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## Single neuron responses in humans during execution and observation of actions

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### Summary

Direct recordings in monkeys have demonstrated that neurons in frontal and parietal areas discharge during execution and perception of actions [1-8]. Since these discharges ‘reflect’ the perceptual aspects of actions of others onto the motor repertoire of the perceiver, these cells have been called *mirror neurons*. Their overlapping sensory-motor representations have been implicated in observational learning and imitation, two important forms of learning [9]. In humans, indirect measures of neural activity support the existence of sensory-motor mirroring mechanisms in homologue frontal and parietal areas [10,11], other motor regions [12-15], and also the existence of multi-sensory mirroring mechanisms in non-motor regions [16-19]. We recorded extracellular activity from 1177 cells in human medial frontal and temporal cortices while patients executed or observed hand grasping actions and facial emotional expressions. A significant proportion of neurons in supplementary motor area, and hippocampus and environs, responded to both observation and execution of these actions. A subset of these neurons demonstrated excitation during action-execution and inhibition during action-observation. These findings suggest that multiple systems in humans may be endowed with neural mechanisms of mirroring for both the integration and differentiation of perceptual and motor aspects of actions performed by self and others.

## Highlights

1. Cells in SMA respond during execution and observation of actions
2. Cells in medial temporal lobe respond during observation & execution of actions
3. Some respond with excitation during execution and inhibition during observation

## Results

We recorded extracellular activity from a total of 1177 neurons in 21 patients while they observed and executed grasping actions and facial gestures. In the observation conditions, subjects observed various actions presented on a laptop screen. In the execution conditions, the subjects were cued to perform an action by a visually presented word. In a control task, the same words were presented and the patients were instructed not to execute the action (see Experimental procedures and figure S1A). In the medial frontal cortex, we recorded from 652 neurons (369 single units, and 283 multi units) in the supplementary motor area (SMA; both SMA-proper and pre-SMA), and anterior cingulate cortex (ACC; both the dorsal and rostral aspects [20]). In the medial temporal lobe we recorded from 525 neurons (296 single units, and 229 multi units) in the amygdala, hippocampus, parahippocampal gyrus (PHG) and entorhinal cortex (EC) (see figure S1B for anatomical location of electrodes). The number of cells recorded in each region is provided in Table 1A.

Significant changes in firing rate were tested using two-tailed paired t-test between the firing rate during baseline (−1000 ms to 0 ms relative to trial onset) and a window of +200 to +1200ms after stimulus onset (see Experimental procedures). For each action (smile, frown, precision grip, or wholehand grip) we examined the neural response during action-observation and action-execution. A response to action-execution was considered only if there was no significant response to the corresponding control task.

After examining the cell's response to each action separately, the cell was classified as follows:

### Action-observation neuron

a cell responding only during one or more action-observation conditions and not during any of the action-execution conditions (e.g. a cell responding to smile observation and frown observation).

### Action-execution neuron

a cell responding only during one or more action-execution conditions and not during any of the action-observation conditions (e.g. a cell responding to precision-grip execution).

### Action Observation/Execution non matching neuron

a cell responding during action-observation in one condition and action-execution in a different condition (e.g. a cell responding to smile observation and frown execution).

### Action Observation/Execution matching neuron

a cell responding during both the execution and the observation of the same action (e.g. a cell responding to smile observation and smile execution).

Table 1B provides the number of cells in each category described above, according to anatomical region. The majority of cells responded to one dimension of the stimuli (observation or execution). In the SMA ( $\chi^2(1) = 14.5$ ,  $p = 10^{-3}$ ) and pre-SMA ( $\chi^2(1) = 4.2$ ,  $p$

= 0.03), the proportion of responses to action-execution relative to action-observation was significantly higher. In the other regions examined (ACC and medial temporal lobe) there was no significant difference between the two conditions. Six cells responded to observation, execution, and also the control task of one action and were therefore not considered as *Action Observation/Execution matching cells* (three cells in PHG, two in EC and one in SMA). Within the population of *action-observation* cells, there were more responses to hand grasps (precision grip or wholehand prehension) in PHG relative to facial gestures (smile or frown; ( $\chi^2(1) = 3.9, p = 0.04$ )), and more responses to observations of facial gestures relative to hand grasps in ACCd ( $\chi^2(1) = 4.8, p = 0.02$ ). The distribution of responses within the population of *action-observation* and *action-execution* cells is provided in Table S1.

We subsequently focused our analyses on the Action Observation/Execution Matching cells responding during both observation and execution of particular actions. Figure 1A displays one such cell in the SMA responding to the observation and execution of two grip types (Precision and Wholehand). This cell did not respond to the Control tasks or any of the facial gesture conditions. Figure 1B displays another cell in entorhinal cortex responding to observation and execution of facial gestures (Smile and Frown). Again, this cell did not respond to the Control tasks or to observation and execution of the various Grips.

Next, we tested whether the proportion of Action Observation/Execution matching neurons in each anatomical region is significantly higher than that expected by chance (chance level set at 5%). We performed a chi-square test on the proportion of such cells in each region (except for the amygdala where we performed Fischer's exact test due to small number of cells). The proportion of cells in the hippocampus ( $\chi^2(1) = 12.5, p = 2 \times 10^{-4}$ ), parahippocampal gyrus ( $\chi^2(1) = 17.4, p < 10^{-4}$ ), entorhinal cortex ( $\chi^2(1) = 3.3, p < 0.05$ ), and SMA ( $\chi^2(1) = 19.4, p < 10^{-4}$ ) was significantly higher than expected by chance. In Amygdala, pre-SMA, ACCd and ACCr the proportions were not significantly higher than chance. In addition to the chi-square test, we performed a bootstrap analysis to test whether or not the number of Action Observation/Execution matching neurons is higher than the null distribution (see Experimental procedures). Figure S2A displays the null distribution (blue) together with the actual number of cells in our data set (red arrow). In agreement with the chi-square test described above, the number of cells in SMA ( $p = 0.003$ ), entorhinal cortex ( $p = 0.001$ ), hippocampus ( $p < 10^{-4}$ ), and parahippocampal gyrus ( $p < 10^{-4}$ ) were significantly higher than expected by chance. In addition, we performed the same analysis, this time taking into account only cells defined as single units and obtained similar results (SMA ( $p = 0.02$ ), EC ( $p = 0.004$ ), H ( $p = 0.02$ ) and PHG ( $p = 0.007$ ); see figure S2B). Furthermore, the proportion of Action Observation/Execution matching neurons in these regions was significantly higher compared with Poisson generated spike trains with similar firing rates (figure S2C). The distribution of joint p-values for these Action Observation/Execution matching neurons is provided in figure S2D for the different regions.

Next, we focused on the Action Observation/Execution matching neurons in the anatomical regions where the proportion of such cells was significant (SMA, parahippocampal gyrus, hippocampus, and entorhinal cortex). Figure 2 displays the responses of six additional neurons from these various regions. The complete response details of all Action Observation/Execution Matching cells are provided in Table S2. The majority of these cells (40 out of 68) were classified as single units (see Experimental procedures). Among the 68 Action Observation/Execution Matching cells, 33 increased their firing rate during both observation and execution of a particular action (e.g. Figure 2 A-D). In contrast, 21 other neurons decreased their firing rate during both conditions (Figure 2E). These types of responses have been previously reported in monkeys (e.g. [21]) and birds [22]. Furthermore, 14 neurons *increased* their firing rate during one condition and *decreased* it during the other.

The majority of these cells ( $n = 11$ ) increased their firing rate during action-execution and decreased their firing rate during action-observation (Figure 2F) while the remaining neurons did the opposite ( $\chi^2(1) = 6.2$ ,  $p = 0.01$ ). For anatomical distribution of response types see Table S3A. Obviously, the breaking down of responses by type and anatomical region makes it difficult to test for regional differences and therefore to draw any firm conclusion on these distributions.

We subsequently examined the temporal profiles of neural activity by computing the average response profile of all Action Observation/Execution matching neurons. This was conducted separately for cells exhibiting excitation to both conditions (Figure 3A), inhibition to both conditions (Figure 3B), and cells exhibiting excitation during action-execution and inhibition during action-observation (Figure 3C). In order to accommodate for differences in firing rates across different cells before averaging, similar to [21] we normalized each excitatory response to range between 0 and +1, and each inhibitory responses to range between 0 and -1 (see Experimental procedures). Excitatory cells reached peak firing rate faster during action-observation compared with action-execution and inhibitory cells returned to baseline faster during action-observation. It is interesting to note that excitatory observation/execution matching cells had firing rates significantly lower than baseline during the control task (Figure 3A). Average baseline firing rates for cells exhibiting excitation during both action-execution and action-observation was  $4.8 \pm 3.7$  Hz, whereas the average baseline firing rates for cells exhibiting inhibition during both conditions was  $9.4 \pm 6.0$  Hz (mean  $\pm$  s.d.). Average baseline firing rate for cells exhibiting excitation to action-execution and inhibition to action-observation was  $6.5 \pm 3.2$ . For relative and absolute response amplitudes see figure S3. In terms of response latencies, no significant difference between observation and execution was found (see table S3B).

The majority of Action Observation/Execution matching neurons in our data-set matched only one action (54 cells), while 14 cells matched the execution and observation of two actions. No significant difference between the proportion of cells matching facial gestures or hand grasps was found ( $\chi^2(1) = 0.6$ ,  $p = 0.4$ ; see Table S1C).

## Discussion

We recorded extra-cellular neural activity in 21 patients while they executed and observed facial emotional expressions and hand grasping actions. In agreement with the known motor properties of SMA and pre-SMA, our results show a significantly higher proportion of cells responding during action-execution compared with action-observation in these regions. While the majority of responding cells across all regions responded only to one aspect of a particular action (either perception or execution) we also found cells responding to both. Significant proportions of such cells were found both in medial frontal lobe (SMA) and in medial temporal lobe – namely, hippocampus, parahippocampal gyrus and entorhinal cortex. In the amygdala, ACC (both rostral and dorsal aspects), and pre-SMA, the number of such cells did not reach significance levels. Finally, within the population of cells responding to both observation and execution of action, our results indicate a sub-population of cells responding with excitation during action-execution and inhibition during action-observation.

What is the relationship between the cells recorded in SMA – on the medial wall of the frontal lobe - that responded during both execution and observation of actions and the ‘mirror neurons’ reported previously in monkeys? The critical feature of mirror neurons is the functional matching between a motor response and a perceptual one [23]. The population of cells we found exhibited this critical functional feature for grasping actions and facial expressions. In this regard, there is obviously similarity between the human and the monkey cells. In monkeys, however, neurons with mirroring properties have been reported in a

variety of areas on the lateral wall of the primate brain [3,7,21,24,25]. In the current study we did not record from these regions since the placement of electrodes was determined only by clinical considerations. Neurophysiological data suggest that while areas on the lateral wall such as F5 seem to contain a vocabulary of actions, from grasping to facial expressions, areas on the medial wall such as SMA seem relevant to movement initiation and movement sequences [26]. Thus, it is possible that the action observation/execution matching neurons we recorded from SMA represent cellular mirror mechanisms for these particular aspects of hand and facial actions.

One of the striking features of our findings is the presence of action observation/execution matching neurons in the medial temporal lobe (MTL). Connections such as the uncinate fasciculus and other cortico-cortical white matter tracts between the MTL and motor regions in the frontal lobe exist [27-31]. Although there is some evidence for responses in the hippocampus during voluntary actions [32], unlike SMA, lesions in the medial temporal lobe do not result in obvious motor deficits, and electrical stimulation in these areas does not result in overt movement. It might be argued that the visual input (rather than the motor output) during action-execution is what elicited the responses in these medial temporal lobe neurons. In our study, however, the visual inputs during action-observation and action-execution were widely different (only a word is visually presented to cue action-execution compared to a video/picture presented during action-observation). Furthermore, the visual input during the control and action-execution of the face experiment is identical although these cells did not respond to the control condition (see figures 1-2). Additionally, in some patients we used auditory tones to cue action-execution (and as appropriate control) and we obtained similar results for these patients (i.e. responses to the tone during action-execution and not during the control condition). It follows that the purely visual explanation for action observation/execution matching cells cannot hold, at least for the execution of facial expressions where no additional visual input is available. In principle, the visual input of the patient's grasping hand may explain the discharge of the cells during grasping execution and grasping observation. However, this argument would require two separate mechanisms to explain the mirroring responses for facial expressions and for grasping: a 'true' mirroring mechanism for facial expression and a 'purely visual' mechanism for grasping action. While this possibility cannot be excluded, it is less parsimonious than invoking a unitary mirroring mechanism for both facial expressions and grasping actions.

It may also be argued that the neurons with mirroring properties respond in an invariant manner to different visual stimuli sharing the same concept e.g., a picture of a smiling face and the execution cue word "smile" [33]. Indeed we found six neurons that responded to observation, execution and also to the control condition of a specific action. However the argument that the observation/execution matching neurons in the medial temporal lobe represent the concept of the action is untenable since we only considered cells that did not respond during the control conditions where the word stimuli were presented again but did not cue the patient to perform an action. An alternative account for the responses in medial temporal lobe during action-execution is that they represent proprioceptive processing. At this stage we cannot rule out this alternative account.

We have recently demonstrated that neurons in medial temporal lobe are re-activated during spontaneous recall of episodic memory [34]. The action observation/execution matching neurons in the medial temporal lobe may match the sight of actions of others with the memory of those same actions performed by the observer. Thus during action-execution, a memory of the executed action is formed, and during action-observation this memory trace is reactivated. This interpretation is in line with the hypothesis of multiple mirroring mechanisms in the primate brain, a hypothesis that can easily account for the presence of mirroring cells in many cortical areas [1,3-5,7,8,24,25].

The functional significance of the mirror mechanism most likely varies according to the location of mirror neurons in different brain areas [35]. For example, the mirror mechanism in the insula might underlie the capacity to understand a specific emotion (disgust) in others [16,19], while the mirror mechanism in the parieto-frontal circuit may help understanding the goal of observed motor acts and the intentions behind them [21]. Here we show cellular mirroring mechanisms in areas relevant to movement initiation and sequencing (SMA), and memory (medial temporal lobe). While these hypothesis have yet to be tested more carefully, these results demonstrate the presence of mirror mechanisms in humans at the single neuron level and in areas functionally different from the ones previously described in the literature.

Mirroring activity, by definition, generalizes across agency and matches executed actions performed by self with perceived action performed by others. While this may facilitate imitative learning, it may also induce unwanted imitation. Thus, it seems necessary to implement neuronal mechanisms of control. The subset of mirror neurons responding with *opposite* patterns of excitation and inhibition during action-execution and action-observation seem ideally suited for this control function. Indeed, extensive brain lesions are associated with compulsory imitative behavior in neurological patients [36,37]. Recently, it has been reported that the majority of pyramidal tract neurons in monkey F5 that display mirror like activity suppress their firing rate during action observation [6], in accord with our own data. Interestingly, some fMRI studies have also reported decreased BOLD signal in primary motor cortex during action-observation [12]. A recent model proposes a direct mirror pathway for automatic, reflexive imitation and an indirect mirror pathway for parsing, storing and organizing motor representations [38]. The observation/execution matching cells with opposite response patterns are compatible with the direct pathway. Finally, mirroring may generate the problem of differentiating between actions of the self and of other people. The opposing pattern of activity for actions of self and others may also form a simple neuronal mechanism for maintaining self-other differentiation.

To conclude, these data demonstrate mirroring spiking activity during action-execution and action-observation in human medial frontal cortex and human medial temporal cortex - two neural systems where mirroring responses at single cell level have not been previously recorded. A subset of these mirroring cells exhibited opposing pattern of excitation and inhibition during action-execution and action-observation, a neural feature that may help preserving the sense of being the owner of an action during execution, and exert control on unwanted imitation during observation. Taken together, these findings suggest the existence of multiple systems in the human brain endowed with neural mirroring mechanisms for flexible integration and differentiation of the perceptual and motor aspects of actions performed by self and others.

## Experimental Procedures

For detailed description of methods see Supplemental Experimental Procedures.

## Patients

We recorded extracellular single and multi unit activity from 21 patients with pharmacologically intractable epilepsy. Patients were implanted with intracranial depth electrodes to identify seizure foci for potential surgical treatment. Electrode location was based solely on clinical criteria and the patients provided written informed consent to participate in the experiments. The study conformed to the guidelines and was approved by the Medical Institutional Review Board at UCLA.

## Experiment design

The entire experiment was composed of three parts – ‘*Facial expressions*’, ‘*Grasping*’ and a ‘*Control*’ experiment. Stimuli were presented on a standard laptop at the patient's bed. In the ‘*Grasping*’ experiment there were two conditions: action-observation, and action-execution. In the action-observation conditions, the subjects observed a 3sec video clip depicting a hand grasping a mug with either precision grip or whole hand prehension. In the action-execution condition, the word ‘*Finger*’ appearing on the screen cued the subject to perform a precision grip on a mug placed next to the laptop. Similarly, the word ‘*Hand*’ cued the subject to perform a whole hand prehension. Observation and execution trials were randomly mixed. The ‘*Facial expressions*’ experiment was also composed of execution and observation trials. In the execution trials, the subjects smiled or frowned whenever the word ‘*Smile*’ or ‘*Frown*’ respectively appeared on the screen. In the observation conditions they simply observed an image of a smiling or frowning face. Observation and execution trials were randomly mixed. In the ‘*Control*’ experiment, the subjects were presented with the same cue words used in the execution conditions of the ‘*Facial expressions*’ and ‘*Grasping*’ experiments (i.e. the words ‘*Finger*’, ‘*Hand*’, ‘*Smile*’, or ‘*Frown*’). This time, the subjects had to covertly read the word and refrain from making facial gestures or hand movements.

## Recording and analysis

Data was recorded at 28kHz using a 64-channel acquisition system (Neuralynx, Tucson, AZ) and the signals were band-pass filtered between 1Hz and 9kHz. During off-line analysis, the raw signal was band-pass filtered between 300 and 3000 Hz and action potentials were clustered and manually sorted using an algorithm based on super paramagnetic clustering. For each neuron, and each condition, we assessed responsiveness by comparing the firing rate during baseline (–1000ms to 0ms relative to stimulus onset) and firing rate during the experimental condition (+200ms to +1200ms relative to stimulus onset) on a trial by trial basis using a two-tailed paired t-test. The statistical significance threshold for the paired t-test across trials was set at 0.05. In order to calculate the average response profile of cells during execution/observation (Figure 3), Excitatory responses were normalized by subtracting the average response during baseline (–1000 to 0ms relative to trial onset), and dividing by the maximum firing rate of the response (bin size = 200ms). Inhibitory responses were normalized by removing the average response during baseline and dividing by the absolute value of the minimum of the response (see Supplemental Experimental Procedures for further details).

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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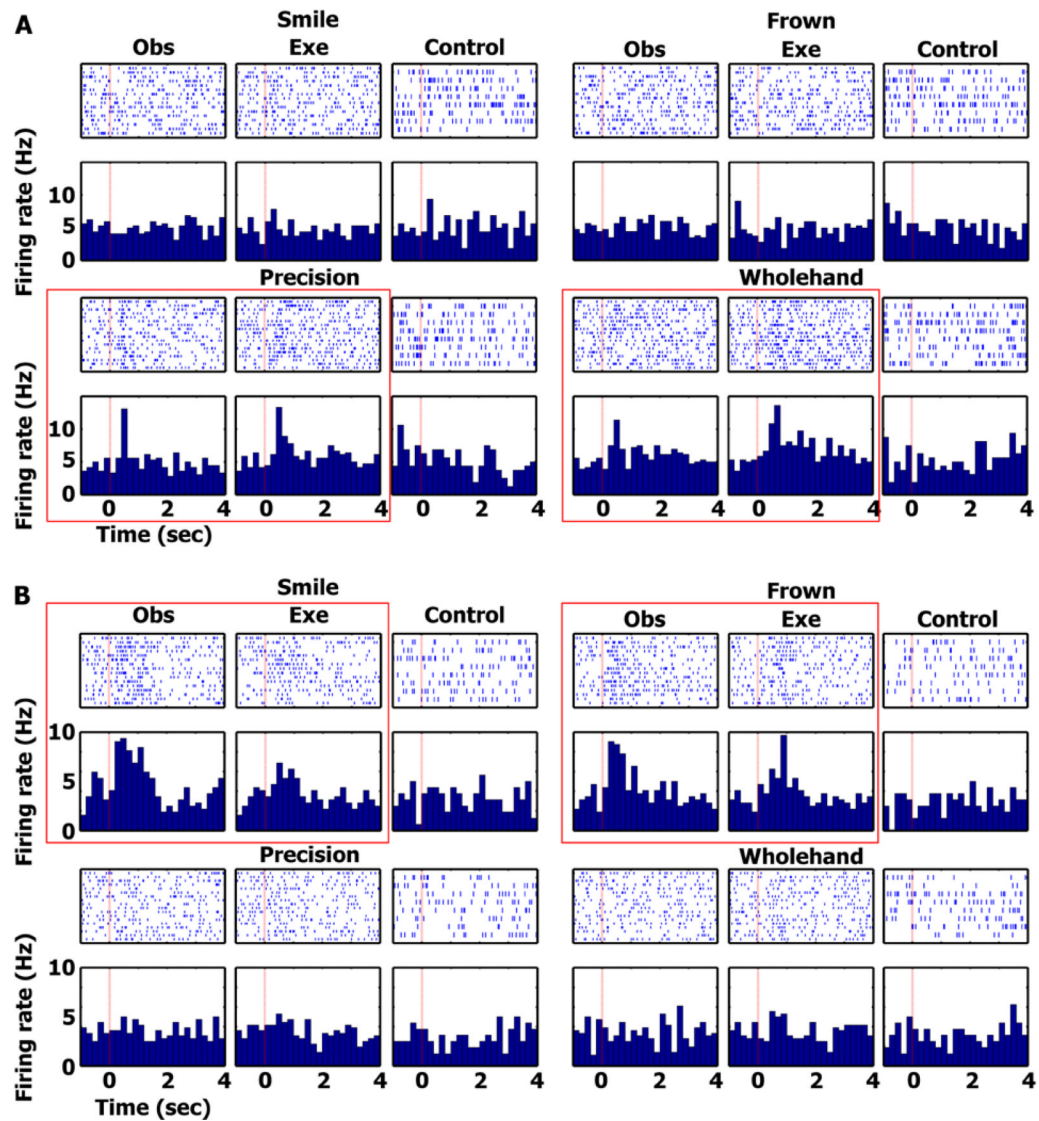
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## References

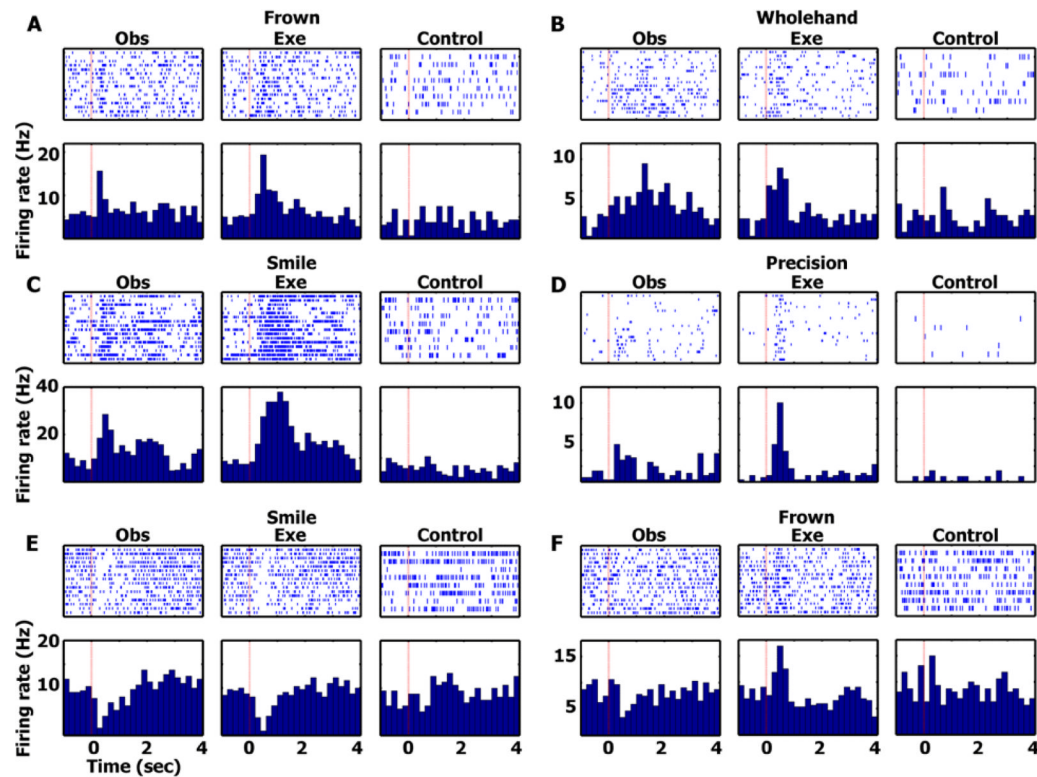
1. di Pellegrino G, Fadiga L, Fogassi L, Gallese V, Rizzolatti G. Understanding motor events: a neurophysiological study. *Exp Brain Res*. 1992; 91:176–180. [PubMed: 1301372]
2. Dushanova J, Donoghue J. Neurons in primary motor cortex engaged during action observation. *Eur J Neurosci*. 2010; 31:386–398. [PubMed: 20074212]
3. Gallese V, Fadiga L, Fogassi L, Rizzolatti G. Action recognition in the premotor cortex. *Brain*. 1996; 119(Pt 2):593–609. [PubMed: 8800951]
4. Keysers C, Kohler E, Umiltà MA, Nanetti L, Fogassi L, Gallese V. Audiovisual mirror neurons and action recognition. *Exp Brain Res*. 2003; 153:628–636. [PubMed: 12937876]
5. Kohler E, Keysers C, Umiltà MA, Fogassi L, Gallese V, Rizzolatti G. Hearing sounds, understanding actions: action representation in mirror neurons. *Science*. 2002; 297:846–848. [PubMed: 12161656]
6. Kraskov A, Dancause N, Quallo M, Shepherd S, Lemon RN. Corticospinal Neurons in Macaque Ventral Premotor Cortex with Mirror Properties: A Potential Mechanism for Action Suppression? *Neuron*. 2009; 64:922–930. [PubMed: 20064397]
7. Shepherd SV, Klein JT, Deaner RO, Platt ML. Mirroring of attention by neurons in macaque parietal cortex. *Proc Natl Acad Sci U S A*. 2009; 106:9489–9494. [PubMed: 19470477]
8. Umiltà MA, Kohler E, Gallese V, Fogassi L, Fadiga L, Keysers C, Rizzolatti G. I know what you are doing. a neurophysiological study. *Neuron*. 2001; 31:155–165. [PubMed: 11498058]
9. Hurley, S.a.C.N. *Perspectives on Imitation: From Neuroscience to Social Science*. MIT press; Cambridge, MA: 2005.
10. Iacoboni M, Molnar-Szakacs I, Gallese V, Buccino G, Mazziotta JC, Rizzolatti G. Grasping the intentions of others with one's own mirror neuron system. *PLoS Biol*. 2005; 3:e79. [PubMed: 15736981]
11. Iacoboni M, Woods RP, Brass M, Bekkering H, Mazziotta JC, Rizzolatti G. Cortical mechanisms of human imitation. *Science*. 1999; 286:2526–2528. [PubMed: 10617472]
12. Gazzola V, Keysers C. The observation and execution of actions share motor and somatosensory voxels in all tested subjects: single-subject analyses of unsmoothed fMRI data. *Cereb Cortex*. 2009; 19:1239–1255. [PubMed: 19020203]
13. Grezes J, Decety J. Functional anatomy of execution, mental simulation, observation, and verb generation of actions: a meta-analysis. *Hum Brain Mapp*. 2001; 12:1–19. [PubMed: 11198101]
14. Koski L, Iacoboni M, Dubeau MC, Woods RP, Mazziotta JC. Modulation of cortical activity during different imitative behaviors. *J Neurophysiol*. 2003; 89:460–471. [PubMed: 12522194]
15. Hari R, Forss N, Avikainen S, Kirveskari E, Salenius S, Rizzolatti G. Activation of human primary motor cortex during action observation: a neuromagnetic study. *Proc Natl Acad Sci U S A*. 1998; 95:15061–15065. [PubMed: 9844015]
16. Calder AJ, Keane J, Manes F, Antoun N, Young AW. Impaired recognition and experience of disgust following brain injury. *Nat Neurosci*. 2000; 3:1077–1078. [PubMed: 11036262]
17. Hutchison WD, Davis KD, Lozano AM, Tasker RR, Dostrovsky JO. Pain-related neurons in the human cingulate cortex. *Nat Neurosci*. 1999; 2:403–405. [PubMed: 10321241]
18. Keysers C, Wicker B, Gazzola V, Anton JL, Fogassi L, Gallese V. A touching sight: SII/PV activation during the observation and experience of touch. *Neuron*. 2004; 42:335–346. [PubMed: 15091347]
19. Wicker B, Keysers C, Plailly J, Royet JP, Gallese V, Rizzolatti G. Both of us disgusted in My insula: the common neural basis of seeing and feeling disgust. *Neuron*. 2003; 40:655–664. [PubMed: 14642287]
20. McCormick LM, Ziebell S, Nopoulos P, Cassell M, Andreasen NC, Brumm M. Anterior cingulate cortex: an MRI-based parcellation method. *Neuroimage*. 2006; 32:1167–1175. [PubMed: 16859929]
21. Fogassi L, Ferrari PF, Gesierich B, Rozzi S, Chersi F, Rizzolatti G. Parietal lobe: from action organization to intention understanding. *Science*. 2005; 308:662–667. [PubMed: 15860620]
22. Prather JF, Peters S, Nowicki S, Mooney R. Precise auditory-vocal mirroring in neurons for learned vocal communication. *Nature*. 2008; 451:305–310. [PubMed: 18202651]



23. Rizzolatti G, Sinigaglia C. Further reflections on how we interpret the actions of others. *Nature*. 2008; 455:589. [PubMed: 18833249]
24. Cisek P, Kalaska JF. Neural correlates of reaching decisions in dorsal premotor cortex: specification of multiple direction choices and final selection of action. *Neuron*. 2005; 45:801–814. [PubMed: 15748854]
25. Tkach D, Reimer J, Hatsopoulos NG. Congruent activity during action and action observation in motor cortex. *J Neurosci*. 2007; 27:13241–13250. [PubMed: 18045918]
26. Rizzolatti G, Luppino G. The cortical motor system. *Neuron*. 2001; 31:889–901. [PubMed: 11580891]
27. Blatt GJ, Pandya DN, Rosene DL. Parcellation of cortical afferents to three distinct sectors in the parahippocampal gyrus of the rhesus monkey: an anatomical and neurophysiological study. *J Comp Neurol*. 2003; 466:161–179. [PubMed: 14528446]
28. Kondo H, Saleem KS, Price JL. Differential connections of the perirhinal and parahippocampal cortex with the orbital and medial prefrontal networks in macaque monkeys. *J Comp Neurol*. 2005; 493:479–509. [PubMed: 16304624]
29. Lavenex P, Suzuki WA, Amaral DG. Perirhinal and parahippocampal cortices of the macaque monkey: projections to the neocortex. *J Comp Neurol*. 2002; 447:394–420. [PubMed: 11992524]
30. Mohedano-Moriano A, Pro-Sistiaga P, Arroyo-Jimenez MM, Artacho-Perula E, Insausti AM, Marcos P, Cebada-Sanchez S, Martinez-Ruiz J, Munoz M, Blaizot X, et al. Topographical and laminar distribution of cortical input to the monkey entorhinal cortex. *J Anat*. 2007; 211:250–260. [PubMed: 17573826]
31. Munoz M, Insausti R. Cortical efferents of the entorhinal cortex and the adjacent parahippocampal region in the monkey (*Macaca fascicularis*). *Eur J Neurosci*. 2005; 22:1368–1388. [PubMed: 16190892]
32. Halgren E. Firing of human hippocampal units in relation to voluntary movements. *Hippocampus*. 1991; 1:153–161. [PubMed: 1669290]
33. Quiroga RQ, Reddy L, Kreiman G, Koch C, Fried I. Invariant visual representation by single neurons in the human brain. *Nature*. 2005; 435:1102–1107. [PubMed: 15973409]
34. Gelbard-Sagiv H, Mukamel R, Harel M, Malach R, Fried I. Internally generated reactivation of single neurons in human hippocampus during free recall. *Science*. 2008; 322:96–101. [PubMed: 18772395]
35. Fabbri-Destro M, Rizzolatti G. Mirror neurons and mirror systems in monkeys and humans. *Physiology (Bethesda)*. 2008; 23:171–179. [PubMed: 18556470]
36. De Renzi E, Cavalleri F, Facchini S. Imitation and utilisation behaviour. *J Neurol Neurosurg Psychiatry*. 1996; 61:396–400. [PubMed: 8890779]
37. Lhermitte F, Pillon B, Serdaru M. Human autonomy and the frontal lobes. Part I: Imitation and utilization behavior: a neuropsychological study of 75 patients. *Ann Neurol*. 1986; 19:326–334. [PubMed: 3707084]
38. Ferrari PF, Bonini L, Fogassi L. From monkey mirror neurons to primate behaviours: possible ‘direct’ and ‘indirect’ pathways. *Philos Trans R Soc Lond B Biol Sci*. 2009; 364:2311–2323. [PubMed: 19620103]

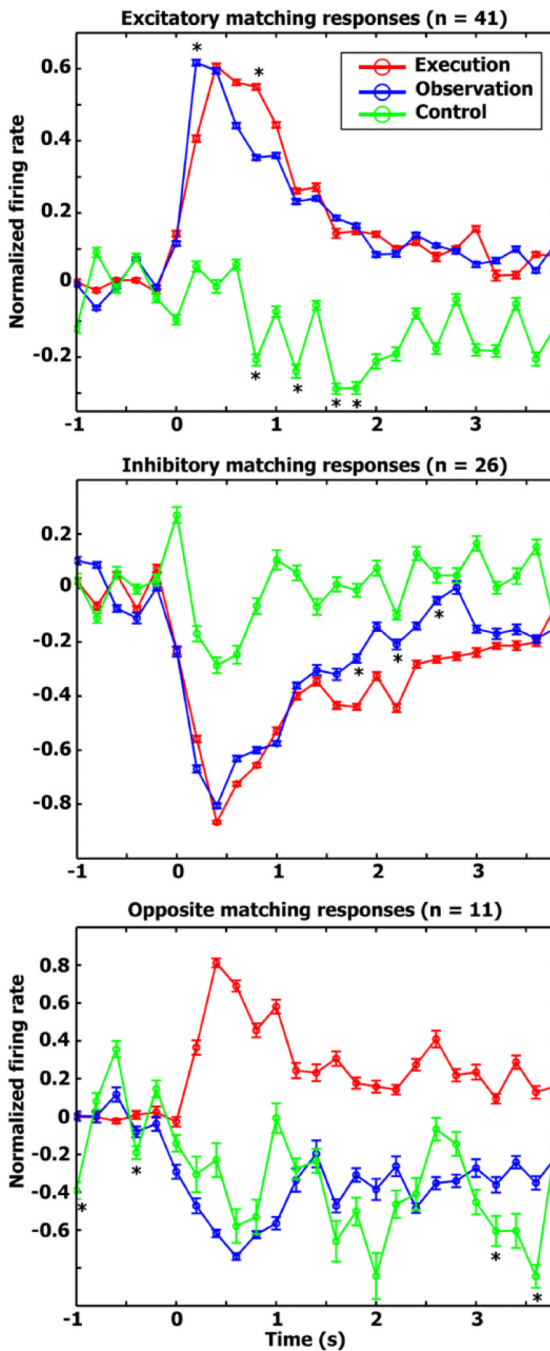


**Figure 1.** Rasters (top) and peri-stimulus time histograms (bottom) of two cells during all experimental conditions and tasks. Rasters are aligned to stimulus onset (red vertical line at time = 0). Bin size = 200ms. Red box highlights responses passing statistical criteria. A) An action observation/execution matching multi unit in left SMA for the two grips (Precision and Wholehand). B) An action observation/execution matching single unit in right entorhinal cortex for two facial gestures (Smile and Frown). See also figure S1.



**Figure 2.**

Raster plots and peri-stimulus time histograms of 6 different observation/execution matching neurons during execution, observation, and the control task. (A) Single unit in left entorhinal cortex increasing its firing rate during both frown execution and frown observation. (B) Single unit in right parahippocampal gyrus increasing its firing rate during whole hand grasp execution and whole hand grasp observation. (C) Single unit in left entorhinal cortex increasing its firing rate during smile execution and smile observation. (D) Single unit in right parahippocampal gyrus increasing its firing rate during precision grip execution and precision grip observation. (E) Single unit in left SMA decreasing its firing rate during smile execution and smile observation. (F) Single unit in left parahippocampal gyrus increasing its firing rate during frown execution and decreasing it during frown observation. See also figure S2.



**Figure 3.**

Average normalized response profile of all Action Observation/Execution matching neurons. (A) Average of 41 excitatory responses (from 33 different neurons) during action execution and action observation. (B) Average of 26 inhibitory response (from 21 different neurons). (C) Average of 11 response profiles (from 11 different neurons) exhibiting excitation during action-execution and inhibition during action-observation. Bins size = 200ms. For normalization procedure see Experimental procedures. Error bars represent standard error of the mean across all neurons. Asterisks on the observation/execution plots denote time bins at which the difference between the temporal profile of action-execution and action-observation were significant (see Experimental procedures). Asterisks on the

control task plot denote time bins at which the control condition is significantly different than zero. See also figure S3.

Location of recorded cells **A)** Number of single units (SU) and multi units (MU) recorded in the left and right hemispheres in various anatomical regions.

**Table 1A**

Region	A	H	EC	PHG	SMA	Pre-SMA	ACCd	ACCr	total
SU/MU	11/22	92/71	102/73	91/63	82/43	79/65	66/59	142/116	665/512
Right	13	77	81	48	23	68	80	168	558
Left	20	86	94	106	102	76	45	90	619
Total	33	163	175	154	125	144	125	258	1177

**B)** Response types of cells across all recorded regions. Absolute number (single unit, multi unit) and percentages of cells (calculated from total number of recorded cells in each region – see table 1A). Last column represents the percentage of responses across all regions. For definition of response types, see text. A – amygdala, H – hippocampus, EC – entorhinal cortex, PHG – parahippocampal gyrus, SMA – supplementary motor area, ACCd – dorsal aspect of anterior cingulate, ACCr – rostral aspect of anterior cingulate. See also supplementary table 2.

**Table 1B**

Region	A	H	EC	PHG	SMA	Pre-SMA	ACCd	ACCr	%
Action-execution	11 (4, 7) (33%)	36 (19, 17) (22%)	37 (18, 19) (21%)	39 (22, 17) (25%)	41 (27, 14) (33%)	34 (23, 11) (24%)	28 (12, 16) (22%)	50 (28, 22) (19%)	23%
Action-observation	4 (1, 3) (12%)	29 (18, 11) (18%)	32 (21, 11) (18%)	35 (19, 16) (23%)	13 (9, 4) (10%)	19 (11, 8) (13%)	26 (15, 11) (21%)	45 (25, 20) (17%)	17%
Observation/Execution matching	2 (1, 1) (6%)	18 (8, 10) (11%)	14 (9, 5) (8%)	19 (13, 6) (12%)	17 (10, 7) (14%)	6 (4, 2) (4%)	2 (2, 0) (2%)	12 (8, 4) (5%)	8%
Observation/Execution non matching	1 (0, 1) (3%)	16 (8, 8) (10%)	11 (5, 6) (6%)	11 (8, 3) (7%)	13 (7, 6) (10%)	10 (5, 5) (7%)	1 (0, 1) (1%)	14 (8, 6) (5%)	7%