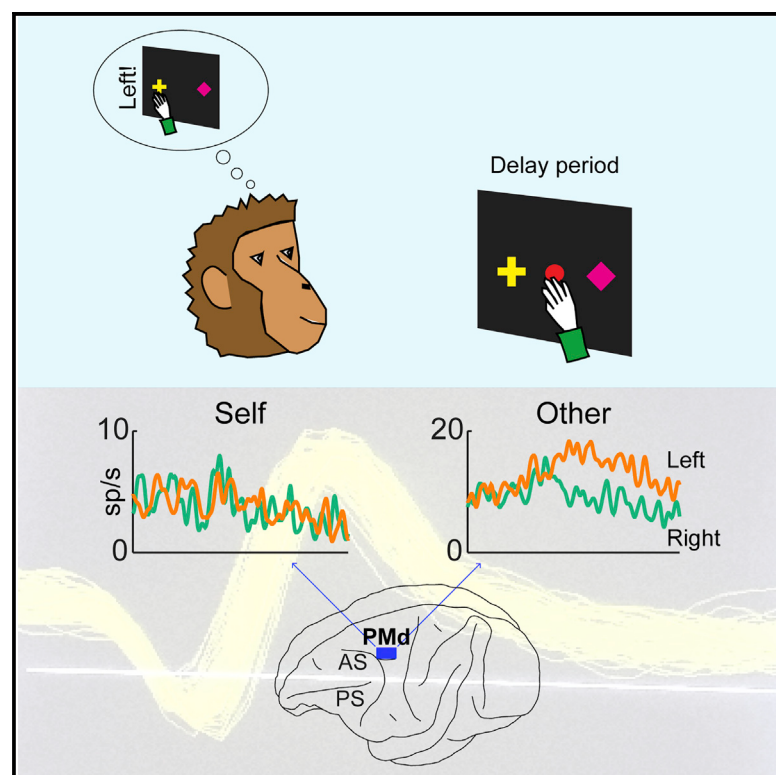


Cell Reports

Coding of Self and Other's Future Choices in Dorsal Premotor Cortex during Social Interaction

Graphical Abstract



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In Brief

Understanding others' intentions is essential to successful primate social life. Cirillo et al. explore the role of dorsal premotor cortex (PMd) in discriminating between self and others' behavior while macaques interacted with humans. They show that the majority of neurons encoding the future choice did so selectively for the monkey or the human agent. PMd thus differentiates self from others' behavior, leading to independent representations of future actions.

Highlights

- During social interaction, a minority of PMd neurons exhibit mirror-like properties
- Some neurons are solely responsive during other's performance but not during one's own
- PMd might be fundamental for the distinction between one's and other's behavior



Coding of Self and Other's Future Choices in Dorsal Premotor Cortex during Social Interaction

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SUMMARY

Representing others' intentions is central to primate social life. We explored the role of dorsal premotor cortex (PMd) in discriminating between self and others' behavior while two male rhesus monkeys performed a non-match-to-goal task in a monkey-human paradigm. During each trial, two of four potential targets were randomly presented on the right and left parts of a screen, and the monkey or the human was required to choose the one that did not match the previously chosen target. Each agent had to monitor the other's action in order to select the correct target in that agent's own turn. We report neurons that selectively encoded the future choice of the monkey, the human agent, or both. Our findings suggest that PMd activity shows a high degree of self-other differentiation during face-to-face interactions, leading to an independent representation of what others will do instead of entailing self-centered mental rehearsal or mirror-like activities.

INTRODUCTION

Social life requires the ability to understand others' behavior and predict others' intentions. Many social behaviors in monkeys are similar to those observed in humans: they can monitor each other's actions (Fujii et al., 2007; Falcone et al., 2016, 2017), cooperate (Haroush and Williams, 2015), learn from observation (Falcone et al., 2012a, 2012b; Monfardini et al., 2014), and show altruistic behaviors (Chang et al., 2011).

Previous reports have described neurons involved in various aspects of social understanding: "mirror" neurons in the ventral premotor cortex (PMv) respond to both performed and observed actions (di Pellegrino et al., 1992; Rizzolatti et al., 1996), neurons in anterior cingulate and orbitofrontal cortex respond to others' reward (Azzi et al., 2012; Chang et al., 2013), and neurons in medial frontal areas represent others' actions or intentions (Yoshida et al., 2011, 2012; Falcone et al., 2017).

A previous study by Cisek and Kalaska (2004) reported that neurons in dorsal premotor cortex (PMd) might be involved in mental rehearsal of processes normally occurring before movement, interpreting this activity as a covert simulation process. The authors showed that a large majority of neurons were direc-

tionally tuned in both performance and observation tasks (84%), and they proposed that the predictive activity of those cells was based on a mental rehearsal process. These observations have led to the interpretation that the neural network responsible for planning and executing actions in PMd overlaps with the network for observation of others' actions.

More recently, Tkach et al. (2007) have shown a similar result looking only at the movement period in a task with no delay. They found that an overwhelming majority of neurons in PMd and primary motor cortex (M1) were endowed with mirror properties. From these two previous reports, it emerges that nearly all tuned neurons in the monkeys' trials responded before (Cisek and Kalaska, 2004) and during the movement observation (Tkach et al., 2007).

It has been shown that it is possible to use the activity of selected M1 and PMd neurons to generate a mapping between neural activity and the motion of a device that can be later used by the animal for neuroprosthetic control (Wahnoun et al., 2006). This study showed that the match between the neural correlates of observation and execution might also lead to important real-life applications. However, it is not clear if these results would effectively extend to a real face-to-face interaction with other agents.

Here, we claim that such functional overlap is not a general feature of neurons in PMd. We suggest that the mental rehearsal or mirror-like interpretation of PMd functionality likely arises from the specific task features of previous studies on PMd (Cisek and Kalaska, 2004; Tkach et al., 2007) such as a non-visible agent, the passive observation of others' behavior without monitoring requirements, and a bias in the selection criterion of neurons. To provide a more realistic interaction, we used an experimental paradigm in which the interacting partner was visible to the monkeys and that required the monitoring of others' actions. Moreover, we avoided task-related neuron selection biases by not preselecting only the neurons that were directionally tuned to the monkey's execution of the movement. We trained two monkeys in two versions of a non-match-to-goal (NMTG) task: a spatial version (S-NMTG) and an object version (O-NMTG). In both versions of the task, monkey and human interacted and alternated their roles as actor and observer. During the task, neural activity was recorded using multielectrode arrays chronically implanted in PMd.

In the delay period, prior to any movement, we found that the majority of PMd neurons exclusively encoded one's own future actions. The remaining neurons encoded other's future actions, either exclusively or together with self-actions.



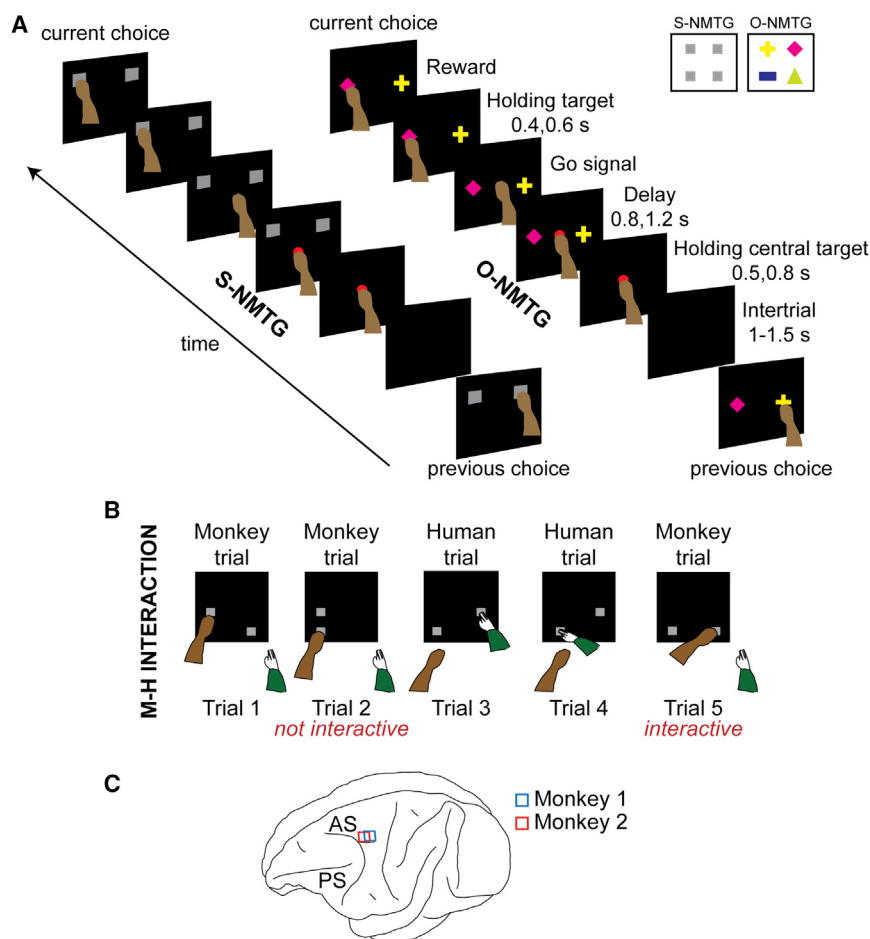


Figure 1. Task and Recording Sites

(A) Temporal sequence of events of one example trial for the S-NMTG and the O-NMTG task. Top right: the peripheral targets used during the two task versions. In both cases, the correct choice depends on previous choice.
(B) Example of a trial sequence with the monkey or the human acting as agent.
(C) Array positions relative to principal sulcus (PS) and arcuate sulcus (AS).

trial, we computed the number of aborted interactive trials. Each monkey aborted interactive trials very rarely (1.1% and 0.4% aborted trials for monkey 1 and monkey 2, respectively). The proportion of aborted trials was not different between monkeys (two-sample *t* test, *p* = 0.38, *t*_[35] = 0.89). This result suggests that the higher proportion of errors in the interactive trials for monkey 2 might reflect a greater difficulty to monitor the human previous choice rather than a low level of motivation.

The oculomotor behavior of monkey 1 (Figure S1A) and monkey 2 (Figure S1B) was similar in both monkey and human trials during the delay and the holding target period of the task for right and left correct target selections.

Single Neuron Activity

Our database included recordings from 328 neurons. For most of the analyses,

we focused on the delay period (0.4–0.8 s; [Experimental Procedures](#)), because in this period the coding of the future choice could be studied independently from any movement. This time window was common to both delay durations (0.8 and 1.2 s), maximizing the number of trials available for the analysis. Moreover, this time window represented the period with higher target position selectivity compared with the preceding one (28% target position cells more than delay 0.08–0.4 s period). During this time interval, the information on the correct target in the monkey trials and for representing the future choice before the action in the human trials was available, because the two peripheral targets appeared at the beginning of the delay. The animal could therefore either plan its future choice or represent the human's future choice, in the monkey and human trials, respectively.

The percentage of cells with significant main effects or interactions in a two-way ANOVA with factors agent (monkey versus human) and target location (right versus left) was computed in four different periods of the task. The percentage of cells with a significant main effect of agent varied from 48% (156 of 328) in the delay period to 62% (204 of 328) in the first 0.4 s of the holding target period. The percentage of cells encoding the target position (main effect of target position) varied from 26% (86 of

Taken together, our results demonstrate that by using a real-interaction paradigm, we can identify different neuronal substrates that help recognize self and other's behaviors and that are not merely based on mental rehearsal activities.

RESULTS

Two monkeys performed two versions of an NMTG task (Figure 1A). In both task versions, two of four potential targets appeared on the right and left parts of a screen, and the task rule was to choose the target that did not match the previously chosen one ([Experimental Procedures](#)). Both monkeys accurately performed trials executed after a correct trial performed by the monkey itself (not interactive trials) or by the human (interactive trials) ([Experimental Procedures](#)). Performance in not interactive and interactive trials was $90.9 \pm 1.2\%$ and $86 \pm 1.2\%$ ($\pm$ SEM) for monkey 1, respectively, and $90.1 \pm 1\%$ and $75.3 \pm 2.4\%$ ($\pm$ SEM) for monkey 2, respectively. For monkey 1 the mean reaction time (RT) in not interactive trials did not differ from the mean RT in interactive trials (*t* test, *p* = 0.07, *t*_[2] = 3.58). For monkey 2, the mean RT in the not interactive condition was faster than the mean RT in the interactive condition (*t* test, *p* = 0.02, *t*_[3] = 4.87). To assess monkeys' motivation to continue performing the task after a human

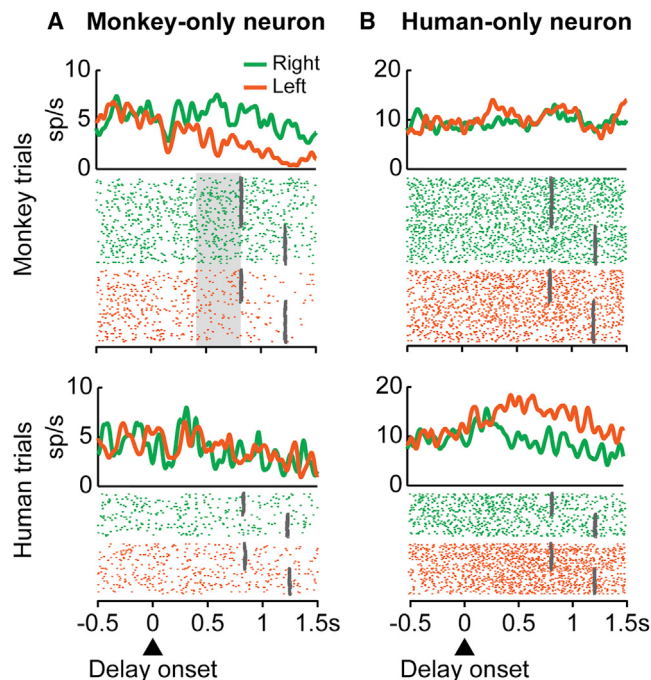


Figure 2. Example Neurons

(A and B) Raster plots of two neurons recorded within the same session: a monkey-only (A) and a human-only (B) cell. Top: the mean firing rate in monkey (top) or human (bottom) trials for right (green) or left (orange) target spatial position. Bottom: the neuronal spikes relative to the delay onset. The gray rectangle indicates the analyzed period. The trials are sorted by the agent performing the trial (monkey/human) and the chosen target position (right/left).

328) in the delay period to 31% (100 of 328) in the movement time (MT).

A post hoc analysis (Fisher's least significant difference [LSD] test, $p < 0.05$) revealed which cells showed a significant difference between target positions for each agent. We then categorized the cells in three different subgroups: "monkey-only," "human-only," and "both-agents" cells. The monkey-only cells encoded a specific target position in monkey trials only, the human-only cells did so in human trials only, and the both-agents cells coded a target position in both monkey and human trials. Figure S2A shows the percentage of cells belonging to each group during the four task epochs. The percentages were calculated on the basis of the total number of target position-selective cells for each task period. In every epoch, we observed a prevalence of monkey-only cells and a smaller proportion of human-only and both-agents cells. The proportion of cells in each subgroup was similar across delay, MT, and holding target epochs ($\chi^2[4, n = 290] = 1.93, p = 0.75$), while in the RT period, the percentage of human-only and both-agents cells was smaller compared with the other three epochs ($\chi^2[6, n = 389] = 12.96, p = 0.04$). Figure S2B shows that most cells encoded the target position specifically to one epoch and more rarely maintained the same coding across epochs. This result confirms the peculiarity of the prospective nature of the delay period.

During the delay period we identified 80 of 328 target position-selective cells (24%) broadly distributed in each monkey's array. Even if the array of monkey 2 was centered in a more rostral position compared with the array of monkey 1, 49% of the significant cells were recorded in the estimated overlapping portion of the two arrays. Moreover, the proportion of cells in each subgroup in the overlapping portion was similar to that obtained in Figure S2A for the delay period (67% versus 64% monkey-only, 10% versus 17% human-only, 23% versus 19% both-agents, in the overlapping portion and Figure S2A, respectively).

Figure 2A shows an example of a monkey-only cell with a preference for the right target position. Figure 2B represents a human-only cell with higher activity for the left target position but with no difference between the two target positions in the delay period of the monkey trials.

Figure 3 shows two examples of both-agents cells. Most of the both-agents cells had a preference for the same target position during both monkey and human trials, as the cell represented in Figure 3A, which preferred the left target location. On the other hand, only one cell changed its preferred position from monkey to human trials. This cell is shown in Figure 3B, with higher activity for the left target position in monkey trials, but the right target position in human trials.

Population Activity

To assess the strength of the cells tuning for the target position in the delay period, and to compare the target position signals between the different cell classes, we looked at the population activity. Figure 4A displays the spatial tuning for the monkey-only ($n = 51$) and human-only ($n = 14$) cells in the form of population histograms. For both groups, the difference in activity between preferred and anti-preferred target positions developed soon after peripheral targets appeared, persisting through the delay period and beyond. For the both-agents cells ($n = 15$), Figure S4A shows that the differences of the population averages between preferred and anti-preferred target positions were similar in both monkey and human trials.

To assess whether the spatial preferences of each cell group were specific to the trials performed by the agent for which they showed significance (monkey or human), we selected, for the monkey-only cells, the trials performed by the human. The preferred and anti-preferred target positions derived from monkey trials were assigned to these trials. Population histograms in Figure S3A show that there was no tendency for the monkey-only cells to share the same spatial preference for human and monkey trials. This analysis was repeated for the human-only cells, but the preferred and anti-preferred target locations obtained from human trials were assigned to the monkey trials. We also found that this group of cells exhibited no tendency to share a similar spatial preference for monkey and human trials. Furthermore, soon after the analysis period, there was an inversion of preference for the human-only cells if considered in monkey trials. This suggests that the spatial preference observed in human trials was specific to the trials performed by that agent. As expected, when the same analysis was repeated for the both-agents cells (Figure S4B), assigning the human rank to

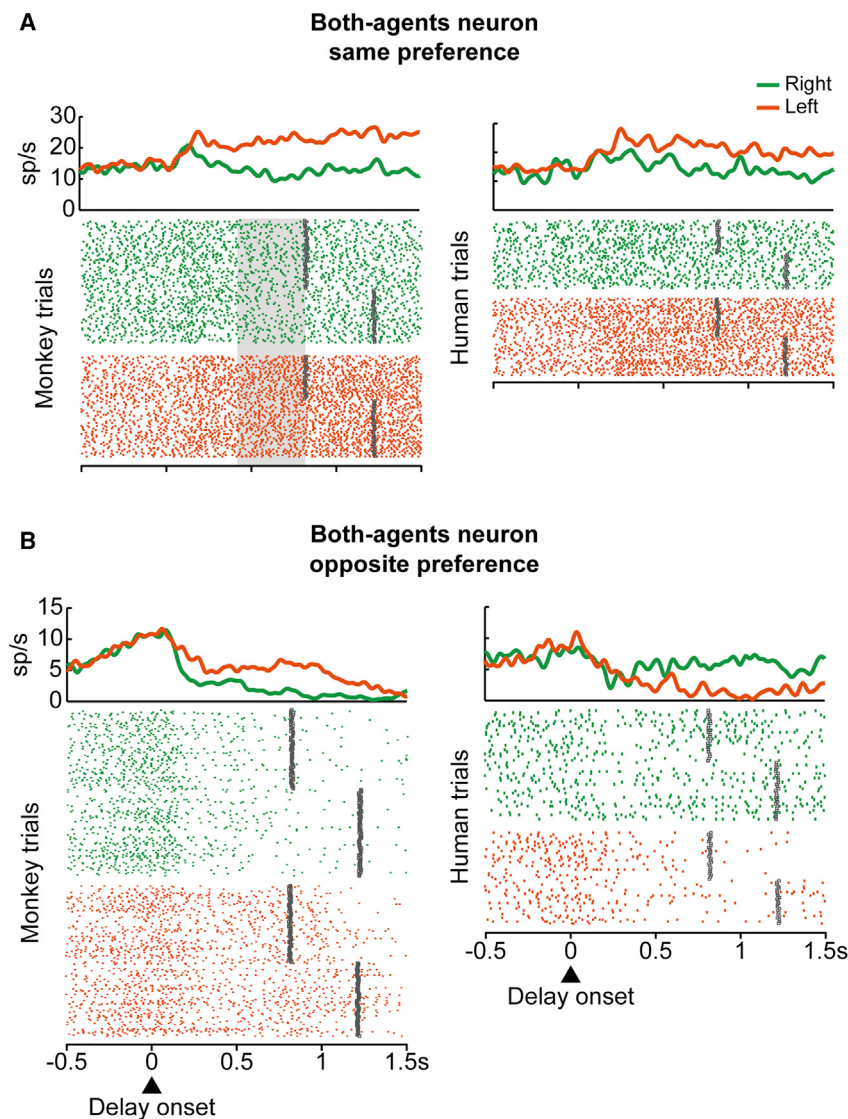


Figure 3. Examples of Both-Agents Neurons

(A) Neuron with target position coding properties in both monkey and human trials. The neuron maintains the preference for a target position in both types of trials: higher activity for left (orange) than for right (green) target position. (B) Neuron with a significant effect of target position in both monkey and human trials but with a change of spatial preference between trial types. The neuron shows higher activity for left (orange) than right (green) target position during monkey trials but higher activity for right than left target position during human trials. The plot conventions are the same as those in Figure 2.

monkey trials and vice versa, these cells showed a tendency to share similar spatial preferences for both kinds of trials. Indeed, as noted above, only one cell changed its preferred position from monkey to human trials.

Population representations of the target spatial positions were then analyzed using a neuron-dropping analysis. Figure 4B shows the neuron-dropping curves for each cell class in monkey (left) and human trials (right). As expected, the neuron-dropping curves computed for monkey-only cells in monkey trials showed much better target position's estimations than human-only cells (red versus blue curves). However, the human-only cells provided a better than chance estimation of the target position in monkey trials. Also as predicted, in human trials, human-only cells yielded better estimations of the target position than monkey-only cells, even if this latter group reached a high percentage of correct classification. Neuron-dropping curves for both-agents cells provided similar estimations for monkey and human trials, even showing higher estima-

tions than monkey-only and human-only cells (Figure 4B, green curves). Taken together, the resultant neuron-dropping curves show that the groups of selective cells yielded more than chance reliable estimations of the target position, in accordance with their tuning in the delay period. Nevertheless, Figure 4B indicates that there is no sharing of the tuning preference between monkey-only and human-only cells, while the both-agents cells showed high estimations irrespective of the agent. Classification of each target position was above chance for even a single neuron tuned to that location in monkey and human trials and increased as the number of neurons increased. Figure S3B shows the neuron-dropping curves for all recorded cells ($n = 328$) computed in the delay period, both in monkey and human trials. The curves show that the percentage of correct estimations of the target position was well above chance level in both monkey and human trials. This result supports, at the entire neuronal population

level, the idea that PMd neurons provided reliable estimations of the correct target position during observation when the human was performing the task.

DISCUSSION

In this study, we used a social cognitive task to investigate the activity of PMd neurons during the interaction of monkey and human agents. We found that only a minority of neurons exhibited directional activities in both self and other's trials before action execution. Some neurons represented the human's future choice, without coding the monkey's own response. This differs from previous research (Cisek and Kalaska, 2004) that demonstrated similar pre-movement activity patterns in both the monkey and other's trials. However, the present findings are consistent with previous reports of other-selective cells in lateral and medial frontal areas (Falcone et al., 2016, 2017). Here, we demonstrate that not all neurons in frontal areas exhibit

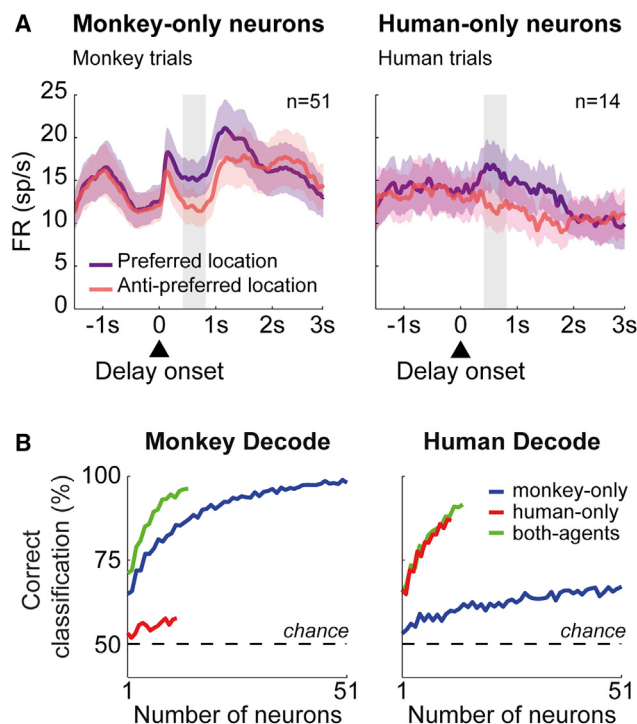


Figure 4. Population Activity and Decoding of Spatial Position

(A) Mean firing rate (FR) of monkey-only neurons during monkey trials (left) and of human-only neurons during human trials (right), aligned on delay onset. The gray rectangle indicates the analyzed period. Error bars are $\pm$ SEM.

(B) Proportion of correctly classified trials during the delay for monkey-only (blue curves), human-only (red curves), and both-agents (green curves) cells during monkey (left) and human (right) trials. Dashed lines indicate chance levels.

mirror-like properties, even in a brain area widely considered to predominantly contain neurons that “mirror” the actions of others.

We focused most of our analyses on the delay period because all the information defining the behavioral goal has already been acquired by this time, and the activity during this period can potentially predict the impending human response during human trials. It was possible to analyze the neural correlates of the future partner’s response in the delay period because the human partner’s hand was always in a central position on the screen at this time, and no visual cue indicated the behavioral goal. Therefore, the monkey could only anticipate the human partner’s response using its understanding of the task.

By adopting a monkey-human (M-H) paradigm instead of a monkey-monkey (M-M) paradigm, our task design offered the advantage of avoiding ambiguities in the representation of the other’s future behavior, because the human choices were under experimental control. Our paradigm allowed us to maintain a stable predictive context and constant reward expectation during the partner’s trials. However, this advantage comes with the limitation of not being able to study error-related activity.

Similar to our previous studies (Falcone et al., 2016, 2017), we found agent-related cells that, during the delay period, coded which actor was performing the task. This distinction is essential

for establishing turn-taking, joint action, and understanding or predicting other agents’ behavior. The importance of differentiating self from others is also evident in the compulsory imitative behavior that follows frontal lobe damage (De Renzi et al., 1996), which may be a result of a deficit in this ability. Interestingly, agent-related cells that are preferentially active during others’ actions are absent in the medial frontal cortex of a monkey with autistic traits (Yoshida et al., 2016).

We found three main categories of cells that were modulated by a specific target position: (1) the monkey-only cells, which represented the monkey’s target selection in monkey trials only; (2) the human-only cells, which represented the future correct target position in human trials only; and (3) the both-agents cells, which coded the future correct target position in both monkey and human trials. Strikingly, the majority of cells modulated by the target spatial position were monkey only (64% [51 of 80]) and did not encode any spatial target during the observed human trials. Conversely, a much smaller proportion of PMd cells exhibited the same activity pattern for both self and others’ future choices (both-agents cells, 19% [15 of 80]). These both-agents cells might represent the behavioral goal determined by the task rule, irrespective of the actor performing the task. Neurons that encode abstract goals have been described by Nakayama et al. (2016). We found a similar proportion of human-only cells (17% [14 of 80]), indicating that the cells that represent the partner’s future choices are not necessarily involved in mental rehearsal of one’s own motor plan, as previously suggested (Cisek and Kalaska, 2004). The exact role of the human-only cells cannot be determined in our paradigm, because the human always performs the correct action. It is therefore possible that the predictive activity of these cells represents either what the human agent will do, or what the human should do.

Although our results demonstrate a great self-other dissociation between neural representations of actions, earlier studies (Cisek and Kalaska, 2004; Tkach et al., 2007) emphasized the overlap of encoding self and other’s actions. In these studies, PMd neurons active during performed actions were also active during observation of similar motor acts. The authors interpreted their findings by proposing a simulation mechanism underlying observed events. The common view that the same neural mechanisms are engaged both when an action is performed and observed has been taken up by many neurophysiological and fMRI reports as a general feature of PMd (Cunnington et al., 2006; Hatsopoulos and Suminski, 2011; Landmann et al., 2011; Mendoza and Merchant, 2014; Anat and Miriam, 2017).

To account for the differences between our results and those of previous studies we need to consider the differences between the tasks. The first general difference between our study and those using cursors to represent actions (Cisek and Kalaska, 2004; Tkach et al., 2007) is having a human rather than inanimate agent. A cursor displayed on a screen might not be a good surrogate of a living agent. For example, it has been suggested that neurons in lateral prefrontal cortex (IPFC) modulate their activity depending on the animacy of the rival in a social competitive task (Hosokawa and Watanabe, 2012). IPFC neurons were more sensitive when monkeys interacted with another monkey compared with a computer in this study, implying that the presence of a real

partner modulated the observed neuronal activity. In addition, neuroimaging studies report different patterns of brain activity in humans when interacting with another human agent versus a computer, emphasizing the influence of agency beliefs in social interaction contexts (Wykowska et al., 2014; Caruana et al., 2017).

Another difference from previous PMd studies was our requirement of trial-by-trial monitoring of self and other's actions. Failure to monitor the previous response reduced the possibility of making the correct choice during the monkey's turn, after the other's trial. Analyses of oculomotor behavior confirmed that monkeys monitored the task events comparably during self and other's trials.

Importantly, agents in our study were seated next to, and were visible to, each other, switching actor and observer roles in a real-interaction paradigm. The simulative PMd activity described in previous studies may have been elicited by the departure from real-world interactions, which is inherent to virtual observation conditions. We demonstrated that the majority of PMd neurons distinguished between self and others' actions, and only a small proportion of neurons with shared representations.

In contrast to the study of Tkach et al. (2007), Dushanova and Donoghue (2010) recorded M1 activity during a step-tracking task, in which monkeys used a manipulandum to move a cursor or viewed the cursor being moved by the experimenter. Only half of task-engaged neurons from the initial population were modulated by the observation condition. Another study indicating a difference between computer and living agents has described agent-specific coding in the striatum for actions that produced reward during an interaction with a conspecific, but not with a computer (Báez-Mendoza et al., 2013). The importance of face-to-face interaction in generating specific representations has also been described in monkey parietal cortex (Fujii et al., 2007). Another example of neural flexibility, but limited to the study of mirror neurons in PMv, is the change in the coding of mirror neurons' neural representations, depending on peripersonal or extrapersonal space of the observed action (Caggiano et al., 2009). A similar influence on mirror neuron activity has also now been reported (Maranesi et al., 2014).

To better understand the agency-related features of our neuron categories, research should investigate the same brain region using the same task with an inanimate agent, so the effect of a partner's animacy can be considered at different levels of interaction. The different contexts of our study and that of Cisek and Kalaska (2004) could change the coding of the agent; their task design could have promoted simulation with no need of self-other distinction. The fact that an unseen agent moved the cursor on the screen might have favored the use of some neural control or mental rehearsal in an attempt to move the cursor, although it was not necessary because its motion was under the computer control.

Our results extend to PMd a socio-cognitive role via its inclusion in a network implicated in the representation of self-decisions and predicting others' intentions. This has also been done with other cortical areas (Rudebeck et al., 2006; Yoshida et al., 2012; Azzi et al., 2012; Haroush and Williams, 2015; Falcone et al., 2016, 2017), suggesting that social cognition does not rely on common neuronal activation alone.

Unlike other prefrontal and premotor areas that have been targeted with the same paradigm (Falcone et al., 2016, 2017), we found a prevalence of monkey-only cells over the human-only cells in PMd (as in IPFC and supplementary motor area [SMA]). Conversely, a similar proportion of monkey-only cells and human-only cells was found in the posterior part of the medial prefrontal cortex (pmPFC) and in pre-SMA). When considering the both-agents cells, we found that almost all the examined cells shared the same spatial preferences, in contrast to our previous study, in which we found that cells in pmPFC could switch or maintain their spatial preferences in similar proportions (Falcone et al., 2017). The human-only cells could represent a neural substrate, or prerequisite, of a fundamental capacity in the complex primate social environment: mentalizing. Mentalizing is defined as the ability to understand others' intentions, beliefs, attitudes, and goals (Frith and Frith, 2005; Luyten and Fonagy, 2015). Given the connectivity of PMd with frontal areas (Wise et al., 1997; Matelli and Luppino, 2001), such as IPFC and SMAs (Johnson and Ferraina, 1996; Falcone et al., 2016), the role of PMd neurons to represent another individual's intentions may be necessary for successful social interactions. In autistic-spectrum and antisocial behavior disorders, deficits in mentalizing ability have been reported (Preckel et al., 2016; Yoshida et al., 2016), and for this reason, it is very important to understand which brain areas constitute the "social brain" network.

We believe that furthering our understanding of primate social cognition is vital for development of therapies designed to treat neuropsychiatric disorders in which anticipating others' intentions, and incorporating them into one's own behavior, are affected (Frith and Frith, 1999).

Here, the great majority of PMd neurons encoded a future response in the monkey trials only, providing strong evidence that PMd neurons can differentiate the behaviors of self and other. Accordingly, this study also serves as a cautionary note when interpreting neurons with mirror-like properties during social interaction.

EXPERIMENTAL PROCEDURES

Animals

Animal care, housing, and experimental procedures conformed to the European (Directive 210/63/EU) and Italian (DD.L. 116/92 and 26/14) laws on the use of non-human primates in scientific research. The research protocol was approved by the Italian Health Ministry (Central Direction for the Veterinary Service). The housing conditions and experimental procedures were in accordance with the European law on humane care and use of laboratory animals. Two male rhesus monkeys (*Macaca mulatta*) participated in this study, monkey 1 (8 years of age, 8 kg) and monkey 2 (12 years of age, 9.5 kg).

Behavioral Task

Two male rhesus monkeys (*Macaca mulatta*), monkey 1 and monkey 2, performed a NMTG task. There were two versions of the task, which differed only in the peripheral stimuli, while the duration of task periods and the basic rule were identical. Monkey 1 and monkey 2 performed the first version of the task (S-NMTG); monkey 2 also performed the O-NMTG task. We then decided to use the two different versions of the task to obtain comparable performance from the two monkeys. S-NMTG was used for monkey 1 and O-NMTG for monkey 2, because the latter did not learn interaction during the spatial version (performance criterion $\geq 70\%$ after human), showing performance close to chance. The monkeys sat in a primate chair with the head restrained facing

a touch-screen monitor (Microtouch; 19 inches, 800 × 600 pixel resolution) 20 cm away. In both task versions, each trial started with a red central stimulus (7° diameter circle), which appeared on the screen. Once the monkeys touched the central stimulus they had to hold it for 0.5 or 0.8 s. Subsequently, in the S-NMTG task (Figure 1A, left), two spatial targets, represented by identical filled gray rectangles (7.1° × 7.7°), appeared in two of four possible screen positions: center left (23.5° left of center), bottom left (17.5° below and 23.5° left of center), center right (23.5° right of center), and bottom right (17.5° below and 23.5° right of center). In the O-NMTG task (right of Figure 1A), the peripheral stimuli were represented by four objects, differing in color and shape, that appeared in pairs; one to the right and one to the left of the central stimulus (23.5° right and left of center). After the peripheral targets onset, a delay period of 0.8 or 1.2 s began, during which the monkeys had to continue touching the central stimulus until the disappearance of the central target. This served as a “go” signal, which instructed the monkeys to select one of the two peripheral targets. After target selection, the monkeys had to touch it for a holding target period of 0.4 or 0.6 s. On correct trials, the monkeys received water with juice as a reward. Both correct and incorrect trials were followed by a 1–1.5 s inter-trial interval. On next trial, the previously chosen target reappeared on the screen together with another target, randomly selected from a list of the three remaining targets. This could be either a new target or the target not chosen in the previous trial. The task rule was to reject the previously selected target and choose the alternative one. Choosing the same target that was selected in the previous trial was an error that did not lead to reward delivery, and a correction trial followed. An error in a correction trial was followed by another correction trial. The first choice of every session was always accepted as correct and the reward was delivered.

M-H Interaction

During the recording sessions (three for monkey 1 and four for monkey 2), the monkey interacted with a human partner in a subset of trials (26% and 24% of trials for monkey 1 and for monkey 2, respectively). The human partner was sitting close to the animal. The human partner could only start his turn as the actor after the monkey completed a trial, without interrupting it. The human partner indicated his turn during the inter-trial period by moving his hand toward the center of the screen. The monkeys learned to let the human perform the trial without interfering. The human partner performed sequences of one to four consecutive trials, always correct. When the human partner drew back his arm at the end of the last trial in the sequence, the monkey started a new trial. The interaction with the human partner started only after monkeys had learned the task alone. The human partner was not the same for the two monkeys. After a trial correctly executed by the human, the monkey received the reward as in the trials correctly executed by the monkey itself.

Trial Types

During the M-H interaction phase of the experiment (Figure 1B), we assigned monkey trials to two categories: not interactive and interactive trials. The not interactive trials were the trials performed by the monkey after a trial performed by the monkey itself. The interactive trials were the trials performed by the monkey preceded by a trial performed by the human partner. The interactive trials were designed to test the monkeys’ ability to monitor the previous trial performed by the human agent. We refer to this trial classification only for behavioral analyses. For neuronal analyses we refer to the current trials performed by the monkey as “monkey trials,” and to the current trials performed by the human as “human trials,” regardless of the preceding trial type.

Single-Unit Activity

All neurophysiological analyses were performed on the activity of neurons in correct trials, and they excluded correction trials (trials preceded by an incorrect trial).

We recorded 400 single neurons in PMd while the monkeys performed the NMTG task alongside the human partner: 248 cells from monkey 1 and 152 from monkey 2. From the initial population of neurons, we selected a subpopulation of 328 cells, 210 from monkey 1 and 118 from monkey 2, using a single-unit stability method (Supplemental Experimental Procedures) to consider only units that were not the same across recording sessions.

We selected trials with both delay durations (0.8 and 1.2 s). We analyzed the neural activity during four periods: the interval from 0.4 to 0.8 s within the delay period; the RT period; the MT period, defined as the time from the detachment of the hand from the central stimulus to the touch of one target; and the first 0.4 s of the holding target period. We performed a two-way ANOVA with agent and chosen target position as factors. In the delay period of the S-NMTG task, as in O-NMTG, the monkeys could represent the spatial target that the human would select, just by knowing the task rule as in the self-performed trials. For the S-NMTG task, the center and bottom positions of the same side of the screen (with respect to the central stimulus) were collapsed and assigned either to the right or to the left position to make the analysis of the two task versions comparable with each other, because in the O-NMTG task there were only two target positions (right and left).

We focused on the delay period and performed a post hoc analysis (Fisher’s LSD test, $p < 0.05$) on the cells used for the two-way ANOVA ($n = 328$) to evaluate whether the target position differences depended on the agent who performed the task. We then classified the neurons into three different groups, “monkey-only,” “human-only,” and “both-agents” cells, on the basis of whether the target position modulated the activity of neurons only in monkey, only in human or in both kinds of trials, respectively.

Population Analysis

We computed the mean firing rate of different populations of cells. For each cell, we determined its preferred target position as the one with the maximum mean firing rate during the delay 0.4–0.8 s, and we sorted the trials by this target spatial position. We did so for the population activity of monkey-only, human-only, and both-agents cells. To assess whether the spatial preferences of each group were exclusively related to the trials performed by the agent for which they exhibited a significant modulation of their activity, we selected for the monkey-only cells the trials performed by the human, assigning to these trials the preferred and anti-preferred target positions derived from monkey trials. We did the opposite for the human-only cells. We then performed the same analysis for the both-agents cells.

Neuron-Dropping Analysis

To assess the strength of the neural representation of the target position in monkey and human trials, we performed a classification procedure (Genovesio et al., 2006) with neuron-dropping analysis (Foffani and Moxon, 2004). Neuron-dropping curves represent how well a spatial position can be decoded from the activity of a sample neuronal subpopulation, as a function of the sample size (see Supplemental Experimental Procedures for more details).

SUPPLEMENTAL INFORMATION

Supplemental Information includes Supplemental Experimental Procedures and four figures and can be found with this article online at <https://doi.org/10.1016/j.celrep.2018.07.030>.

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AUTHOR CONTRIBUTIONS

A.G. and R.C. designed the experiment. R.C. collected the data. R.C., L.F., and E.M. analyzed the data. R.C., L.F., E.M., S.F., and A.G. wrote the manuscript. A.G. supervised the research.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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