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## Selectivity for grip type and action goal in macaque inferior parietal and ventral premotor grasping neurons

Luca Bonini,<sup>1</sup> Francesca Ugolotti Serventi,<sup>2</sup> Stefania Bruni,<sup>2</sup> Monica Maranesi,<sup>2</sup> Marco Bimbi,<sup>2</sup> Luciano Simone,<sup>2</sup> Stefano Rozzi,<sup>2</sup> Pier Francesco Ferrari,<sup>2,3</sup> and Leonardo Fogassi<sup>2,4</sup>

<sup>1</sup>Istituto Italiano di Tecnologia (IIT), Brain Center for Social and Motor Cognition (BCSMC), Parma, Italy; <sup>2</sup>Rete Multidisciplinare Tecnologica (RTM) and Dipartimento di Neuroscienze, Università di Parma, Parma, Italy; <sup>3</sup>Dipartimento di Biologia Evolutiva e Funzionale, Università di Parma, Parma, Italy; and <sup>4</sup>Dipartimento di Psicologia, Università di Parma, Parma, Italy

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**Bonini L, Ugolotti Serventi F, Bruni S, Maranesi M, Bimbi M, Simone L, Rozzi S, Ferrari PF, Fogassi L.** Selectivity for grip type and action goal in macaque inferior parietal and ventral premotor grasping neurons. *J Neurophysiol* 108: 1607–1619, 2012. First published June 27, 2012; doi:10.1152/jn.01158.2011.—Grasping objects requires the selection of specific grip postures in relation to the objects' physical properties. Furthermore, grasping acts can be embedded in actions aimed at different goals, depending on the context in which the action is performed. Here we assessed whether information on grip and action type integrate at the single-neuron level within the parieto-frontal motor system. For this purpose, we trained three monkeys to perform simple grasp-to-eat and grasp-to-place actions, depending on contextual cues, in which different grip types were required in relation to target features. We recorded 173 grasping neurons: 86 from the inferior parietal area PFG and 87 from the ventral premotor area F5. Results showed that most neurons in both areas are selective for grip type, but the discharge of many of them, particularly in PFG, appears to differ in relation to action context. Kinematics data and control experiments indicated that neuronal selectivity appears more likely to depend on the action goal triggered by the context than on specific contextual elements. The temporal dynamics of grip and goal selectivity showed that grasping neurons reflect first “how” the object has to be grasped (grip), to guide and monitor the hand shaping phase, and then “why” the action is performed (goal), very likely to facilitate subsequent motor acts following grasping. These findings suggest that, in the parieto-frontal system, grip types and action goals are processed by both parallel and converging pathways, and area PFG appears to be particularly relevant for integrating this information for action organization.

area PFG; area F5; affordance; contextual information; motor control

IN BOTH HUMANS AND MONKEYS, the visuo-motor transformations of objects' physical properties into specific types of grip occur in a cortical circuit formed by the anterior intraparietal area (AIP) and the ventral premotor cortex (PMv) (Davare et al. 2011; Grafton 2010; Rizzolatti and Luppino 2001).

Single-neuron recording studies in monkeys demonstrated that AIP (Baumann et al. 2009; Murata et al. 1996, 2000; Sakata et al. 1995, 1997; Taira et al. 1990) and the ventral premotor area F5 (Fluet et al. 2010; Murata et al. 1997; Raos et al. 2006) play crucial roles in the visuo-motor transformations necessary for grasping objects. In fact, the disruption of neuronal activity of area AIP in both monkeys and humans

(Gallese et al. 1994; Tunik et al. 2005), and of area F5 in the monkey (Fogassi et al. 2001), impairs hand shaping during visually guided grasping. Unlike AIP, PMv also exerts a strong influence on M1 (Buch et al. 2010; Cattaneo et al. 2005; Davare et al. 2009; Prabhu et al. 2009; Shimazu et al. 2004; Umiltà et al. 2007) and the spinal cord (Borra et al. 2010; Dum and Strick 1991; He et al. 1995; Lemon 2008), enabling the actual grasping execution.

The studies considered so far provide a comprehensive picture of the neural mechanisms underlying object grasping. However, grasping acts are usually embedded in actions aimed at specific final motor goals, which in turn are strictly related to the context in which the action has to be performed. Therefore, sensory-motor transformations for grasping have to be integrated within higher-order neuronal systems devoted to action organization. For instance, when grasping a fruit, a specific grip type has to be chosen depending on the physical properties of the fruit (i.e., its size and shape). However, the agent could grasp the fruit in order to eat it or to place it in a basket. Thus the same grip can be used to attain different action goals.

It is noteworthy that recent studies showed that grasping neurons in the inferior parietal area PFG and in area F5 of the monkey can be differentially activated depending on the action (grasp-to-eat or grasp-to-place) in which the coded act is embedded (Bonini et al. 2010; Fogassi et al. 2005). Control experiments have investigated the specific factors determining grasp-to-eat or grasp-to-place neuronal selectivity. For example, grasp-to-place neurons did not change their selectivity when the container in which the target had to be placed was located near the target or near the mouth, revealing that neuronal selectivity is largely independent from the kinematics of the motor acts following grasping (Bonini et al. 2010; Fogassi et al. 2005). Furthermore, a recent study showed that both grasp-to-eat and grasp-to-place neurons did not change their selectivity in relation to the rewarding value of the food obtained by the monkey for correct task accomplishment (Bonini et al. 2011). Finally, the same study also demonstrated that the neuronal selectivity of PFG and F5 grasping neurons is the same during the execution of both simple and complex action sequences and crucially depends on the availability of contextual information about the final action goal (Bonini et al. 2011). On the basis of these findings it has been suggested that the discharge of PFG and F5 neurons reflects the goal of the action in which the coded act is embedded, and that the cortical circuit

Address for reprint requests and other correspondence: L. Bonini, Istituto Italiano di Tecnologia (IIT)—Brain Center for Social and Motor Cognition, Via Voltumo 39, 43125 Parma, Italy (e-mail: luca.bonini@unipr.it).

formed by areas PFG and F5 plays an important role in the organization of goal-directed actions (Bonini et al. 2010, 2011; Fogassi et al. 2005). However, in these latter studies neuronal activity was always recorded during the execution of a single type of grip (precision grip), thus leaving an important issue unresolved: whether information on grip and action type integrate at the single-neuron level or are processed in parallel by distinct neuronal systems.

Here we addressed this issue by recording neuronal activity from inferior parietal area PFG and ventral premotor area F5 of three monkeys while they executed simple grasp-to-eat and grasp-to-place natural actions, each performed with different grip types. To induce the monkey to perform different actions and grip types, we manipulated contextual information and object features.

## MATERIALS AND METHODS

The study was carried out on three macaque monkeys (2 female *Macaca nemestrina* and 1 male *Macaca mulatta*), which will be referred to as *M1*, *M2*, and *M3*, respectively.

Before recordings, each monkey was habituated to sit comfortably in a primate chair, to interact with the experimenters, and to become familiarized with the experimental setup. Each monkey was then trained to perform the motor task described below, using the hand contralateral to the hemisphere to be recorded. At the end of training, a head fixation system and a cylindrical recording chamber (Alpha Omega Engineering, Nazareth, Israel; inner diameter 18 mm) were implanted based on stereotaxic coordinates of the cortical regions to be recorded (Fig. 1A) under general anesthesia (ketamine hydrochloride 5 mg/kg im and medetomidine hydrochloride 0.1 mg/kg im)

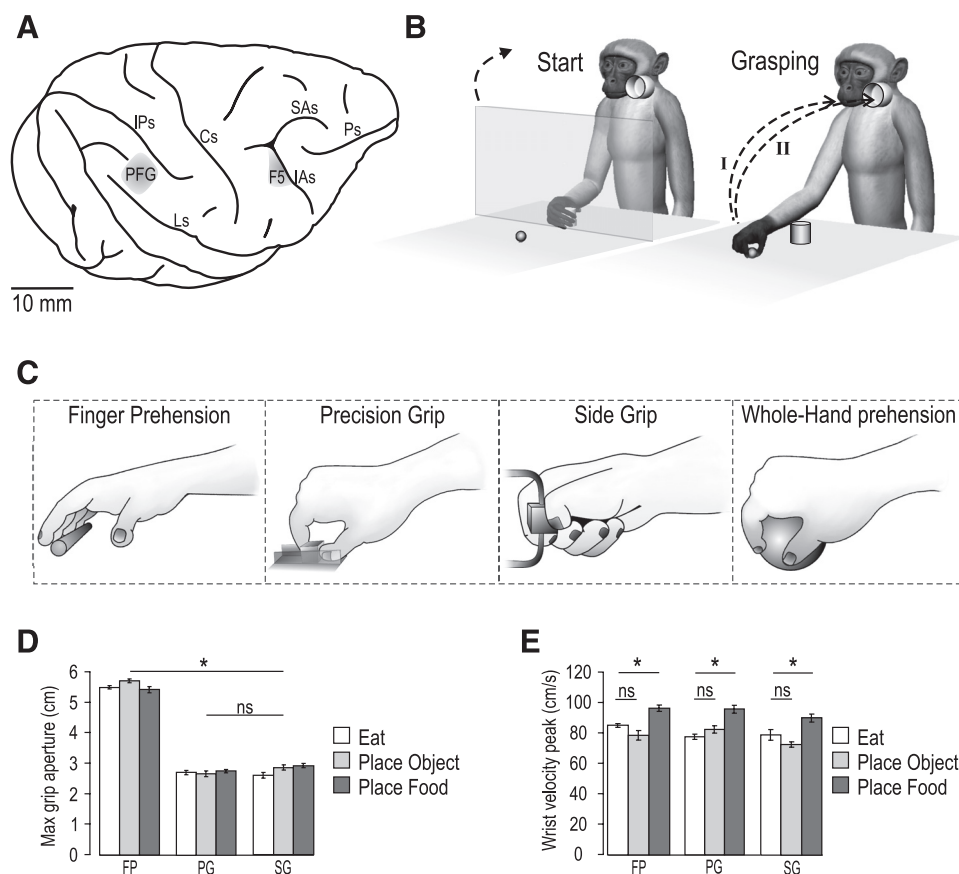
followed by postsurgical pain medications (Bonini et al. 2010; Rozzi et al. 2006). All experimental protocols were approved by the Veterinarian Animal Care and Use Committee of the University of Parma and complied with European law on the humane care and use of laboratory animals.

**Behavioral task and apparatus.** Monkeys were trained to perform a modified version of a motor task previously described (see Fogassi et al. 2005 and Bonini et al. 2010 for further details on the apparatus).

Figure 1B shows the basic motor task employed in this study. The monkey held its hand in a fixed starting position while the experimenter positioned a piece of food (apple, carrot, or potato) or an object (of the same size and shape as the food) as the target in one of the specific devices described below. During set preparation, a transparent plastic screen was interposed between the monkey and the target, preventing the monkey from reaching the target but allowing it to know what action would be performed. The first part of the task was identical across all conditions. When the screen was removed (go signal), the monkey reached for and grasped the target (food or object) and ate the food (eating condition) or placed the object into a container located near the mouth (placing condition) (Fig. 1B, I and II, respectively). After correct execution of grasp-to-place trials, a piece of food identical to that used during eating trials was delivered as the reward.

To verify whether the different target used during eating and placing actions could influence neuronal discharge, a considerable part of the recorded neurons were tested by requiring the monkey to grasp and place a food morsel identical to that used during grasp-to-eat actions. To this purpose, before each grasp-to-place trial, the monkey was briefly (1–2 s) visually presented with a preferred food reward before the onset of the trial. After a variable delay (2–5 s), the screen was lifted and monkey grasped the food and placed it into the container in order to receive the preferred reward.

Fig. 1. A: lateral view of the right hemisphere of monkey *M3*. Gray shading indicates the regions of the inferior parietal lobule (area PFG) and ventral premotor cortex (area F5) in which neurons were recorded. IPs, intraparietal sulcus; Ls, lateral sulcus; Cs, central sulcus; IAs, inferior arcuate sulcus; SAs, superior arcuate sulcus; Ps, principal sulcus. B: motor task. The monkey started from a fixed position, with a transparent screen interposed between its hand and the target. When the screen was removed (Start), the monkey reached for and grasped the target (Grasping) in order to bring it to its mouth and eat it (I) or place it into a container located near its mouth (II). C: grip types employed for grasping target objects. D: maximal finger aperture during the execution of grasp-to-eat, grasp-to-place an object, and grasp-to-place food with finger prehension (FP), precision grip (PG), and side grip (SG). Error bars indicate SE. \* $P < 0.001$ . ns, Not significant. E: wrist velocity peak during the execution of grasp-to-eat, grasp-to-place an object, and grasp-to-place food with FP, PG, and SG. Conventions as in D.



To study possible grip selectivity, monkeys were trained to perform both conditions of the motor task using different grip types. To this end, we employed different devices for holding the target of the monkeys' grasp-to-eat and grasp-to-place actions, in order to force them to employ a specific grip. Figure 1C shows the different grip types employed for studying neuronal activity. Monkeys were trained to perform 1) "finger prehension" (FP), by using all the fingers but the thumb when a thin cylindrical piece of food or a metal object (diameter 0.5 cm, length 5 cm) had to be grasped from a tray positioned horizontally in front of the monkey; 2) "precision grip" (PG), by using the pulpar surface of the distal phalanges of the thumb and the index finger when a small piece of food or an object of the same size and shape of the food (a cube of 1 cm) had to be grasped from a groove; 3) "side grip" (SG), by using the thumb and the radial surface of the distal phalanx of the index finger with 90° supination of the hand when the same small object (or food) used for PG had to be grasped from the arms of small spring tongs oriented vertically; and 4) "whole hand prehension" (WH), by using all fingers, including the thumb, in opposition with the hand palmar surface, when a large sphere (4 cm in diameter) or a large piece of food of the same size and shape had to be grasped from a tray positioned horizontally in front of the monkey. The center of mass of all target objects was located at a fixed distance of 15 cm from the hand starting position.

Grasp-to-eat and grasp-to-place trials, performed with different grip types, were presented in a pseudorandom fashion. If the monkey detached its hand from the starting position before the go signal, or failed to correctly grasp the target, the trial was discarded and not included in the data set. Furthermore, if the monkey ate the food used as the target for the grasp-to-place actions, the preferred food was not delivered and the trial was discarded. Failed trials were repeated in order to collect at least 10 correct trials for each experimental condition.

Contact-detecting electric circuits were used to signal the main behavioral events necessary for subsequent alignment of neuronal activity and for statistical analysis of neuronal discharge in different epochs. The recorded events were 1) detachment of the hand from the starting point, 2) contact of the hand with the target (food or object) of the action, and 3) contact of the hand with the rim of the container in which the object/food had to be placed.

**Recording techniques.** Single-neuron recordings were carried out by using single glass-coated tungsten microelectrodes (impedance 0.5–1 M $\Omega$ ) inserted through the intact dura, perpendicularly to the cortical surface. The microelectrode was mounted on an electrode-driving terminal (MT, Alpha Omega Engineering) fixed to the recording chamber. The electrode was moved into the brain by a computer-controlled micromanipulator (EPS, Alpha Omega Engineering). Neuronal activity was amplified (MCPplus, Alpha Omega Engineering) and monitored on an oscilloscope. Single-neuron action potentials were also isolated online with a dual voltage-time window discriminator (Bak Electronics, Germantown, MD) for more detailed testing of neuronal properties (see below). Raw analog signal, isolated action potentials, and the digital events related to the behavioral paradigm were acquired and stored by means of LabVIEW-based software. Single spikes' shapes were further extracted and sorted off-line with dedicated software (Wave-Clus; Quiroga et al. 2004).

**Preliminary testing of neuronal activity in recording sites.** After chamber implantation, the regions of interest (hand regions of parietal area PFG and of ventral premotor area F5) were functionally identified by studying single neurons and multiunit activity and through intracortical microstimulation (ICMS) (Fogassi et al. 2005; Raos et al. 2006; Rozzi et al. 2008).

In particular, the hand region of the PMv is located laterally to the genu of the arcuate sulci and includes the medial convexity sector of the postarcuate cortex in which ICMS could evoke hand movements at relatively high thresholds (typically 40  $\mu$ A or higher, with monophasic pulse trains of 50 or 100 ms at 330 Hz). We did not record

neuronal activity from regions in which ICMS or functional properties were related to axial, arm, or mouth movements.

Before acquisition of neuronal activity with the motor tasks, single and multiunit activity on each site were systematically tested as follows. To ensure that each neuron's activity was related to hand grasping, we did a preliminary test of their discharge in a few trials in which monkeys grasped a piece of food in proximity to their bodies (no reaching required) with their eyes closed. Similarly, to verify the possible presence of mouth-related activity, we studied neuronal responses with the monkeys' eyes closed by giving them small pieces of food directly into their mouths. Furthermore, we also tested possible tactile responses during mechanical stimulation of the pulpar surface of the fingers and the palm of the contralateral hand, since these responses could be a potential source of apparent grip motor selectivity. Typically, the effector activated by ICMS matched that activated during the preliminary testing of neuronal activity. Only cortical sites in which neurons responded specifically during hand motor acts were further tested with the motor task and therefore included in this study. Note that, although we adopted these criteria in order to limit the possible impact of potential confounding factors on neuronal discharge and selectivity, these criteria may have prevented us from studying neurons that show suppression of activity during grasping.

**Kinematics analyses.** Kinematics analyses were carried out on *monkey M3* in order to verify the presence of possible differences in the parameters of hand movement when monkeys grasped-to-eat or grasped-to-place different target objects (piece of food or metallic object) with different types of grip (FP, SG, and PG). Only a few neurons were tested during WH, because using big food morsels as targets of the grasp-to-eat action resulted in a rapid loss of the monkey's motivation. For this reason, this grip was not considered in the kinematics analyses. In accordance with previous kinematics studies (Gentilucci et al. 1991; Jeannerod 1984), we focused on two main parameters: hand maximal aperture, defined as the maximal distance between the tip of the thumb and index finger, and the peak of wrist tangential velocity. A white-colored marker was placed on the monkey's wrist and on the tip of the last phalanx of the thumb and index finger. By means of a digital video camera we captured trials of grasp-to-eat, grasp-to-place food, and grasp-to-place an object and analyzed videos off-line with homemade dedicated software, at a sampling rate of 50 frames/s.

**Definition of grasping epochs and data analyses.** Neuronal activity was stored from 2 s before until 2 s after the detachment of the monkey's hand from the starting position (4 s for each trial). In a preliminary analysis, for each neuron we verified the presence of a significantly higher response during grasping compared with the baseline activity, as follows. First, we adopted a largely accepted broad definition of "hand grasping," which includes both the hand shaping and actual grasping phases (Chen et al. 2009; Jeannerod 1988; Mason et al. 2004). Accordingly, we defined two epochs of interest (see Bonini et al. 2010; Fogassi et al. 2005): 1) grasping epoch, from 300 ms before the hand contacted the target object (food or metallic solid) to 300 ms after this event (total duration 600 ms), and 2) baseline epoch, starting 2 s before the hand-target contact and lasting for 600 ms, when the hand was at rest on the starting position and the transparent screen was interposed between the hand and the target. Note that the grasping epoch does not include the introduction of the food into the mouth (during eating trials) or the contact of the monkey's hand with the rim of the container (during placing trials). In fact, hand-target contact occurred  $541 \pm 68$  ms (mean  $\pm$  SD) before the food was introduced into the mouth and  $499 \pm 62$  ms before the contact of the hand with the rim of the container. This also indicates that most of the arm flexion phase for bringing the target to the mouth (during eating trials) or into the container located near the mouth (during placing trials) was excluded from the grasping epoch employed for data analyses. A repeated-measures ANOVA (factors: grip, action context, and epoch) was employed, followed by Bonferroni

post hoc tests. All the neurons presented in this study displayed a statistically significant response during the above-defined grasping epoch, with respect to the baseline activity, either as a main effect or as an interaction with a certain grip and/or action context. All analyses were performed with a significance criterion of  $P < 0.05$ . Only neurons steadily recorded for at least 10 trials in each condition that showed a significant activation during grasping, based on this analysis, were considered in this study and further analyzed.

Subsequently, once identified as described above, the response of grasping neurons was analyzed by means of an ANOVA for repeated measures (factors: grip, action context, and epoch), followed by Bonferroni post hoc tests in case of significant interaction effects. In this case, the factor epoch included two distinct levels, namely, precontact (300 ms before hand-target contact) and postcontact (300 ms after hand target contact) epochs, but not the baseline period. This analysis enabled us to more precisely identify possible differences in the timing of grip type and action context selectivity.

To quantitatively assess the preference expressed by single neurons for the type of grip or the action context, preference indexes (PIs) were calculated as follows:

$$PI = (R_p - R_n) / (R_p + R_n)$$

where  $R_p$  and  $R_n$  are the mean firing rates of the neuron in its preferred and not preferred conditions, respectively. The selection of the trials to be included in the calculation of  $R_p$  and  $R_n$  was based on the findings of single neurons' statistical analysis, in terms of main or interaction effects. For example, to calculate a PI for grip preference, both the eating and placing trials were used to calculate  $R_p$  and  $R_n$  if a neuron showed only a significant main effect for the factor grip. Alternatively, if there was an interaction effect between the factors grip type and action context,  $R_p$  and  $R_n$  were calculated by using either eating or placing trials of both the grip types to be compared, depending on the condition that provided the significant interaction effect. PIs ranged from 0 (discharge identical between the compared conditions) to 1 (complete selectivity for the preferred condition).

Population analyses were carried out taking into account single neurons' response expressed in terms of normalized mean activity, calculated as described elsewhere (Bonini et al. 2010). To compare the time course of neuronal selectivity between different neuronal populations we transformed the normalized mean activity into normalized differential activity. To this end, for each neuron of a certain population we first averaged the activity in each of the two conditions to be compared (preferred and not preferred) across trials during a time window of 60 ms, slid forward in steps of 20 ms, according to previous studies (Bonini et al. 2010). These time intervals appear to be the shortest possible intervals for reliably identifying the neurons' peak of activity. Each value was divided by the highest value among those obtained in both conditions, so that the normalized activity time course ranged from 0 to 1. We then computed the difference between each corresponding value of the preferred and not preferred conditions. This procedure, applied along the entire acquisition period, allowed us to describe the time course of the differential activity. The time in which the highest differential activity value occurred corresponded with the timing of the peak of selectivity. To identify the time when each neuron began to show its selectivity, we calculated the mean differential activity between preferred and not preferred conditions during the 600-ms baseline epoch and added to it its standard deviation; then, we subtracted this value from each value of the differential activity time course. The time corresponding to the occurrence of the last one of a series of at least three subsequent bins with values  $\leq 0$  before the peak of selectivity was taken as the onset time of the neuronal selectivity.

*Histological reconstruction and identification of recorded regions.* About 1 wk before the animals were killed (7 days for *M1*; 10 days for *M2*; 8 days for *M3*), electrolytic lesions (10- $\mu$ A cathodic pulses per 10 s) were performed at known coordinates at the external borders of the recorded regions. Each animal was then deeply anesthetized and

perfused as previously described (Rozzi et al. 2006). The brain was then extracted, photographed, and cut (slice thickness 60  $\mu$ m). Each second and fifth section of a series of five was stained by the Nissl method (thionin 0.1% in 0.1 M acetate buffer, pH 3.7). The locations of penetrations were then reconstructed on the basis of the electrolytic lesions, stereotaxic coordinates, depths of penetration, and functional properties. Subsequently, the cytoarchitectonic features of inferior parietal lobule (IPL) convexity and PMv were identified on the basis of the criteria defined by Luppino and colleagues (Belmalih et al. 2009; Gregoriou et al. 2006) and attributed to the different cytoarchitectonic areas.

## RESULTS

We recorded a total of 173 grasping neurons in the three monkeys. In particular, 86 grasping neurons were recorded from the convexity of the inferior postarcuate cortex (area F5c; Belmalih et al. 2009) of the right hemisphere of *monkeys M1* and *M2* and the left hemisphere of *monkey M3*. Furthermore, we recorded 87 grasping neurons from the convexity of the inferior parietal area PFG (Gregoriou et al. 2006) of the right hemispheres of *monkeys M2* and *M3*. Figure 1A shows the anatomical location of the two investigated regions reported on the right hemisphere of *monkey M3*.

Neuronal activity was recorded while monkeys performed the task in each of the two conditions (eating and placing; see Fig. 1B) employing at least two different grip types (Fig. 1C). Fig. 1, D and E, show the results of kinematics analyses of the monkey's hand movement, carried out in order to verify possible differences in finger aperture and wrist velocity during grasp-to-eat, grasp-to-place food, and grasp-to-place an object performed with different types of grip.

Concerning finger aperture (see MATERIALS AND METHODS), a  $3 \times 3$  repeated-measures ANOVA (factors: grip and condition) showed a significant main effect for the factor grip [ $F(2,18) = 1,382.8$ ,  $P < 0.001$ ] and for the interaction between grip and condition [ $F(4,36) = 2.73$ ,  $P < 0.05$ ] but no main effect for the factor condition. Bonferroni post hoc tests revealed that during FP finger aperture was greater than during SG and PG ( $P < 0.001$ ), which did not differ significantly from each other in this respect. Importantly, finger aperture was not significantly different during grasp-to-eat, grasp-to-place a piece of food, and grasp-to-place an object across any of the studied grip types.

Concerning the peak of wrist velocity, the same repeated-measures ANOVA was applied, revealing a significant main effect for the factors grip [ $F(2,18) = 6.03$ ,  $P < 0.05$ ] and condition [ $F(2,18) = 61.2$ ,  $P < 0.001$ ] but not for the interaction between them. Bonferroni post hoc tests showed that the wrist velocity was higher during FP and PG compared with SG ( $P < 0.05$  for both comparisons). In addition, while wrist velocity peak did not differ between grasp-to-eat and grasp-to-place an object, it was significantly higher when the monkey grasped a piece of food to place it ( $P < 0.001$  for both comparisons).

Forty-seven percent of F5 neurons and 42% of PFG neurons were tested with grasp-to-place of a metallic solid, while the remaining neurons in each area were tested with grasp-to-place of a piece of food. Note that if any unspecific factor related to the grasped object (e.g., its texture or behavioral value) influenced neuronal discharge, one would expect a considerable difference in grip or action context selectivity between the

Table 1. Grip type and action context selectivity of PFG recorded neurons

Grip Selectivity	Action Context Selectivity			No Action Context Selectivity	Total PFG Neurons
	Eating	Placing	Total		
PG (64)	2	4	6	6	12
SG (73)	7	1	8	12	20
FP (59)	9	6	15	12	27
WH (6)	0	4	4	0	4
Total grip selective	18	15	33	30	63
No grip selectivity	4	4	8	16	24
Total PFG neurons	22	19	41	46	87

Total number of neurons tested with each grip type is reported in parentheses. PG, precision grip; SG, side grip; FP, finger prehension; WH, whole hand prehension.

subpopulations tested during grasp-to-place the food or the object. On the contrary, in both areas these neuronal subpopulations contain a remarkably similar proportion of neurons that reflect the grip type and the action context [PFG:  $\chi^2 = 0.1$ , not significant (ns); F5:  $\chi^2 = 0.0$ , ns], suggesting that the type of target (food or object) does not influence grasp-to-eat or grasp-to-place neuronal selectivity, in line with previous studies (Bonini et al. 2011; Fogassi et al. 2005). Thus from this point onward, neurons tested during grasp-to-place an object or a piece of food will be pooled together.

Statistical analyses of single-neuron activity (see Tables 1 and 2) revealed that >70% of neurons in both areas (72% in PFG and 71% in F5) showed selectivity for the grip type. FP was the most frequently preferred grip in both PFG (43%) and F5 (48%). Furthermore, several neurons in both areas also showed a selectivity for the action context (47% in PFG and 36% in F5), with a slightly higher proportion of neurons selective for grasp-to-eat (54% in PFG and 67% in F5) than for grasp-to-place.

Figure 2A shows the proportion of the recorded neurons that showed grip selectivity, action context selectivity, or no selectivity in the two areas. Interestingly, 38% of PFG neurons and 23% of F5 neurons encoded both the grip type and the action context (overlapping regions in Fig. 2A). Fisher's exact probability test revealed that area PFG contains more neurons that integrate information on grip type and action context compared with F5 ( $P = 0.027$ ). In contrast, area F5 had a higher proportion of neurons that show only grip selectivity compared with PFG, although this difference did not reach statistical significance ( $P = 0.054$ ).

Table 2. Grip type and action context selectivity of F5 recorded neurons

Grip Selectivity	Action Context Selectivity			No Action Context Selectivity	Total F5 Neurons
	Eating	Placing	Total		
PG (71)	3	3	6	10	16
SG (52)	5	0	5	11	16
FP (59)	5	4	9	20	29
WH (5)	0	0	0	0	0
Total grip selective	13	7	20	41	61
No grip selectivity	8	3	11	14	25
Total F5 neurons	21	10	31	55	86

Total number of neurons tested with each grip type is reported in parentheses.

Figure 2B is based on the total number of neurons recorded in each area and shows the proportion of neurons showing a significant grip or action context selectivity during either pre- or postcontact epochs or during both of these epochs (see MATERIALS AND METHODS). Grip selectivity was present during both pre- and postcontact epochs in more than half of the recorded neurons of both areas, while action context selectivity was more frequently found during a single epoch (PFG:  $\chi^2 = 7.4$ ,  $P < 0.01$ ; F5:  $\chi^2 = 3.9$ ,  $P < 0.05$ ). In particular, action context selectivity appeared more often during the postcontact epoch (PFG:  $\chi^2 = 11.2$ ,  $P < 0.001$ ; F5:  $\chi^2 = 14.7$ ,  $P < 0.001$ ).

*Grip selectivity regardless of action context.* Figure 3 shows examples of neurons showing only grip selectivity and discharging similarly during grasp-to-eat and grasp-to-place actions. The neuron in Fig. 3A increased its firing rate when the monkey's hand detached from the starting position for grasping a target with FP and reached its peak of activity immediately after the contact of the hand with the target. Grasping with other grip types (i.e., WH and PG) evoked no significant response. Notably, the firing pattern was the same during both grasp-to-eat and grasp-to-place. Figure 3B shows a neuron with broader grip selectivity. This neuron discharged strongly after the contact of the monkey's hand with the target, during finger closure. The response was present only during grasping with the opposition of the thumb and the index finger (i.e., during PG and SG) and not when the monkey performed FP. Also in this neuron, the response did not differ significantly between grasp-to-eat and grasp-to-place.

Most of the neurons that showed grip selectivity alone (PFG: 21 of 30, F5: 30 of 41) were tested by comparing their

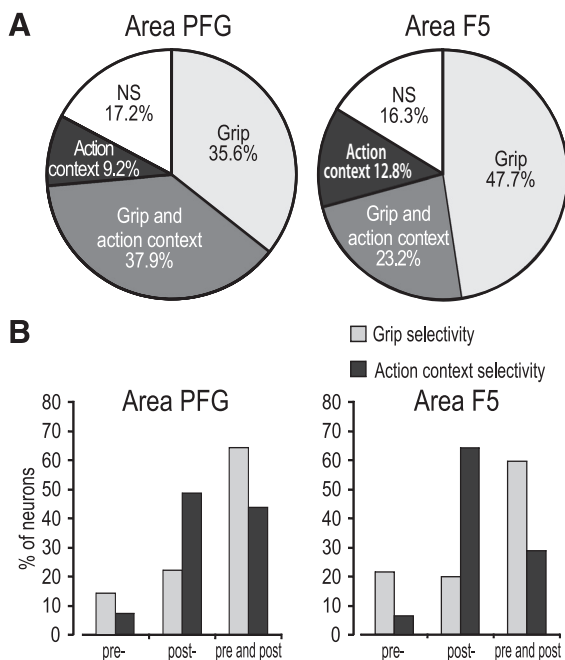


Fig. 2. *A*: proportion of neurons selective only for the grip type (light gray) or the action context (dark gray), selective for a combination of both factors (overlapping region), or unselective for both factors (NS, white) recorded in areas PFG and F5. *B*: % of PFG and F5 neurons showing grip and action context selectivity during precontact epoch, postcontact epoch, or both epochs.

discharge during a grip requiring the opposition of the thumb and the index finger (i.e., PG or SG) with that during FP or WH, which require the use of all the fingers. The majority of the neurons tested in these conditions had a preference for FP (PFG: 62%, F5: 63%), while a lower percentage discharged more strongly during either PG or SG. Note that during FP the absence of any preference for grasp-to-eat rules out the possibility that the amount of reward had an influence on these neurons' discharge. For the remaining grip-selective neurons (PFG:  $N = 9$ , F5:  $N = 11$ ), activity was tested by comparing PG and SG, showing that the large majority had a preference for SG (PFG: 7 of 9, F5: 9 of 11).

Figure 4 shows the time course and intensity of the activity of neuronal populations of both areas selective only for grip type, aligned on the hand-target contact. Grip selectivity was assessed by considering a 300-ms baseline epoch and the two epochs of grasping: the precontact epoch (300 ms before hand-target contact) and the postcontact epoch (300 ms after hand-target contact). A  $2 \times 3$  repeated-measures ANOVA (factors: grip and epoch), was then applied to F5 and PFG neuronal populations, including area as a grouping factor. This analysis showed a significant main effect for both grip [ $F(1,70) = 359.8$ ,  $P < 0.001$ ] and epoch [ $F(2,140) = 173.2$ ,  $P < 0.001$ ] but not for the area factor. Furthermore, there was also a significant interaction between grip and epoch [ $F(2,140) = 69.0$ ,  $P < 0.001$ ]. Bonferroni post hoc tests revealed that neuronal activity was significantly higher in the preferred compared with the not preferred condition during both the pre- and postcontact epochs ( $P < 0.001$  for both comparisons), while there was no difference between preferred and not preferred conditions during the baseline period. To quantitatively compare the grip selectivity of PFG and F5, we calculated a preference index (PI, see MATERIALS AND

METHODS) for each of these neurons. An independent-samples  $t$ -test revealed that PFG and F5 neuronal populations selective for grip type only have a similar degree of grip preference ( $t = 0.22$ , ns).

We further investigated possible differences in the timing of grip selectivity between the neuronal populations of the two areas by comparing the rising and the peak time of neuronal selectivity (see MATERIALS AND METHODS), but no significant differences emerged. Grip selectivity starts to rise  $274 \pm 187$  ms before the hand-target contact in PFG and  $261 \pm 167$  ms before the same event in F5 ( $t = 0.29$ , ns) and reaches its peak  $25 \pm 116$  ms before the hand-target contact in PFG and  $12 \pm 126$  ms after this event in F5 ( $t = 1.25$ , ns).

Taken together, these data demonstrate that grasping neurons of area F5 and PFG that showed only grip selectivity were remarkably similar in both the magnitude and time course of their preferences.

*Action context selectivity regardless of grip type.* A subset of neurons in both areas ( $N = 8$  in PFG,  $N = 11$  in F5) showed selectivity only for the action context, with no difference in discharge intensity during actions performed with different grip types. Some of these neurons discharged more strongly during grasp-to-eat than grasp-to-place (4 in PFG, 8 in area F5), while the remaining were selective for grasp-to-place. The proportion of selectivity for eating and placing was not different between the two areas ( $\chi^2 = 1.03$ , ns).

Figure 5 shows examples of this type of neuron. The neuron shown in Fig. 5*A* discharged more strongly during grasp-to-eat compared with grasp-to-place, while the neuron shown in Fig. 5*B* exhibited the opposite selectivity, discharging more strongly during grasp-to-place than during grasp-to-eat. Note that both neurons have no grip preference, and action context selectivity is present in all the tested types of grip.

Figure 6 shows the time course and intensity of the activity of neuronal populations of both areas selective only for the action context, aligned on the hand-target contact. Neuronal selectivity was assessed with the same procedures and epochs of interest described above for grip selectivity. A  $2 \times 3$  repeated-measures ANOVA (factors: action context and epoch) was applied to F5 and PFG neuronal populations, including area as a grouping factor. This analysis showed significant main effects for both action context [ $F(1,17) = 57.97$ ,  $P < 0.001$ ] and epoch [ $F(2,34) = 48.24$ ,  $P < 0.001$ ] but not for area [ $F(1,17) = 0.1$ ,  $P = 0.75$ ]. Furthermore, it also showed a significant interaction between action context and epoch [ $F(2,34) = 20.23$ ,  $P < 0.001$ ]. Bonferroni post hoc tests revealed that neuronal activity was significantly higher in the preferred compared with the not preferred condition during both the pre- and postcontact epochs ( $P < 0.001$  for both comparisons), while it was not different during the baseline period. To quantitatively compare the PFG and F5 selectivity for action context, we also calculated a PI (see MATERIALS AND METHODS) for each of these neurons. Independent-samples  $t$ -test revealed that PFG and F5 neuronal populations selective only for action context have a similar degree of selectivity ( $t = 0.78$ , ns).

*Selectivity for both grip type and action context in parietal and premotor neurons.* A considerable portion of neurons in both areas, rather than showing either grip or action context selectivity, encoded a specific interaction between these two factors. Figure 7 shows examples of this type of neuron.

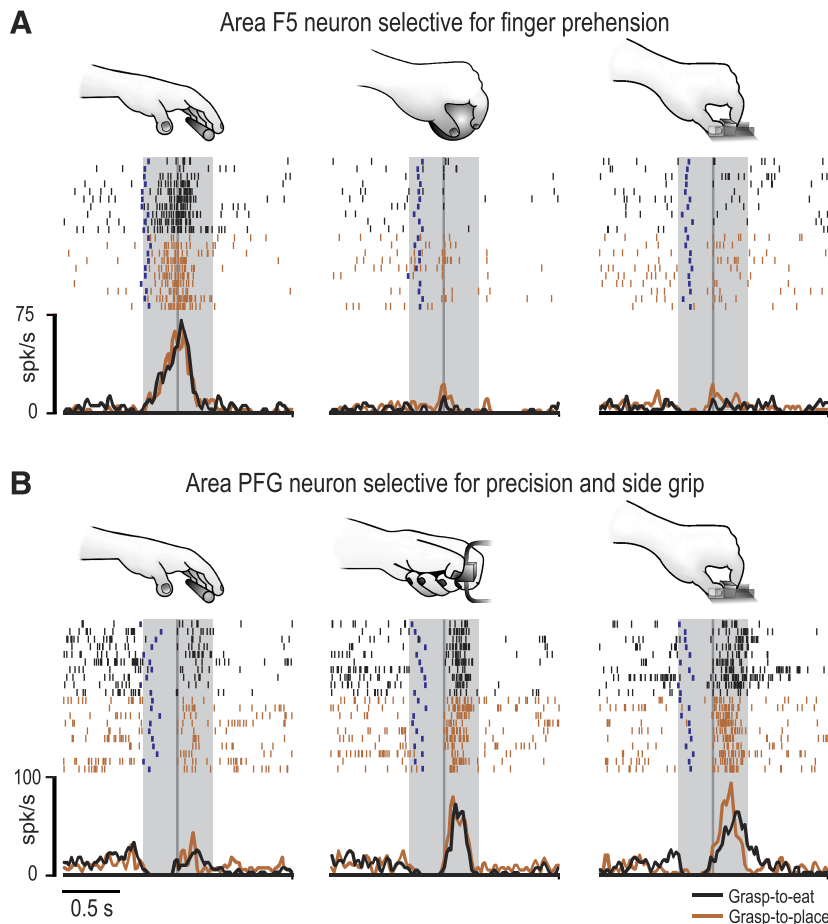


Fig. 3. Examples of neurons selective only for the type of grip recorded during grasp-to-eat (black) and grasp-to-place (red) performed with different grip types. *A*: this neuron was tested with food as the target for grasp-to-place performed with FP and PG, while an object was employed for grasp-to-place with whole hand prehension (WH). *B*: this neuron was tested with food as the target in all grasp-to-place actions. Rasters and histograms are aligned with the moment the monkey's hand touched the target object. The gray shaded region indicates the grasping epoch. Blue bars indicate, for each trial, the moment when the monkey's hand detached from the starting position.

Figure 7A shows a neuron discharging more strongly for grasp-to-place than grasp-to-eat during all the tested grip types. Nevertheless, the neuron discharged more strongly when grasp-to-place was performed with PG compared with any other tested grip. A consistent percentage of neurons combining grip and action context selectivity in both areas (PFG: 45.5%, F5: 45%) showed this behavior, being modulated according to a specific action context during all grip conditions, in addition to showing clear grip selectivity. The remaining neurons displayed a preference for action context only when grasping was performed with a specific grip type: in a few cases the less preferred type (PFG:  $N = 1$ , F5:  $N = 2$ ), most frequently the preferred type (51.5% in PFG, 45% in F5).

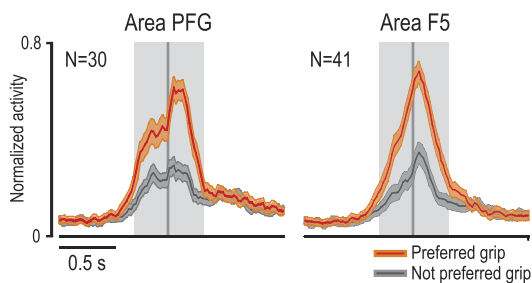


Fig. 4. Temporal profile of the normalized activity of the whole neuronal populations selective only for the type of grip of areas PFG and F5 in their preferred vs. not preferred grip. The activity is aligned on the moment when the monkey's hand touched the target. The vertical gray shaded regions indicate the grasping epochs. Red and grey shadings around each line represent 1 SE.

For example, the neuron shown in Fig. 7B discharged significantly more strongly during grasp-to-eat than grasp-to-place, but only during FP, which is preferred by this neuron. Note that, among neurons selective for both grip type and action context, the preference for grasp-to-eat when the target is a large food morsel (i.e., during FP or WH) could be specifically due to an enhancement of the neuronal discharge determined by the higher rewarding value of the target rather than by the interaction between a specific grip type and the action context. However, this occurred in only four neurons of the whole data set, and all of them were, nevertheless, more strongly activated during grasp-to-place with FP than during grasp-to-eat with all other tested grip types: this clearly suggests that the mere rewarding value of the target does not determine neuronal selectivity, in line with previous findings (Bonini et al. 2011). The neuron shown in Fig. 7C shows a discharge pattern that further supports this claim. In fact, it activated specifically during WH, discharging more strongly when grasp-to-place rather than grasp-to-eat was performed with this type of grip.

Figure 8A shows the time course and intensity of the activity of PFG (*left*) and F5 (*right*) neuronal populations selective for both grip type and action context in their preferred and not preferred grip (*top*) and action context (*bottom*) conditions. We analyzed the grip type and action context selectivity in the pre- and postcontact epochs, separately for the two areas, by means of  $2 \times 2$  repeated-measures ANOVAs (factors: condition and epoch). Concerning the grip (Fig. 8A, *top*), the analysis revealed significant main effects for both factors condition [PFG:



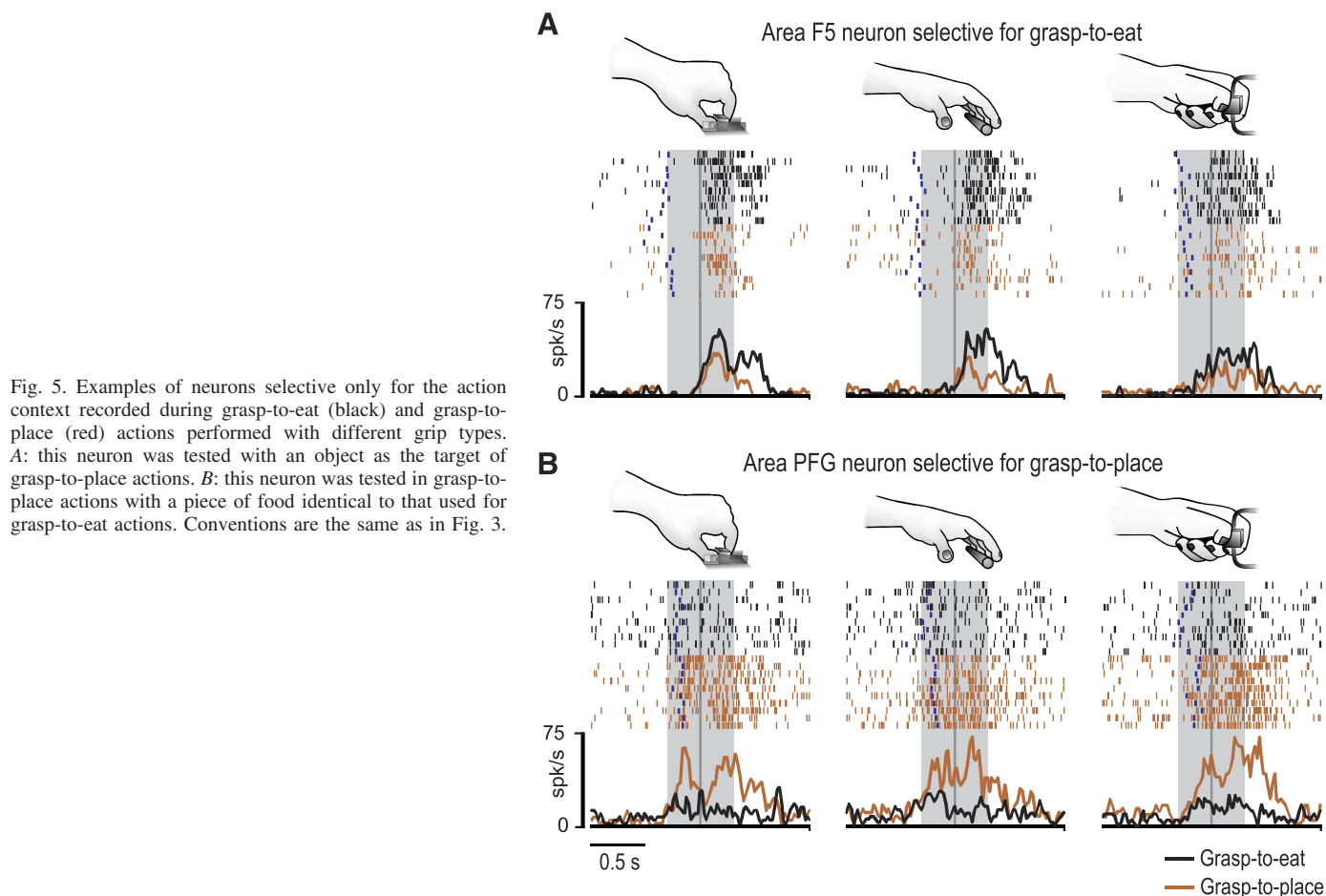


Fig. 5. Examples of neurons selective only for the action context recorded during grasp-to-eat (black) and grasp-to-place (red) actions performed with different grip types. *A*: this neuron was tested with an object as the target of grasp-to-place actions. *B*: this neuron was tested in grasp-to-place actions with a piece of food identical to that used for grasp-to-eat actions. Conventions are the same as in Fig. 3.

$F(1,32) = 246.8, P < 0.001$ ; F5:  $F(1,19) = 88.6, P < 0.001$ ] and epoch [PFG:  $F(1,32) = 8.5, P < 0.05$ ; F5:  $F(1,19) = 8.4, P < 0.05$ ]. Bonferroni post hoc tests showed that the neuronal response was higher during the execution of the preferred compared with the not preferred grip ( $P < 0.001$  for both areas). Furthermore, the neuronal activity significantly increased in the postcontact grasping epoch ( $P < 0.001$  for both areas). Concerning the action context (Fig. 8A, bottom), the analysis revealed a significant main effect for factors condition [PFG:  $F(1,32) = 70.3, P < 0.001$ ; F5:  $F(1,19) = 71.5, P < 0.001$ ] and epoch [PFG:  $F(1,32) = 13.4, P < 0.001$ ; F5:  $F(1,19) = 7.6, P < 0.05$ ] and their interaction [PFG:  $F(1,32) = 11.7, P < 0.05$ ; F5:  $F(1,19) = 6.5, P < 0.05$ ]. Bonferroni post hoc tests showed that, in both areas, the response associated with the

preferred action was significantly higher than that for the not preferred action, but only during the postcontact epochs ( $P < 0.001$  for both areas). Furthermore, the comparison of the grip and action context selectivity shown by the same neurons in terms of PI (see MATERIALS AND METHODS) revealed that in both areas grip selectivity is greater than action context selectivity (PFG: PI grip = 0.37, PI action context = 0.27,  $t = 4.60, P < 0.001$ ; F5: PI grip = 0.40, PI action context = 0.29,  $t = 2.2, P < 0.05$ ).

To more deeply explore the temporal relationship between grip and action context preference in these neuronal subpopulations, we calculated the rising time and the peak time of each neuron's selectivity for both factors (see MATERIALS AND METHODS). Figure 8, B and C, show the frequency distribution of PFG and F5 neurons based on their selectivity rising time (Fig. 8B) and peak time (Fig. 8C). The grip selectivity starts rising significantly earlier than the action context selectivity in PFG (grip:  $345 \pm 154$  ms before hand-target contact, action context:  $25 \pm 232$  ms after hand-target contact;  $t = 8.21, P < 0.001$ ) as well as in F5 (grip:  $184 \pm 168$  ms before hand-target contact, action context:  $79 \pm 204$  ms before hand-target contact;  $t = 2.72, P < 0.05$ ). Accordingly, the grip selectivity peaks significantly earlier than the action context selectivity, both in PFG (grip:  $25 \pm 112$  ms after hand-target contact, action context:  $158 \pm 224$  ms after hand-target contact;  $t = 3.31, P < 0.005$ ) and in F5 (grip:  $44 \pm 144$  ms after hand-target contact, action context:  $134 \pm 190$  ms after hand-target contact;  $t = 2.28, P < 0.05$ ). Interestingly, comparing the rising time of grip and action context selectivity between the two areas, we found that in PFG the grip selectivity starts earlier than

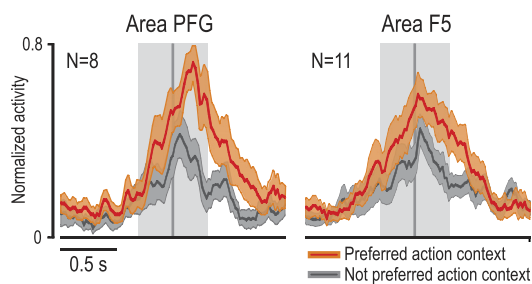


Fig. 6. Temporal profile of the normalized activity of the whole neuronal populations selective only for the action context of areas PFG and F5 in their preferred vs. not preferred conditions. The activity is aligned on the moment when the monkey's hand touched the target. Conventions as in Fig. 4.

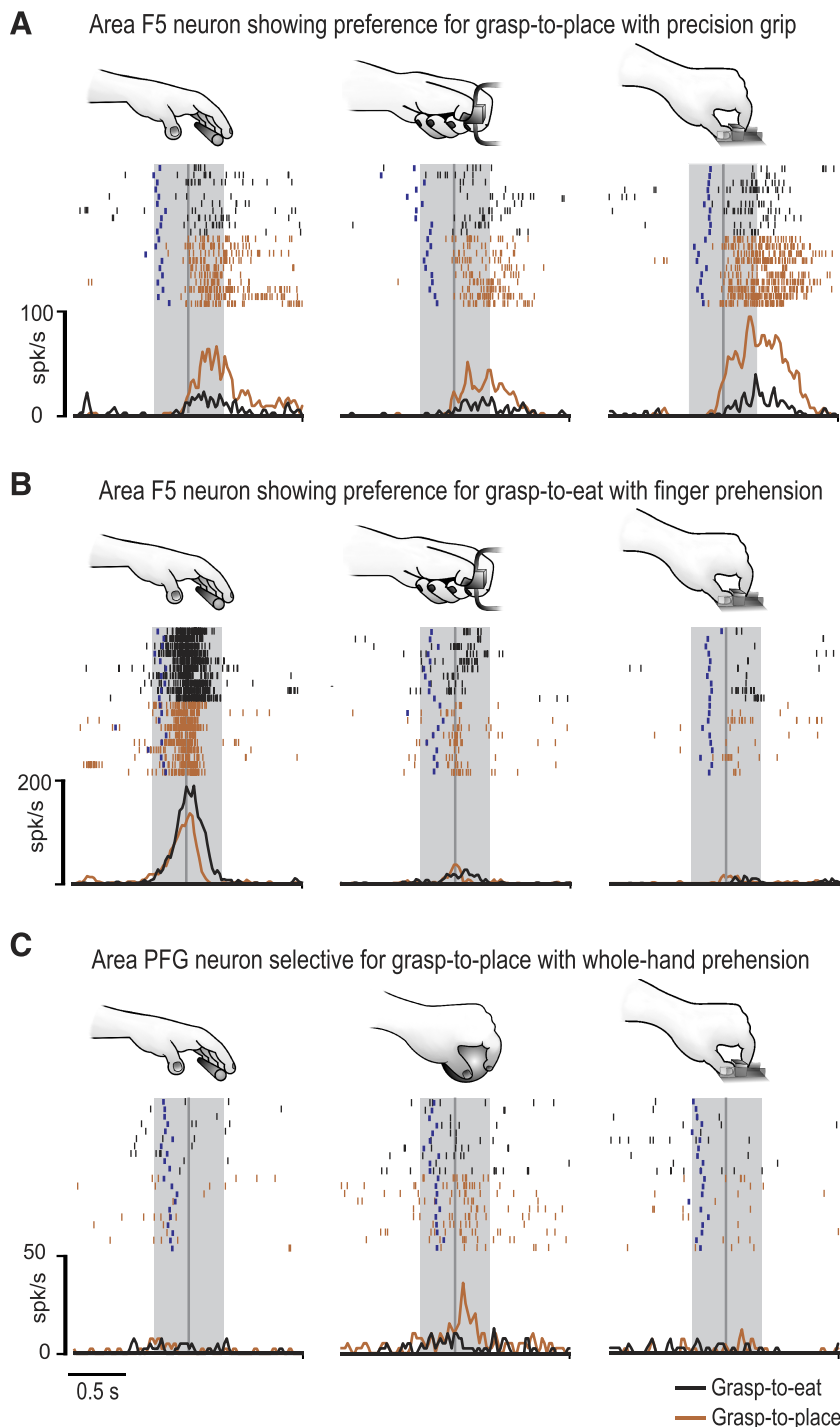


Fig. 7. Examples of neurons combining grip and action context selectivity recorded during grasp-to-eat (black) and grasp-to-place (red) actions performed with different grip types. All neurons shown in this figure were tested by comparing grasp-to-eat with grasp-to-place an object. Notably, the neuron shown in *B* was also tested, during FP, by comparing grasp-to-eat with grasp-to-place food (not shown): its selectivity remained unchanged. *A*: preference for grasp-to-place with PG. *B*: preference for grasp-to-eat with FP. *C*: preference for grasp-to-place with WH. Conventions as in Fig. 3.

in F5 ( $t = 3.58$ ,  $P < 0.001$ ), although the timing of the peak of selectivity is similar ( $t = 0.54$ , ns). This finding appears to be linked to these specific populations of neurons sensitive to both factors, since among neurons selective only for the type of grip the same comparison did not produce any significant result (see above). Finally, there was no difference between the two areas in the rising time ( $t = 1.66$ , ns) or the peak time ( $t = 0.39$ , ns) of action context selectivity.

Figure 8*D* shows the correlation of the PIs (see MATERIALS AND METHODS) for the grip type and the action context calculated for these same neurons. It is clear that in PFG there is a

positive and significant correlation between the magnitude of preference for the grip and that for the action context ( $r = 0.59$ ,  $P < 0.001$ ), while this is not the case in area F5.

#### DISCUSSION

The most common paradigm for studying possible neuronal selectivity for grip type requires the use of target objects of different sizes and shapes (see Taira et al. 1990), while in order to assess possible selectivity for the type of action (e.g., grasp-to-eat or grasp-to-place) previous studies kept the object's size and shape constant but varied contextual information or the type of

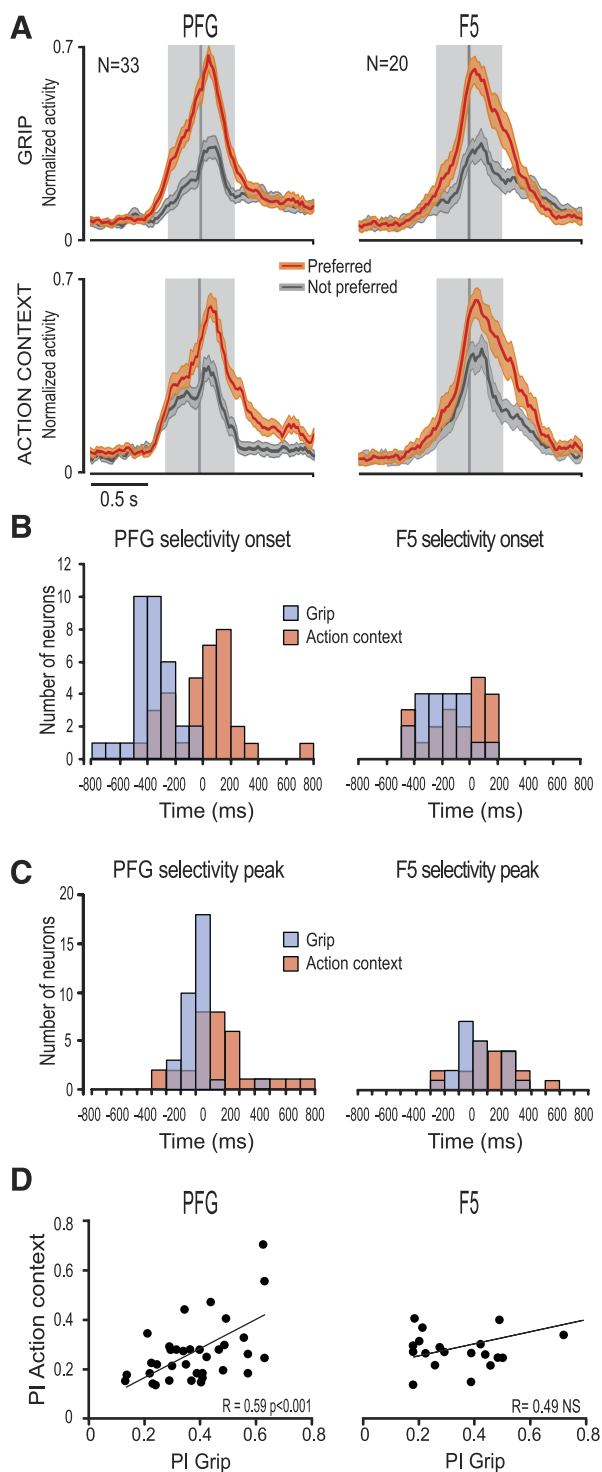


Fig. 8. *A*: temporal profile of the normalized activity of the whole neuronal populations of areas PFG and F5 selective for both grip type and action context, in their preferred vs. not-preferred grip type (*top*) and action context (*bottom*). Conventions as in Fig. 4. *B*: frequency distribution of PFG and F5 neurons selective for both grip type and action context based on their timing of selectivity onset for both the grip (blue) and the action context (red). *C*: frequency distribution of PFG and F5 neurons selective for both grip type and action context based on their timing of selectivity peak for both the grip (blue) and the action context (red). Conventions as in *B*. *D*: correlation between grip type and action context preference indexes (PIs) of PFG and F5 neurons selective for both factors. NS, not significant.

target object (see Bonini et al. 2010, 2011; Fogassi et al. 2005). Here we wanted to explore whether and how the selectivity for grip and action type interact at the single-neuron level. To this purpose, we used food and nonfood target objects that afforded one of two distinct actions (i.e., eating and placing) and manipulated the size and shape of the target to prompt specific grip types among those most commonly employed by macaques in their natural environment (Macfarlane and Graziano 2009).

While grip selectivity necessarily depends on the affordances provided by the object's physical properties, neuronal selectivity for specific types of action can derive from many contextual elements, such as action utility value, type of target object, or spatial differences in the action end point. For example, when using bigger food items to test certain grip types (i.e., FP or WH), a stronger neuronal discharge may result from the higher rewarding value of the grasped food morsels. However, we showed that the value of the target does not appear to have any role in determining neuronal selectivity in our data set, since the distribution of grip and action context selectivity was remarkably similar in the subsets of neurons tested with grasp-to-place foods and grasp-to-place objects. Furthermore, several previous studies based on similar motor tasks demonstrated that the discharge of parietal and premotor grasping neurons is not affected by the type of object grasped (Bonini et al. 2010; Fogassi et al. 2005) or by the reward contingency associated with a certain action (Bonini et al. 2011). The possible influence of the target to be grasped on neuronal selectivity for the two types of action could in principle derive from target-related differences in hand kinematics. However, kinematics analyses showed that during grasp-to-eat and grasp-to-place an object finger aperture and reaching velocity were similar in all studied grip types. The only kinematics difference we found concerns the velocity of reaching movement during grasp-to-place a piece of food, which was higher than that of all the other conditions (grasp-to-eat and grasp-to-place an object) in all tested grip types. Although this could bias the proportion of neurons showing a preference for grasp-to-place when tested with food as target, we showed that grasp-to-place selectivity occurred with the same frequency when the target was food or an object, suggesting that kinematics differences between eating and placing actions did not play a relevant role in determining neuronal selectivity. One might further argue that the even smaller differences in the end point between grasp-to-eat (the mouth) and grasp-to-place (the container located close to the mouth) might have accounted for some of the differences observed between the conditions. Although in the present work we did not systematically assess neuronal discharge during grasping acts embedded in the same action (i.e., grasp-to-place) but with different end points (i.e., a container located near the mouth or near the target), these tests were previously carried out in both the parietal (Fogassi et al. 2005) and premotor cortex (Bonini et al. 2010) and showed that none of the grasp-to-place neurons tested in those studies exhibited any difference in discharge intensity when the object was placed in the container located near the target or near the mouth. All these control experiments, carried out in the present and previous studies, appear to indicate that neuronal selectivity depends on the action goal triggered by the context rather than on specific contextual elements. Therefore, this point onward we will refer to neurons

showing action context selectivity as neurons selective for the action goal.

The main finding of our study is that, among all the recorded neurons in both areas, there is a large prevalence of neurons showing selectivity for the type of grip (73.5% in PFG and 70.9% in F5), encoded alone or in combination with a specific action goal. Furthermore, the discharge of 47% of PFG grasping neurons and of 36% of those recorded in F5 reflects the goal of the action in which grasping is embedded, in most cases showing also a clear-cut selectivity for the type of grip.

*Parallel processing of information on grip type and action goal.* Single-neuron analyses revealed that in both PFG and F5 grip selectivity is much more represented than goal selectivity. In particular, 36% of PFG grasping neurons and 48% of those recorded in area F5 show selectivity only for the grip type.

Previous studies demonstrated the presence of grip-selective neurons in premotor areas F5 (Fluet et al. 2010; Murata et al. 1997; Raos et al. 2006; Rizzolatti et al. 1988) and F2 (Raos et al. 2004) as well as in the parietal areas AIP (Baumann et al. 2009; Gardner et al. 2007; Murata et al. 2000; Sakata et al. 1995; Taira et al. 1990) and V6A (Fattori et al. 2010). However, no systematic investigation of grip selectivity in the convexity of the IPL is available. The present findings constitute, therefore, the first quantitative evidence of grip coding in area PFG.

By comparing the timing of onset and peak of selectivity between PFG and F5 grip-selective neuronal populations, we did not find any significant difference. Furthermore, the magnitude of grip preference was similar as well. These remarkable similarities between F5 and PFG grip selectivity suggest that this latter area should be included in the parieto-frontal system for the control of hand grip postures, typically identified only with the AIP-F5 circuit. The well-documented anatomical connections between anterior IPL regions and the PMv (Bonini et al. 2010; Caspers et al. 2011; Petrides and Pandya 1984; Rozzi et al. 2006) and that between area PFG and AIP (Borra et al. 2008) strongly support this conclusion. In particular, this latter connection suggests that grip selectivity in area PFG could largely depend on the sensory-motor transformations performed by area AIP, thus allowing exploitation of information on how objects have to be grasped for action organization. It is noteworthy that the discharge of grip-selective neurons is not influenced by the action in which grasping is embedded, indicating that these neurons constitute a multipurpose neuronal system employed for several different actions.

Compared with neurons showing pure grip selectivity, those showing action goal selectivity alone were less frequently found in both areas. Previous studies have suggested that grasping neurons discharging differently according to a certain action (i.e., eating or placing) would reflect the agent's motor intention, as part of a dedicated neuronal chain encoding the sequence of acts forming that action (Bonini et al. 2010; Fogassi et al. 2005). The small percentage of neurons selective only for the goal of the action in which grasping was embedded resembles that of neurons with early action goal preference described in a previous work (Bonini et al. 2011), suggesting that their discharge might reflect the action goal at a more abstract level, that is, relatively independent from the way in which the motor acts forming the action are performed.

Interestingly, among neurons having a certain degree of action goal selectivity, most (80% in PFG, 65% in F5) also

display grip selectivity, suggesting that the agent's motor intention and the way in which an object is grasped are not only separately processed by different, parallel pathways (Fogassi and Luppino 2005) but also largely integrated at the single-neuron level.

*Functional interactions between grip type and action goal.* The fact that a consistent number of neurons show selectivity for both the grip and the action goal allowed us to analyze in detail how these two factors interact at the single-neuron level.

Almost all the neurons selective for both factors, in both areas, show their action goal preference during the execution of their preferred grip, although the discharge of half of these is also modulated in relation to other grip types. Furthermore, although they are significantly tuned to both the grip and the goal, they show a stronger selectivity for the grip type than for the action goal.

The priority of grip coding also emerged in the temporal domain. In fact, population analyses of the time course of grip and goal selectivity revealed that grip selectivity appears during both pre- and postcontact epochs, during hand shaping and actual grasping phases, in line with previous findings concerning posterior parietal cortex grasping neurons (Gardner et al. 2007). In contrast, goal selectivity appears more strongly during the postcontact epoch, as shown previously (Bonini et al. 2010, 2011). These results are in line with those reported in human studies (van Schie and Bekkering 2007), showing that slow-wave brain potentials recorded during action execution differentiated between the grip selection (occurring in the earliest phase of action unfolding) and the final goal (manifested during hand transport components leading to task accomplishment). More specifically, by comparing the temporal dynamics of grip and goal selectivity at the single-neuron level, we showed that in both areas grip selectivity rises and peaks significantly earlier than goal selectivity. Furthermore, in PFG grip selectivity rises earlier than in area F5, while no differences were found between the two areas concerning the timing of goal selectivity. Taken together, the present and previous findings support the idea that the specification of the grip type is an overriding condition for determining grasping neurons' discharge, as well as their action goal selectivity during later stages of grasping execution.

Notably, in PFG but not F5 neurons we found a positive correlation between grip and goal selectivity. This result, together with the presence of a higher number of neurons selective for both the grip type and the action goal in PFG than in F5, indicates that the parietal cortex plays a major role in integrating information related to the type of prehension and the goal of the action, depending on the behavioral context. This is in line with recent human data (Marangon et al. 2011) suggesting that, in the IPL, grasp representations are prospectively selected on the basis of the final hand posture required by the forthcoming motor acts, very likely revealing context-based grip selection during intentional actions.

*Conclusions.* Since the first proposal by Fagg and Arbib (1998), several general models of the organization of reaching and grasping actions have been proposed (Badre and D'Esposito 2009; Cisek 2007; Cisek and Kalaska 2010; Grafton 2010). While most of the experiments from which these models were derived investigated "actions" by focusing on relatively simple motor chunks, such as saccades or reaching and grasping acts, we tried to deepen our understanding of the neural underpin-

nings of natural actions, which consist of longer sequences of motor acts aimed at a unitary final goal.

The present findings allow us to draw a more complete picture of the mechanisms underlying the organization of intentional actions. In fact, we provide here the first systematic assessment of grip selectivity by neurons of the inferior parietal convexity (area PFG), showing that this area should be included in the cortical system for the control of hand grip. Furthermore, we also show that neural selectivity for grip is prevalent compared with that for the action goal, and appears to constitute an overriding condition for the selection and organization of motor acts into actions. Finally, although the cortical mechanisms underlying grip selection and action organization appear to work in parallel with one another, we show that there are grasping neurons, particularly in the IPL, that integrate information on both grip type and action goal: these neurons could be exploited for the organization of specific goal-directed actions, providing the details about both “how” and “why” each motor act has to be done.

As previously suggested (Bonini et al. 2011), this organization requires a neural mechanism involved in context-based action selection, which previous studies have identified in prefrontal cortical regions (Fuster 2008; Tanji and Hoshi 2008). Since almost all of these studies have investigated arbitrarily arranged motor sequences, future research should examine the contributions of prefrontal areas to the encoding of action goal and motor patterns during planning and execution of natural action sequences.

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#### DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

#### AUTHOR CONTRIBUTIONS

Author contributions: L.B., S.R., P.F.F., and L.F. conception and design of research; L.B., F.U.S., S.B., M.M., and L.S. performed experiments; L.B., F.U.S., S.B., and M.B. analyzed data; L.B. and L.F. interpreted results of experiments; L.B. and F.U.S. prepared figures; L.B. and F.U.S. drafted manuscript; L.B., F.U.S., S.B., M.M., M.B., L.S., S.R., P.F.F., and L.F. edited and revised manuscript; L.B., F.U.S., S.B., M.M., M.B., L.S., S.R., P.F.F., and L.F. approved final version of manuscript.

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