Parietal Lobe: From Action Organization to Intention Understanding

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Parietal Lobe: From Action Organization to Intention Understanding

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Inferior parietal lobule (IPL) neurons were studied when monkeys performed motor acts embedded in different actions and when they observed similar acts done by an experimenter. Most motor IPL neurons coding a specific act (e.g., grasping) showed markedly different activations when this act was part of different actions (e.g., for eating or for placing). Many motor IPL neurons also discharged during the observation of acts done by others. Most responded differentially when the same observed act was embedded in a specific action. These neurons fired during the observation of an act, before the beginning of the subsequent acts specifying the action. Thus, these neurons not only code the observed motor act but also allow the observer to understand the agent's intentions.

The posterior part of the parietal lobe has been traditionally considered as a typical association cortex. In this view, in the posterior parietal cortex, afferents from two or more sensory channels integrate, and this multimodal sensory association is the basis for some types of percepts, such as space. However, the works of Mountcastle (*1*) and Hyvärinen (*2*), and subsequent studies carried out in several laboratories (*3*–*7*), showed that the posterior parietal cortex, besides "putting together" different sensory modalities (association function), also codes motor actions and provides the representations of these motor actions with specific sensory information. This view stresses the importance of sensorimotor integration in the emergence of perception.

Recently, we reexamined the functional properties of the convexity of IPL (PF/PFG complex) in monkeys, testing the activity of single neurons in response to sensory stimuli and during monkey's active movements (*8*). As previously reported (*2*), we found that IPL convexity has a motor somatotopic organization. Most interestingly, we found that many IPL neurons discharge both when the monkey performs a given motor act and when it observes a similar motor act done by another individual; these neurons are known as parietal mirror neurons (*9*–*11*). Here, we present data on the motor organization of IPL and on its mirror properties.

The coding of motor acts in the inferior parietal lobule. Neurons were recorded from the rostral sector of IPL (Fig. 1A) in two monkeys. All studied neurons (n = 165) were active in association with grasping movements of the hand (grasping neurons). They were formally tested in two main conditions. In the first condition, the monkey, starting from a fixed position (Fig. 1B, left), reached for and grasped a piece of food located in front of it and brought the food to the mouth (Fig. 1B, right, I). In the second condition, the monkey reached for and grasped an object, located as described above, and placed it into a container (Fig. 1B, right, II). In the first condition, the monkey ate the food brought to the mouth; in the second it was rewarded after correct accomplishment of the task.

Although some neurons discharged with the same strength regardless of the motor act that followed grasping, the large majority were influenced by the subsequent motor act. Examples are shown in Fig. 1C. Unit 67 discharged during grasping when grasping was followed by bringing the food to the mouth. In contrast, its discharge was virtually absent when grasping was followed by placing. Unit 161 exemplifies the opposite behavior. This neuron discharged very strongly when grasping was followed by placing, whereas only a weak discharge was present when grasping was followed by bringing to the mouth. Finally, Unit 158 did not show any significant difference in discharge intensity in the two conditions.

Table 1A summarizes the behavior of all recorded neurons. About two-thirds of neurons discharged preferentially ($P < 0.05$) when grasping was embedded into a specific motor action (*12*). The neuron selectivity remained unmodified when the conditions were blocked, as in Fig. 1, or interleaved (fig. S1).

Figure 1D shows the intensity and time course of neuron discharge of the grasp-to-eat and grasp-to-place populations in the two basic conditions. The population analysis (*12*), based on all selective neurons recorded from monkey M2, confirmed the data observed in individual neurons.

To control for the possibility that the differential discharge of neurons during the same motor act could be due to differences in the stimuli that the monkeys grasped, monkeys were trained to grasp an identical piece of food in both conditions. Food placing was achieved by showing the monkey a piece of food that the monkey particularly liked before each trial. After correct placing, the monkey received the preferred food. Unit 122 (Fig. 2) demonstrates that neuron selectivity did not depend on the stimulus used. The same result was found in all tested neurons (n = 28), regardless of whether they coded grasping to eat (n = 22) or grasping to place (n = 6) (*12*).

It is well known from human studies that the first motor act of an action is influenced by the next acts of that action (*13*). We also found that reaching-to-grasp movement followed by arm flexion (bringing the food to

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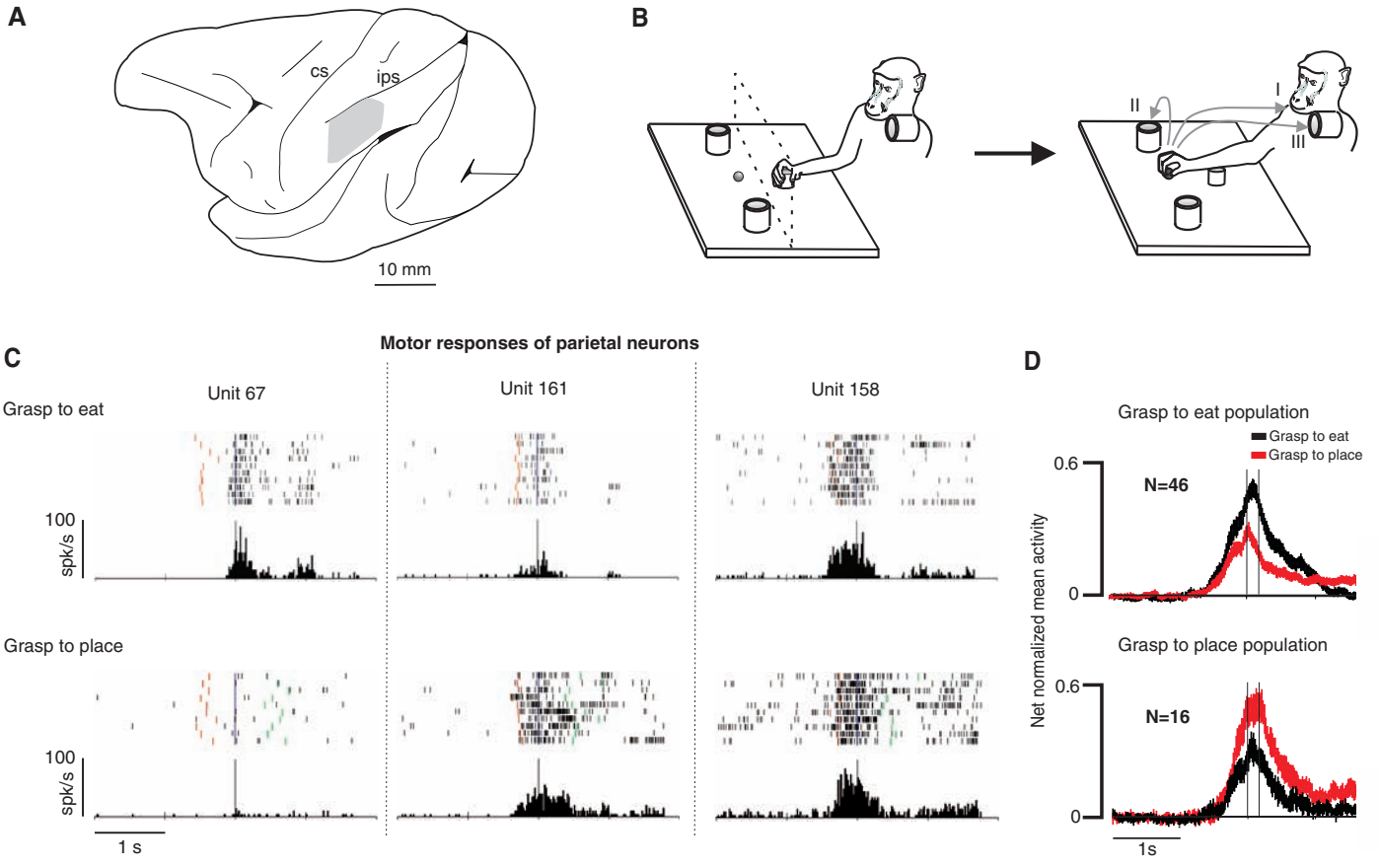

Fig. 1. (**A**) Lateral view of the monkey brain showing the sector of IPL (gray shading) from which the neurons were recorded. cs, central sulcus; ips, inferior parietal sulcus. (**B**) The apparatus and the paradigm used for the motor task. (**C**) Activity of three IPL neurons during grasping in conditions I and II. Rasters and histograms are synchronized with the moment when the monkey touched the object to be grasped. Red bars, monkey releases the hand from the starting position; green bars, monkey touches the container; *x* axis, time, bin = 20 ms; *y* axis, discharge frequency. (**D**) Responses of the population of neurons selective for grasping to eat and grasping to place tested in conditions I and II. The two vertical lines in the two panels indicate the moment when the monkey touched the object and the moment in which the grasping was completed, respectively. The *y* axes are in normalized units. [For description of population analysis, see (*12*).]

the mouth) was executed significantly faster than the same movement followed by arm abduction (placing the food into the container), the wrist peak velocity being 68.4 and 62.8 cm/s, respectively ($t = 2.75$, $P < 0.05$). To render the reaching-to-grasp movement for placing kinematically more similar to that for eating, we introduced a third experimental condition. In this condition, the monkey was trained to grasp a piece of food (or an object) and to place it into a container located near the monkey's mouth (Fig. 1B, III). In terms of the goal, this new placing condition was identical to the previous one, but it required an arm flexion, as in the bringing-to-the-mouth condition. The kinematic analysis showed that the wrist peak velocity (74.8 cm/s) in the new placing condition was faster not only than that in the original placing condition ($t = 6.45$, $P < 0.0001$) but also than that in the grasping-to-eat condition ($t = 2.31$, $P < 0.05$). [For further kinematics data, see (*12*) and fig. S2].

The analysis of neurons studied in the three conditions ($n = 18$) showed that the grasping selectivity was independent of kinematics parameters. All neurons that discharged best during the grasping-to-eat condition ($n = 14$) discharged less in the grasping-to-place condition, both when placing was done in the container located near the target (basic condition, wrist velocity lower than in the grasping-to-eat condition) and when placing was done in the container located near the mouth (new condition, wrist velocity greater than in the grasping-to-eat condition). An example is shown in Fig. 2 (Unit 43). Similarly, all neurons that discharged best during grasping to place in the basic condition ($n = 4$) maintained the same selectivity when placing was done in the container located near the mouth, despite the different movement kinematics in the two conditions. The main factor that determined the discharge intensity was, therefore, the goal of the action and not the kinematics [see (*12*) for more details].

To control whether the force exerted by the monkey to grasp the objects placed at the target location could be responsible for the differential activation of IPL neurons, a mechanical device that could hold the objects with two different strengths was used. Twelve neurons were tested with this device. No change in neuron selectivity was found in these neurons when the monkey grasped the objects using the two different forces (*12*).

Visual properties of mirror neurons in the inferior parietal lobule. In the IPL, there are neurons endowed with mirror properties. We studied 41 mirror neurons, all discharging both during grasping observation and grasping execution, in a visual task in which the experimenter performed, in front of the monkey, the same actions that the monkey did in the motor task, that is, grasping to eat and grasping to place (*12*).

Some neurons discharged with the same strength regardless of the motor act following the observed grasping. The majority of neurons, however, were differentially activated depending on whether the observed grasping was followed by bringing to the mouth or by placing. Examples are shown in Fig. 3. Unit 87 discharged vigorously when the monkey observed the experimenter grasping a piece of food, provided that he subsequently brought the food to his mouth. In contrast, the neuron's discharge was much weaker when, after grasping an object, the ex-

perimenter placed it into the container. Unit 39 illustrates the opposite behavior. Finally, Unit 80 did not show any significant difference in discharge intensity in the two conditions.

Table 1B summarizes the behavior of all tested mirror neurons. As in the motor conditions, the majority of neurons (75.6%) were influenced by the final goal of the action. Neurons responding to the observation of grasping to eat constituted the most represented neuron category.

The difference in discharge observed in the two basic conditions of the experiment could be, in principle, attributed to the two different types of objects (food or solids) grasped by the experimenter. A series of neurons (n = 20) was thus tested in a modified version of the visual task consisting now of three conditions: grasping food to eat, grasping food to place, and grasping solid to place. For all neurons, the selectivity remained the same regardless of which object (food or solid) was grasped by the experimenter (*12*). Twelve of the tested neurons did not show any difference when the experimenter grasped food or solid to place (Fig. 4, Unit 126), whereas eight neurons, all selective for the observation of grasping to eat, discharged more strongly in the placing conditions when the grasped object was food (Fig. 4, Unit 109).

As mentioned above, all 41 neurons tested with the visual task discharged during both grasping observation and grasping execution. In 19 of them, all motorically selective for one type of action (15 grasping-to-eat neurons and 4 grasping-to-place neurons), we studied their higher order visuomotor congruence by comparing their visual and motor selectivity during grasping-to-eat and grasping-to-place actions. The great majority of the tested neurons (16 out of 19) showed the same specificity during grasping observation and grasping execution (13 out of 15 and 3 out of 4 in the case of grasping to eat and grasping to place, respectively). Figure 5A shows an example of a congruent mirror neuron (Unit 169). The analysis of population-averaged responses of all neurons, comparing their visual and motor selectivity, is presented in Fig. 5B (*12*).

The coding of actions in the inferior parietal lobule. IPL neurons discharge in association with specific motor acts. The present study shows that most of them code the same act (grasping) in a different way according to the final goal of the action in which the act is embedded. Control experiments showed that this selectivity is not due to spurious factors such as the force exerted to grasp the object or differences in movement kinematics during object grasping determined by the subsequent arm movements.

Similarly, other factors, such as motivation and attention, that are known to influence the activity of the posterior parietal neurons (*1*, *2*, *7*) cannot explain the present findings. First, the type of reward the monkey received was the same in both grasping-to-eat and grasping-to-place conditions. Second, in the same experimental session we found intermixed neurons

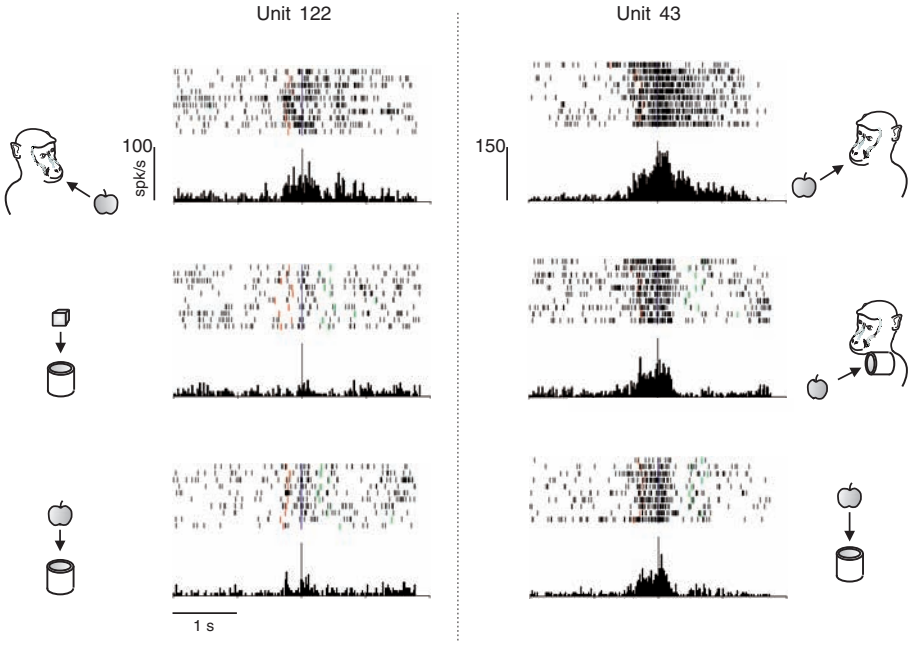

Fig. 2. Discharge of two IPL neurons during active grasping. Unit 122 strongly discharges when the monkey grasps a piece of food to eat (top), whereas it does not respond when the monkey grasps an object (center) or a piece of food (bottom) to place. Unit 43 strongly discharges when the monkey grasps a piece of food to eat (top), whereas the discharge is significantly weaker (*12*) when the monkey grasps a piece of food to place into a container positioned near the mouth (center) or near the grasped object location (bottom). Conventions as in Fig. 1.

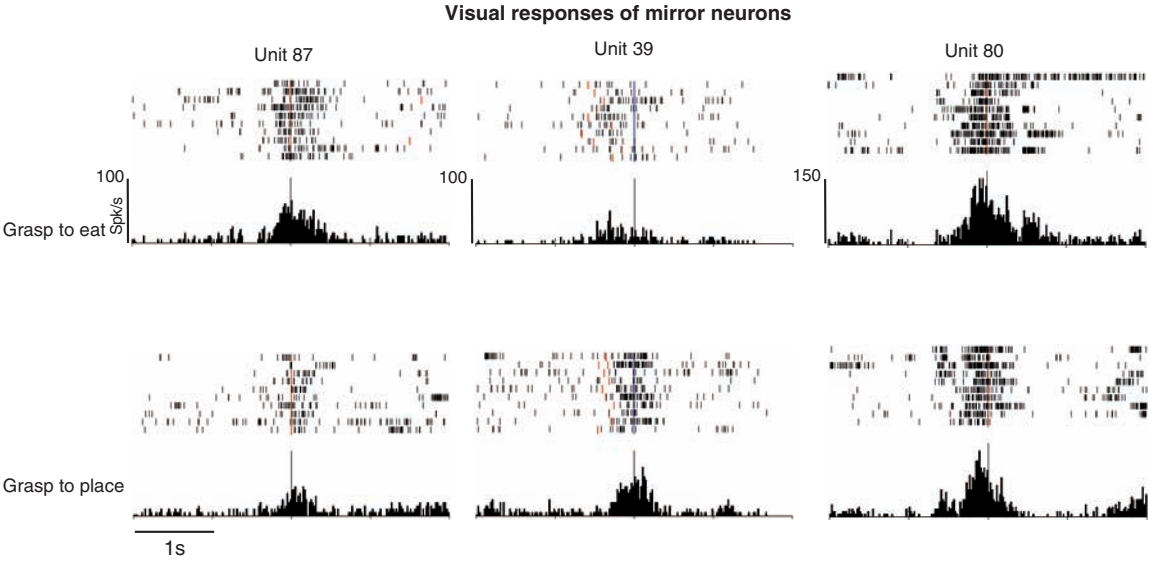

Fig. 3. Visual responses of IPL mirror neurons during the observation of grasping to eat and grasping to place done by an experimenter. Conventions as in Fig. 1.

showing specificity for grasping to place and for grasping to eat. Third, in a few experiments we alternated trials in which the monkey had to grasp to eat with others in which the monkey had to grasp to place. The neuron selectivity remained the same as during blocked trials (fig. S1).

The finding that most IPL neurons code the same motor act differently depending on the final action goal may appear counterintuitive. From an engineering point of view, it should be more economical to have a multipurpose system of neurons for grasping, and for other motor acts, that can be used whenever necessary. This would allow the possibility of having a smaller number of neurons coding the same motor act. There is, however, another aspect of motor organization that must be taken into consideration. One of the most striking aspects of action execution in animals is the fluidity with which the different motor acts follow one another. This "kinetic melody" (*14*) requires a close link between the different motor acts forming the entire action so that its execution can occur without any gap. The system we found in the parietal lobe appears to have exactly this function. Motor acts are not related to one another independent of the global aim of the action but appear to form prewired intentional chains in which each motor act is facilitated by the previously executed one (*15*).

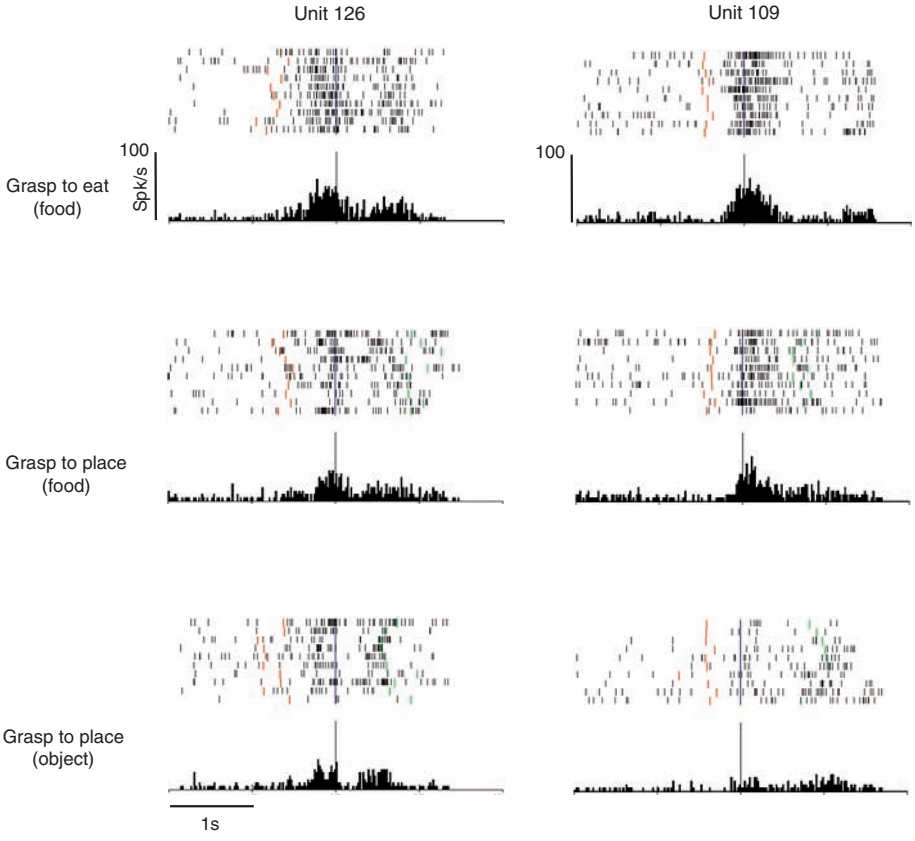

Fig. 4. Visual responses of two IPL mirror neurons during the observation of grasping done by an experimenter. Unit 126 illustrates the case of a neuron selective for grasping to eat whose responsiveness is not influenced by the type of target (food or object) grasped by the experimenter. Unit 109 shows the responses of another grasping-to-eat neuron. As for Unit 126, the visual selectivity remains the same regardless of the object grasped by the experimenter, but the intensity of the discharge is modulated by the type of grasped stimulus.

Table 1. IPL neurons tested during execution and observation of grasping to eat and grasping to place.

(**A**) Number of neurons tested during the execution of the motor task.

Influenced by the final goal		Not influenced by the final goal	Total
Eating > Placing	Placing > Eating	Eating = Placing	
77 (72.6%)	29 (27.4%)		
106 (64.2%)		59 (35.8%)	165 (100%)

(**B**) Number of neurons tested during the observation of the motor task done by the experimenter.

Influenced by the final goal		Not influenced by the final goal	Total
Eating > Placing	Placing > Eating	Eating = Placing	
23 (74.2%)	8 (25.8%)		
31 (75.6%)		10 (24.4%)	41 (100%)

The organization of IPL receptive fields also favors a model that postulates a chain between neurons coding subsequent motor acts. Frequently, IPL neurons that respond to the passive flexion of the forearm have tactile receptive fields located on the mouth, and some of them respond in addition during grasping actions of the mouth (*16*). These neurons appear to facilitate the mouth opening when an object is touched or grasped by the monkey's hand. Recently, several examples of this predictive chained organization in IPL have been described (*7*).

There are no available data on the possible specificity of ventral premotor cortex neurons in coding the same motor act according to the action to which it belongs. Two series of considerations suggest, however, that the same chained organization also exists in this region. First, the IPL is anatomically connected directly with the ventral premotor cortex (*17–19*). Thus, it is hard to believe that the parietal specificity would be lost in the next motor station. Second, and most important, the receptive field organization of the ventral premotor cortex shows characteristics similar to that just mentioned for the IPL (*20*).

Reading the intention of others: The inferior parietal mechanism. When an individual starts the first motor act of an action, he or she has clearly in mind what the final goal of the action is to which the motor act belongs. In the present study, the monkey's decision on what to do with the object is undoubtedly made before the onset of the grasping movement. The action intention is set before the beginning of the movements and is already reflected in the first motor act.

This motor reflection of action intention and the chained motor organization of IPL neurons have profound consequences on a fundamental cognitive capacity, that of understanding the intention of others.

It is generally accepted that the fundamental role of mirror neurons is to allow the observing individual to understand the goal of the observed motor act (*21–23*). The rationale of this interpretation is the following: Because the monkey knows the outcome of the motor act it executes, it recognizes the goal of the motor act done by another individual when this act triggers the same set of neurons that are active during the execution of that act.

The finding of the present experiment is that IPL mirror neurons, in addition to recognizing the goal of the observed motor act, discriminate identical motor acts according to the action in which these acts are embedded. Because the discriminated motor act is part of a chain lead-

ing to the final goal of the action, this neuronal property allows the monkey to predict the goal of the observed action and, thus, to "read" the intention of the acting individual.

This mechanism for understanding intention appears to be rather simple. Depending on which motor chain is activated, the observer is going to have an internal representation of what, most likely, the action agent is going to do. What is more complex is to specify how the selection of a particular chain occurs. After all, what the observer sees is just a hand grasping a piece of food or an object.

Various factors may determine this selection. The first is the context in which the action is executed. In our experiment, the presence or absence of the container clearly indicated the action that the experimenter was intending to do. The second factor is the type of object that the experimenter grasped. Typically, food is grasped to be eaten, whereas this is, of course, not the case for solids. Thus, because of this food-action association, the observation of a motor act directed toward food more likely triggers neurons coding grasping to eat than neurons coding grasping for other purposes. This association is, obviously, not mandatory. If it were, the vision of a piece of food would always trigger the chain of motor acts that code eating.

The two factors (context and object type) were found to interact. In several instances (e.g., Unit 109, Fig. 4), we observed that neurons coding grasping to eat also discharged, although weakly, during grasping to place when the object to be placed was food but not when it was a solid. It was as if the eating chain were activated, although slightly, by food despite the presence of contextual cues indicating that placing was the most likely action. A few neurons, instead of showing an intermediate discharge when the nature of the stimulus (food) and context conflicted, decreased their discharge with time when the same action was repeated. It was as if the activity of the placing chain progressively inhibited the activity of neurons of the eating chain (fig. S3).

It is outside the aim of the present study to describe the effects of these factors and their reciprocal influence on the selection of different chains of motor acts in detail. It is important to note, however, that the rich connections of the IPL (*24*, *25*) with areas coding biological actions [areas of the superior temporal sulcus (*26*, *27*)] and object semantics [inferotemporal lobe (*28*, *29*)] render this cortical region particularly suitable for the selection of the coded motor acts according to external contingencies.

Understanding "other minds" constitutes a special domain of cognition (*30*). Brain imaging studies suggest that several areas might be involved in this function (*31*–*33*). Given the complexity of the problem, it would be naïve to claim that the mechanism described in the present study is the sole mechanism underlying mind reading, yet the present data show a neural mechanism through which a basic aspect of understanding intention may be solved. Furthermore, they represent an example of how action and cognition are linked with one another and how the refinement of the motor organization may determine the emergence of complex cognitive functions.

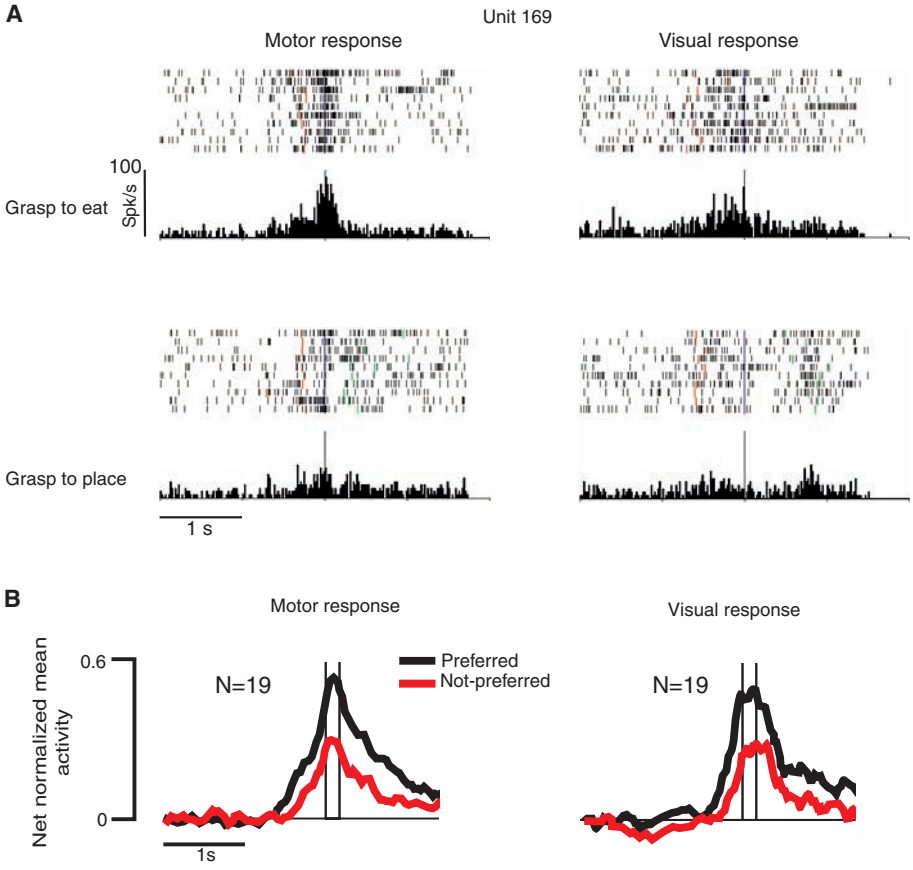

Fig. 5. (**A**) Congruence between the visual and the motor response of a mirror neuron. Unit 169 has a stronger discharge during grasping to eat than during grasping to place, both when the action is executed and when it is observed. Conventions as in Fig. 1. (**B**) Population-averaged responses during motor and visual tasks (*12*).

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REPORTS

Amplification of Acetylcholine-Binding Catenanes from Dynamic Combinatorial Libraries

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Directed chemical synthesis can produce a vast range of molecular structures, but the intended product must be known at the outset. In contrast, evolution in nature can lead to efficient receptors and catalysts whose structures defy prediction. To access such unpredictable structures, we prepared dynamic combinatorial libraries in which reversibly binding building blocks assemble around a receptor target. We selected for an acetylcholine receptor by adding the neurotransmitter to solutions of dipeptide hydrazones [proline-phenylalanine or proline-(cyclohexyl)alanine], which reversibly combine through hydrazone linkages. At thermodynamic equilibrium, the dominant receptor structure was an elaborate [2]-catenane consisting of two interlocked macrocyclic trimers. This complex receptor with a 100 nM affinity for acetylcholine could be isolated on a preparative scale in 67% yield.

Dynamic combinatorial chemistry is a powerful approach for the preparation of unpredictable receptors for recognition and catalysis (*1*–*7*). Its key feature is the dynamic combinatorial library, in which each library member is assembled from building blocks that bond reversibly to one another under the reaction conditions. As a result of this reversibility, all library members can interconvert to give a distribution that is under thermodynamic control. Addition of a guest molecule, or template, that can selectively recognize one receptor in the library will serve to increase the concentration of that host at the expense of unsuccessful structures in the library. The successful host is then isolated and identified. Such systems display feedback amplification of molecules with the desired properties in a manner that is reminiscent of the mammalian immune system. Typically, however, this approach has produced relatively simple structures such as macrocycles or topologically linear species (*8*).

As a neurotransmitter, acetylcholine (ACh) is an attractive target for studies of molecular recognition. We report here that ACh acts as a template to amplify [2]-catenanes from small peptide-hydrazone building blocks whose properties and chemistry we have previously described (*9*). In solution, six of these building blocks assemble around ACh into a remarkably complex receptor structure comprising two linked 42-membered rings.

Library formation was initiated by addition of trifluoroacetic acid (43 equivalents) to a room-temperature 20 mM solution of the peptide building block *p*PFm (**1**) in 95:5 (v/v) chloroform/dimethyl sulfoxide (DMSO) (Fig. 1). High-performance liquid chromatography (HPLC) analysis showed that linear intermediates were formed on a time scale of minutes, converting over the next 60 min into a series of simple cyclic oligomers up to at least the cyclic hexamer. In the absence of added template, the library reached equilibrium in 3 days. The main components of this library were identified by mass spectrometry (MS) as the cyclic dimer (**2**, MH^+ = 781.4), trimer (**3**, MH^+ = 1172.5), and tetramer (**4**, MH^+ = 1562.8), with small amounts of pentamer (**5**, MH^+ = 1952.9), hexamer (**6**, MH^+ = 2342.0), and traces of higher oligomers.

Next, we added of 200 mM ACh chloride to the solution to serve as a binding tem-

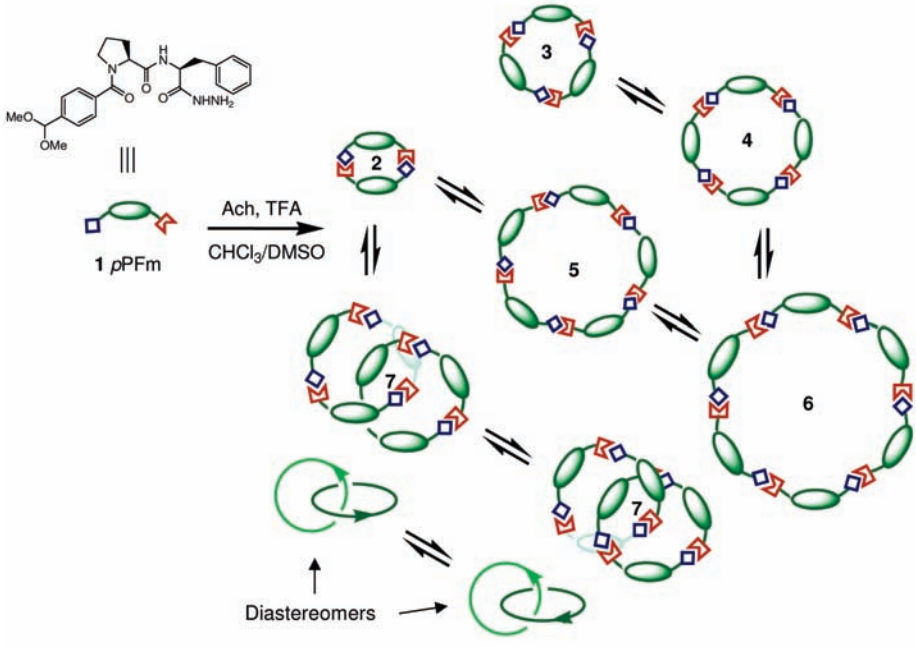

Fig. 1. A *p*PFm dynamic combinatorial library.

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