

# Ventral Premotor Neurons Encoding Representations of Action during Self and Others' Inaction

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## Summary

Our environment offers us a number of opportunities for action. However, sometimes we also have to refrain from acting, for example, when facing a “do not touch” sign placed over a desirable object on the shelf of a shop. Previous findings emphasized the role of mesial frontal and prefrontal regions in the inhibition of stimulus-driven motor responses [1–3], leading to the prediction that motor areas should not become active when one inhibits a motor response. Nevertheless, refraining from performing a specific action might require one to internally represent what one is *not* doing. Is the motor system simply inhibited in this condition, or does it play an active role in the representation of the withheld action? Here, we show that while the majority of macaque ventral premotor neurons remain silent when the monkey refrains from grasping an object, others, recorded simultaneously with the former, discharge both when the monkey grasps an object (“action”) and when it refrains from doing so (“inaction”). The same effect has been shown to be present for mirror neurons [4]. Some of them, besides discharging during action observation, also fire when the observed agent refrains from acting. Notably, neurons discharging during inaction specifically encode either the monkey's own or other's inaction, not both. Our findings indicate that ventral premotor cortex encodes representations of our own or others' action not only when we perform or observe that action but also when its negation is represented.

## Results and Discussion

We recorded grasping neurons from ventral premotor area F5 (Figure 1A) of two macaque monkeys when they performed a go/no-go task (“execution task”) and when they observed an experimenter performing the same task (“observation task”). Both tasks included two main conditions (Figure 1B; see also Figure S1 and Supplemental Experimental Procedures available online). In the first one, the agent (monkey or experimenter) was required to grasp a target object (“action”); in the other one, the agent had to remain still for the entire duration of the trial (“inaction”). In both conditions, the temporal sequence of events was the same and the monkey was required to maintain fixation. The trial started when the monkey, in complete darkness, placed its hand contralateral to the recorded hemisphere in a starting position. A fixation point was then presented. As soon as the monkey engaged fixation,

a cue sound instructed the agent (monkey or experimenter) to grasp (“high tone”) or not to grasp (“low tone”) the subsequently presented target. One among three different graspable objects was then randomly presented (target presentation). When the cue sound ceased (go/no-go signal), the agent had to either reach, grasp, and pull the object (within 1.2 s from the sound off), in the case of the action condition, or remain still until the end of the trial (1.2 s), in the case of the inaction condition. At the end of correctly performed trials of both conditions, the monkey was automatically rewarded with a drop of juice.

After several months of training, both monkeys performed the various trials of the execution task with a high rate of success (86.1%). The analysis of the type and frequency of errors the monkeys made indicated that they tended to erroneously reach to grasp the target object more frequently prior to the go (“false start”) rather than the no-go signal. However, false starts also occurred after the no-go signal (see Figure S2 and Supplemental Results), indicating that the mere ceasing of the sound (even when it was the low tone) could induce the monkey to act. This suggests that the correct performance of the inaction condition in the execution task required voluntary inhibition of the reaching-grasping action.

We recorded 663 area F5 grasping neurons, all tested during both execution and observation tasks. All neurons discharged during action execution. Among them, 188 also fired during action observation and were therefore classified as mirror neurons. Surprisingly, some of the recorded neurons ( $n = 105$ ) also became active during the inaction condition relative to both baseline and the object presentation epoch (see Table S1). Some of them (26 out of 105) were motor (nonmirror) neurons and discharged exclusively during the inaction condition of the execution task. An example is shown in Figure 2A. Neuron 1 is a motor neuron that, besides discharging when the monkey grasped the object (blue), also responded when the monkey refrained from doing so (red). This neuron did not discharge during the observation task. The remaining (79 out of 105) were mirror neurons, and most of them (42 out of 79) discharged exclusively during the inaction condition of the observation task. For example, neuron 2 shown in Figure 2A responded not only during grasping execution and observation but also when the monkey observed the experimenter refraining from grasping the object. Notably, this neuron did not respond in the inaction condition during the execution task. Note that the inaction condition was characterized by the same cue signals and reward contingencies in both task contexts (execution and observation). Figure 2B shows that, with few exceptions ( $n = 7$ ), the neurons encoding inaction responded significantly more strongly ( $p < 0.05$ ) in one of the two tasks, namely, execution ( $n = 45$ , light and dark yellow bars) or observation ( $n = 53$ , light and dark blue bars). Importantly, most of them encoded inaction exclusively in one of the two tasks (36 out of 45 execution; 42 out of 53 observation).

This behavior is also clear at the population level (Figures 2C and 2D; see also Supplemental Results). It is noteworthy that all neurons responding to inaction during the observation task (Figure 2D) were mirror neurons, while the great majority

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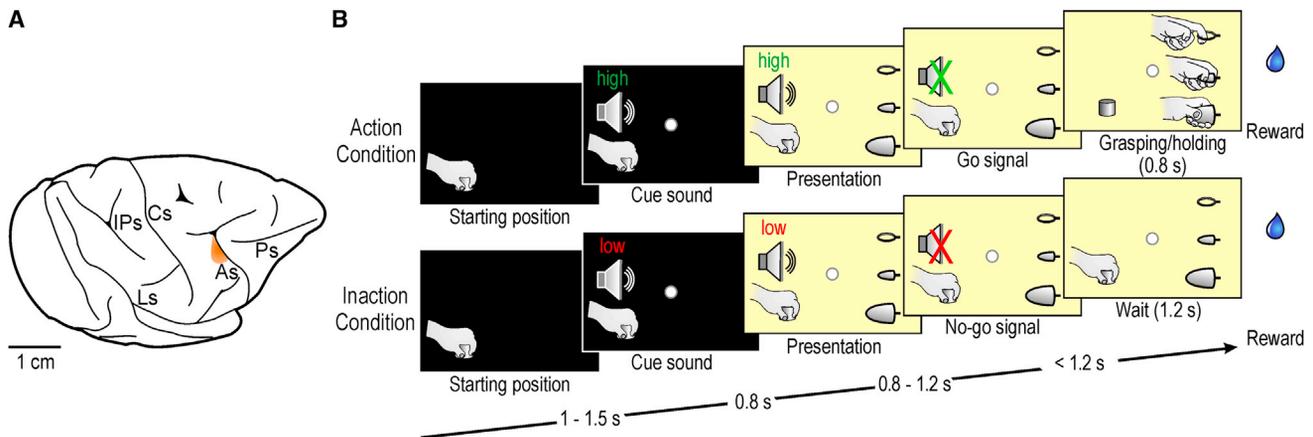


Figure 1. Recorded Region and Behavioral Paradigm

(A) Lateral view of the right hemisphere of the monkey brain. The orange shaded region indicates the sector of the ventral premotor cortex (area F5) from which recordings were carried out. As, arcuate sulcus; Cs, central sulcus; IPs, intraparietal sulcus; Ls, lateral sulcus; Ps, principal sulcus.

(B) Schematic representation of the sequence of events in the action and inaction conditions of the task. Note that the sequence of events was the same when the task was performed by the monkey (execution) as when the task was performed by the experimenter (observation). Task execution and observation were run in different blocks, while action and inaction conditions were randomly presented within each block. Monkeys' arms were not constrained in either of the two contexts.

See also [Figure S1](#).

(26 out of 36) of those responding to inaction in the execution task ([Figure 2C](#)) did not show any significant response to action observation (see also [Table S1](#)).

It might be claimed that neuronal responses during inaction condition could be accounted for by some kind of reward-related anticipatory signal or, alternatively, by subtle, unnoticed monkey movements. However, both these explanations can be ruled out by the following data. First, responses during inaction condition are highly specific for a single task (either execution or observation); this rules out the possibility that they depend on reward-related processes, these being identical in both tasks. Second, the response during inaction condition was more tightly linked with the no-go signal rather than to the end of the trial, as one would expect if it were related to reward delivery. Third, inaction response did not appear to be the result of a global modulation of neuronal activity, typical of unspecific phenomena (such as arousal); indeed, most of simultaneously recorded grasping neurons did not respond during inaction condition (see [Figure S3](#)). In addition, electromyogram (EMG) recordings ([Figures 2E and 2F](#)) showed strong activity during action execution but not during all the conditions (inaction and action observation) in which no movement was required (see also [Supplemental Results](#)), thus demonstrating that monkeys did not move either during inaction conditions in both tasks or during action observation. Taken together, these data indicate that inaction coding is a true functional property pertaining to specific sets of F5 neurons.

What is the relationship between the response of inaction neurons to the action and inaction conditions in the same task? Population responses to executed or observed actions were clearly stronger than those during inaction in the corresponding tasks. Furthermore, the average peak of activity timing in the inaction condition was earlier than that in the action condition, in both tasks ([Figures 3A and 3E](#)). Nevertheless, neurons' peak of activity timing ([Figures 3B and 3F](#)), peak firing rate ([Figures 3C and 3G](#)), and average firing rate ([Figures 3D and 3H](#)) during action and inaction in the same task were

positively and significantly correlated. These findings indicate that the neurons' response pattern underlying the representation of unperformed actions reflects the one associated with overtly executed or observed actions.

Why should some F5 neurons discharge in the absence of any executed or observed movement? One possibility might be that inaction neurons have an inhibitory function. Thus, the response during the inaction condition would contribute to suppressing an action the agent is representing but is required not to perform [5–7]. This explanation might be plausible, however, only for a small portion of the recorded neurons ( $n = 6$ ), namely, those showing opposite (i.e., facilitated-suppressed, or vice versa) activation pattern during action and inaction conditions (see [Figure S4](#)). Since most of inaction neurons showed instead the same activation pattern during the action and inaction condition, a more plausible interpretation is that they provide the monkey with an internal representation of its own or another agent's grasping, both when this representation is associated with an overtly executed or an observed action, and when it has to be intentionally withheld.

Accepting this interpretation, one should expect that neuronal responses during the inaction condition of the execution task are specifically associated with an intentional decision to refrain from grasping, and not with a mere absence of movement due, for instance, to the fact that the monkey neglects the instruction. For example, during some action trials, the monkey, despite the go signal, maintained fixation and (incorrectly) held its hand on the starting position until the end of the wait period (1.2 s; see [Figure 1B](#)). Although from a behavioral point of view, these trials were identical to correctly performed inaction trials, they were incorrect relative to the instruction cue; thus, the monkey was not rewarded ("omitted action"). We analyzed neurons encoding inaction during task execution recorded when the monkey, incorrectly, omitted to act in at least five trials ( $n = 17$ ). Then, we compared their response during action, inaction, and omitted actions. [Figure 4](#) shows that the population response associated with omitted action (gray) is significantly weaker than that during both the

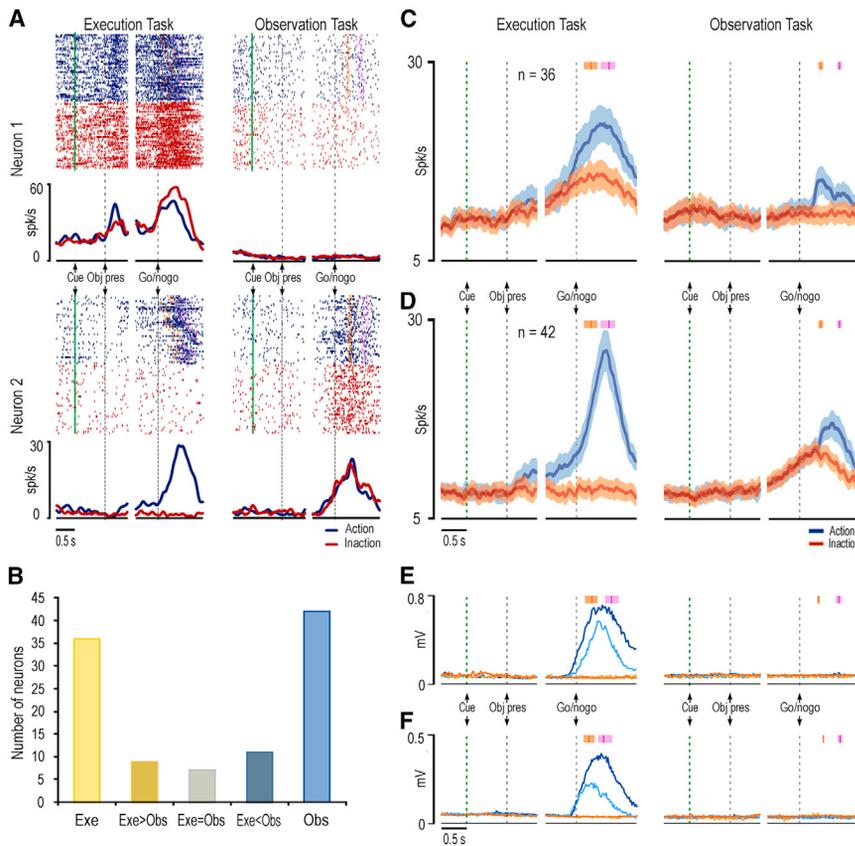


Figure 2. Single-Unit Examples and Population Activity of Neurons Responding to Inaction in Different Task Contexts

(A) Responses of two neurons in the action and inaction conditions during task execution (left) and observation (right). Each panel shows the perievent raster plot (top) and the spike density function (bottom) during the two conditions. Neuron activity is aligned (dashed vertical lines) on object presentation (Obj pres) and go/no-go signal (go/no-go). Small triangles indicate cue sound onset (green), reaching onset (orange), and object-pulling onset (purple).

(B) Histogram showing task context selectivity of all the neurons responding to inaction ( $n = 105$ ). Exe, neurons responding to inaction exclusively during task execution; Obs, neurons responding to inaction exclusively during task observation; Exe>Obs, neurons responding more strongly ( $p < 0.05$ ) to inaction during task execution than during observation; Obs>Exe, neurons responding more strongly to inaction during task observation than during execution; Exe=Obs, neurons responding similarly ( $p > 0.05$ ) to inaction in both task contexts.

(C and D) Population responses during action and inaction conditions in task execution (left) and observation (right) of neurons encoding inaction selectively in the context of task execution (C) or observation (D). Note that only 10 out of 36 of the neurons shown in (C) but all of those shown in (D) are mirror neurons. The red and blue shaded regions around each curve represent 1 SE. Alignments are the same as in (A). The median times of reaching onset and object-pulling onset are indicated with the orange and purple markers, respectively, above each population plot. Shaded areas around each marker represent the 25<sup>th</sup> and 75<sup>th</sup> percentile times of other events of the same type.

(E and F) Average EMG traces from two muscles recorded during action and inaction conditions of one experimental session (45 correct trials for each condition) in monkey M1 (E) and M2 (F). Note that both muscles were active only during the action condition of task execution, but not during either action observation or inaction conditions in both task contexts (see Supplemental Results for details). Muscles are color coded, depending on the experimental condition, as indicated in the insets between (E) and (F): EDC, extensor digitorum communis; Delt, deltoid. Other conventions are as in (C) and (D).

action (blue;  $t = 2.14$ ,  $p < 0.05$ ) and inaction conditions (red;  $t = 4.08$ ,  $p < 0.001$ ), which in turn did not differ from each other ( $t = 0.03$ ,  $p = 0.98$ ). Importantly, whereas the response during the correct performance of the inaction condition was already significant before the no-go signal ( $t = 3.54$ ,  $p < 0.005$ ), the response to omitted actions started only after the go signal (precue:  $t = -0.90$ ,  $p = 0.38$ ). Of course, although we can be

sure that the monkey intentionally refrained from acting during correctly performed inaction trials, we cannot be sure of why the omission occurred after the go signal. Considering that omitted action trials were more frequent at the end of a recording session, a likely possibility is that the monkey needed a pause at a certain point of the task and ignored the instructions. These considerations may justify why there is

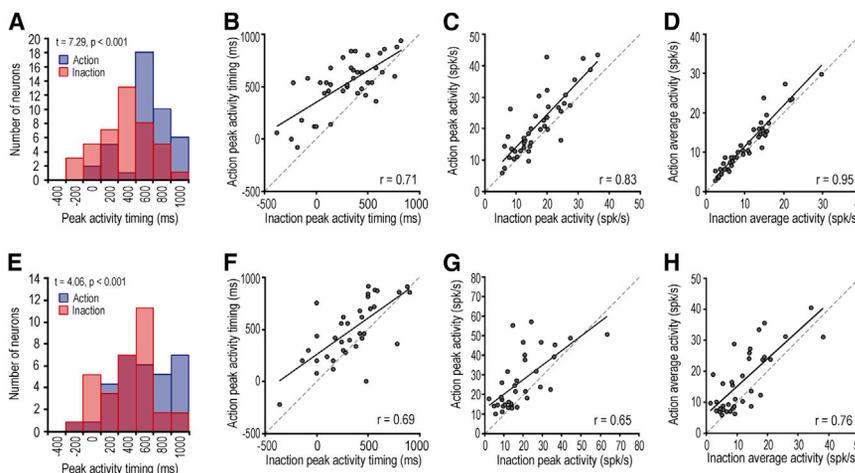


Figure 3. Functional Relationships between Action and Inaction Coding

Relationship between action and inaction coding in neurons selectively responding to inaction during task observation (A–D; same neurons as in Figure 2C) or task execution (E–H; same neurons as in Figure 2D). Peak activity timing has been calculated relative to the go/no-go signal (sound off). All correlation coefficients reported in the figure are significant with  $p < 0.001$ . The dashed gray lines represent the function  $x = y$  in each plot.

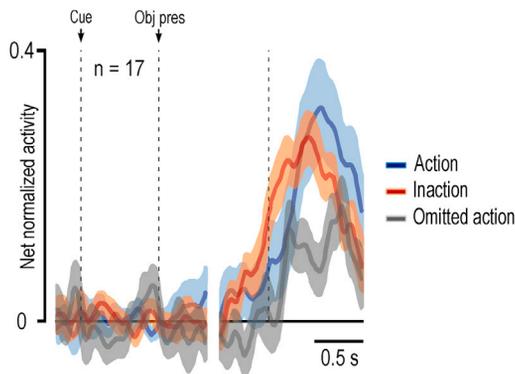


Figure 4. Neuronal Response during Omitted Actions

Population activity of neurons responding during inaction in the context of task execution studied when the monkey erroneously omitted to act (gray line). Other conventions are as in Figure 2.

some neuronal activation even during incorrectly omitted actions, but the lower discharge as compared to correctly performed inaction trials supports the idea that inaction neurons generate motor representations of grasping, which are recruited both when the monkey acts and when it intentionally refrains from doing so.

Previous studies have shown that motor representations can be mentally rehearsed in the absence of any overt movement, based solely on the sight of a moving stimulus usually associated with the monkey's own movement [8]. Our findings demonstrate that ventral premotor neurons can code motor representations even in the absence of any visual stimulus. Furthermore, the tight link between action and inaction responses in the context of task execution or observation suggests that distinct classes of neurons are selectively recruited to encode representations of self (task execution) and other's (task observation) action. Interestingly, a recent study demonstrated that in the presupplementary motor area of the macaque, which is tightly connected with area F5 [9, 10], there are neurons encoding specifically self or others' observed action [11]. Although a no-go condition was not included in this latter study, it is plausible that the interaction between mesial and lateral premotor areas could enable to exploit motor representations related to self and others' action at a more abstract, conceptual level: action concepts might be crucial to understanding not only what we, or others, are doing, but also what we, or others, are refraining from doing. In other words, refraining from grasping an apple necessarily requires the activation of a representation of grasping.

In line with our findings are some previous human event-related potentials studies, in which subjects were required to intentionally not do an action within a free-choice and an instructed paradigm. The results showed that intentionally refraining from performing an action evokes cortical activations similar to those associated with the overt execution of that action [12], suggesting that even intending to not do something activates a representation of what has to not be done. Interestingly, similar results have also been reported by fMRI studies in the domain of human language [13]. Indeed, the representation of affirmative action-related sentences activated specific regions within the frontoparietal cortical action representation system, and these regions were also activated, although more weakly, when action-related sentences were presented in negative terms.

The present findings expand the notion that the motor system is involved in high-order cognitive functions by showing that representations of self and others' action, at the single-neuron level, are activated not only when an action is overtly performed or observed but also, most interestingly, when one needs to represent its negation.

#### Supplemental Information

Supplemental Information includes four figures, one table, Supplemental Results, and Supplemental Experimental Procedures and can be found with this article online at <http://dx.doi.org/10.1016/j.cub.2014.05.047>.

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