

Functional organization of inferior area 6 in the macaque monkey

II. Area F5 and the control of distal movements

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Summary. The functional properties of neurons located in the rostral part of inferior area 6 were studied in awake, partially restrained macaque monkeys. The most interesting property of these neurons was that their firing correlated with specific goal-related motor acts rather than with single movements made by the animal. Using the motor acts as the classification criterion we subdivided the neurons into six classes, four related to distal motor acts and two related to proximal motor acts. The distal classes are: "Grasping-with-the-hand-and-the-mouth neurons", "Grasping-with-the-hand neurons", "Holding neurons" and "Tearing neurons". The proximal classes are: "Reaching neurons" and "Bringing-to-the-mouth-or-to-the-body neurons". The vast majority of the cells belonged to the distal classes. A particularly interesting aspect of distal class neurons was that the discharge of many of them depended on the way in which the hand was shaped during the motor act. Three main groups of neurons were distinguished: "Precision grip neurons", "Finger prehension neurons", "Whole hand prehension neurons". Almost the totality of neurons fired during motor acts performed with either hand. About 50% of the recorded neurons responded to somatosensory stimuli and about 20% to visual stimuli. Visual neurons were more difficult to trigger than the corresponding neurons located in the caudal part of inferior area 6 (area F4). They required motivationally meaningful stimuli and for some of them the size of the stimulus was also critical. In the case of distal neurons there was a relationship between the type of prehension coded by the cells and the size of the stimulus effective in triggering the neurons. It is proposed that the different classes of neurons form a vocabulary of motor acts and that this vocabulary can be accessed by somatosensory and visual stimuli.

Key words: Area 6 – Macaque monkey – Distal movements – Goal related neurons

Introduction

There is a general agreement that the retina and the cochlea are represented several times on the cerebral cortex (see Cowey 1979; Neff et al. 1975; Van Essen and Maunsell 1983; Rosenquist 1985; Zeki 1982). Similarly, there is a broad consensus that each of the various cytoarchitectonic areas that constitute the postcentral gyrus contains an independent somatosensory representation (see Kaas 1983). Until recently, however, there was little evidence in favor of a multiple cortical representation of movements and especially of the distal ones. Electrical stimulation studies demonstrated only two cortical motor maps, one located in the precentral gyrus (Woolsey et al. 1952; see also Wiesendanger 1981) and the other on the medial wall of the frontal lobe (supplementary motor area) (Penfield and Welch 1951; Woolsey et al. 1952), and, as far as this one is concerned, there were doubts about the representation in it of distal movements (Penfield and Jasper 1954; Wiesendanger et al. 1973). Motor system therefore seemed to be organized in way different from that of the sensory systems.

Recent data however have indicated that the principle of a multiple representation of the periphery on the cortex is valid also for the motor system. Single neurons recordings have shown that distal movements are represented both in supplementary motor cortex (Brinkman and Porter 1979; Tanji 1984) and in inferior area 6 (Rizzolatti et al. 1981a, b; Kurata and Tanji 1986). Furthermore, evidence discussed in the accompanying paper indicates that in inferior area 6 there is a third

somatotopically organized motor representation (Gentilucci et al. 1988).

An even richer picture of cortical control of arm movements is suggested by anatomical data. Following injection of horseradish peroxidase in the gray matter of the cervical spinal cord, labelled neurons have been found in a large number of cortical areas (Martino and Strick 1987). Among them are the three physiologically identified motor representations and, in addition, the part of superior area 6 lateral to the superior precentral dimple, the second somatosensory cortex (SII), area 7b and a region of granular insular cortex ventral to SII. Thus there is little doubt that access to the spinal cord is not limited to one or few areas but is diffuse to a constellation of cortical zones on both sides of the central sulcus.

These data raise the problem of specific contribution of these areas to movement organization and in particular to that of distal movements. If these movements are not represented exclusively in area 4, as now it is certain, what is the role of the various areas in controlling them? Are these areas hierarchically organized or do they work in parallel? The aim of this paper is to provide data which may contribute to the solution of these problems. Data will be presented concerning the activity of neurons located in that part of inferior area 6 which control distal movements, i. e. the histochemical area F5 (Matelli et al. 1985). It will be shown that the properties of F5 neurons are more complex than those of the primary motor cortex and that the concept of purpose has to be introduced in order to explain these properties. A preliminary report of these results has been published elsewhere (Rizzolatti et al. 1987).

Methods

The experiments were performed on 3 macaque monkeys (*Macaca nemestrina*). The same animals (MK1, MK2 and MK3) employed in the accompanying paper (Gentilucci et al. 1988) were used. The experimental situation can be summarized as follows. The monkey sat in a primate chair with its arm resting on the chair plastic plane. Pieces of food were presented in various positions of space. At the stimulus presentation the monkey extended its arm, grasped the food and brought it to the mouth. This action, although unitary in its purpose, is constituted by several discrete parts or "motor acts": reaching, grasping with the hand, holding, bringing to the mouth, grasping with the mouth. In turn, each of these motor acts is constituted by various movements. For example, in the case of hand grasping, there is an initial finger extension and abduction followed by a finger flexion and adduction. For each neuron we related the neuron discharge with the animal's movements or motor acts.

Particular attention was paid to animal's grasping movements. Three basic types of hand grasping were distinguished: precision grip, finger prehension, and whole hand prehension. *Precision grip* consists in the opposition of the index finger and thumb. Two

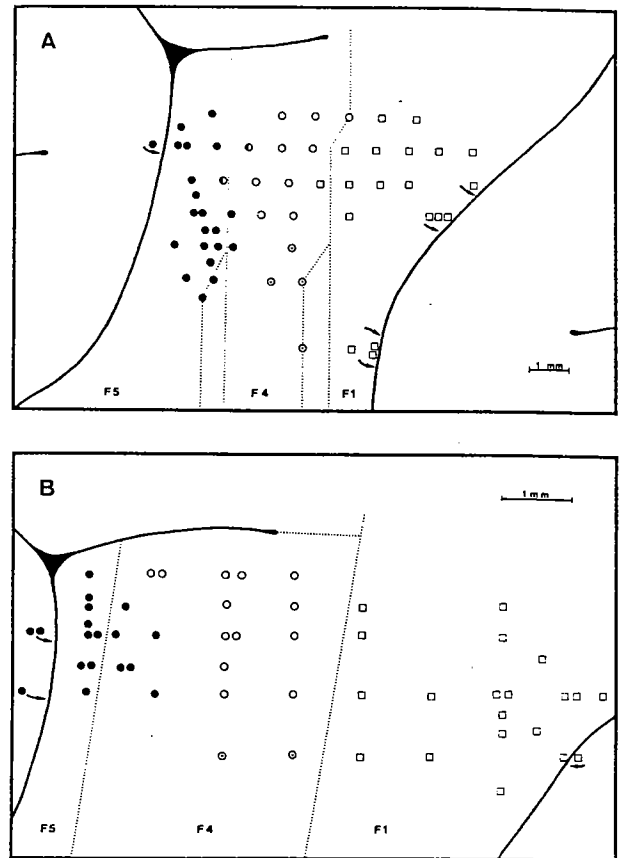


Fig. 1A, B. Spatial distribution of F5, F4 and F1 (primary motor cortex) neurons. A, B Show the inferior part of left frontal agranular cortex of monkey MK2 and MK3. The dashed lines separate the histochemical areas F1 (area 4), F4 and F5. Unmarked areas between F1 and F4, and F4 and F5 are transition zones. Squares, empty circles and full circles indicate penetrations in which F1, F4 and F5 neurons were encountered respectively. Penetrations in which both F4 and F5 neurons were recorded are represented by half full circles. Pointed circles indicate penetrations related to the mouth

varieties of precision grip were observed: "primitive precision grip" and "advanced precision grip". Primitive precision grip is characterized by the opposition of the thumb to the radial (external) side of the index finger. Advanced precision grip consists in the opposition of the first phalanx of the thumb to the first phalanx of the index finger. The monkeys use the primitive precision grip to pick up small objects placed on a flat surface, whereas they use the advanced precision grip to take objects placed inside a slit or to take small objects that cannot be picked up with the primitive grip. *Finger prehension* consists in the opposition of the thumb to the other fingers. The monkeys use finger prehension to pick up middle-size objects such as an orange section or a piece of apple placed on a plane. They use it also to extract objects from a deep, narrow container. *Whole hand prehension* is characterized by a flexion of all fingers around an object in such a way to form a ring around it. The thumb is on one side of the object, the other fingers on the other. Whole hand prehension was tested by presenting to the monkey objects like a carrot or a syringe full of fruit juice.

Table 1. Types of F5 neurons

	N	%		N	%
Grasping-with-the-hand-and-the-mouth	52	24	Reaching	11	5
Grasping-with-the-hand	90	42	Bringing-to-the-mouth-or-the-body	11	5
Holding	20	9			
Tearing	11	5	Complex	21	10

Stimulation procedures and histological techniques have been described in the accompanying paper (Gentilucci et al. 1988) and will not be dealt with here.

Results

Location and general characteristics of the recorded neurons

On the basis of their functional properties two populations of neurons can be distinguished in inferior area 6. The first population is located in area F4, the second chiefly in area F5. In the accompanying paper (Gentilucci et al. 1988), we have described the properties of the first population. In this paper we will present data on the second one. For sake of simplicity we will refer to the neurons belonging to the second population as F5 neurons. In total we have studied 216 F5 neurons. 75 were recorded from monkey MK1, 66 from monkey MK2, and 75 from MK3. Figure 1 shows the penetrations in which F5 neurons were recorded and their location in the various histochemical areas of inferior area 6.

The most important property of F5 neurons was that their firing correlated with specific motor acts and not with individual movements made by the animal. Movements in which the animal used the same muscles as in the effective motor act, but for other purposes, failed to activate the neurons. Using the effective motor act as the classification criterion we subdivided F5 neurons into the classes shown in Table 1. Note that the vast majority of the neurons were related to distal movements.

F5 neurons discharging with distal movements

a) Grasping-with-the-hand-and-the-mouth neurons. The neurons of this class discharged during motor acts aimed to take possession of an object. The discharge was present regardless of whether the

motor act was performed using the hand or the mouth. Figure 2 illustrates the responses of one of these neurons. A strong discharge was present when the animal grasped the food with the mouth (A), with the right hand (B), and with the left hand (C). This discharge did not depend on synergisms between hand and mouth movements, since it was present during mouth grasping movements in the absence of hand movements and during hand grasping movements in the absence of mouth movements.

Twenty-eight neurons (54%) showed selectivity for a particular type of hand prehension, 24 neurons (46%) responded regardless of how the object was taken. The various types of hand prehension effective in triggering the neurons and the temporal relationship between the beginning of their discharge and the hand movements will be described in the next section. Thirty-seven neurons were tested during grasping movements made with the right hand and with the left hand. All of them were activated during movements of either hand.

b) Grasping-with-the-hand-neurons. Grasping-with-the-hand neurons represented the largest class of F5 neurons. Their general functional characteristics were similar to those of the neurons of the class described above, except for the lack of response during mouth grasping movements. One interesting characteristic of grasping neurons was their selectivity for a particular type of grasping. By observing the way in which the monkeys took the food we distinguished three types of hand prehension: precision grip, finger prehension, whole hand prehension. They are illustrated in Fig. 3. This figure also shows the discharge of a neuron during the various types of grasping. For this neuron the strongest discharge was observed during precision grip (A). The response was markedly smaller during finger prehension (B) and it was completely absent during whole hand prehension (C). In order to evaluate separately the contribution of index finger movements to the response, the neuron was also tested when the animal

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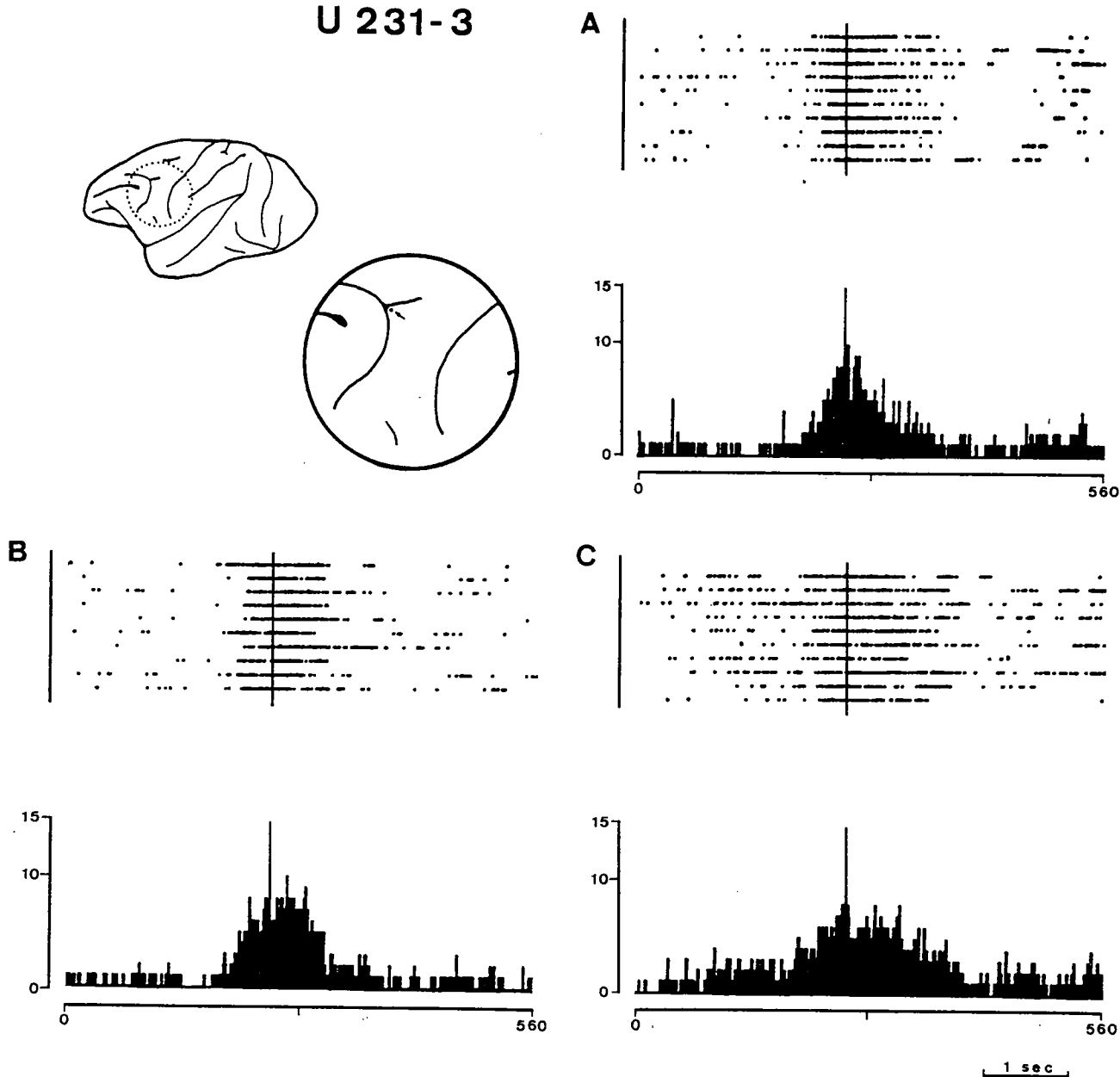


Fig. 2A-C. Study of "Grasping-with-the-hand-and-the-moth" neuron. On the left side of the figure a lateral view of the monkey brain is shown. The arrow indicates the location of the penetration in which the neuron was recorded. A Neuron discharge during grasping with the mouth. B Neuron discharge during prehension with the contralateral hand. C neuron discharge during prehension with the ipsilateral hand. The histograms are aligned with the moment when the animal touched the food. The histograms are the sum of 10 trials. Individual trials are shown above the histograms. Bin width 10 ms

tried to extract food from a hole using its index finger. Practically, no discharge was present (D). Isolated thumb movements were difficult to elicit. However thumb movements which concur to finger prehension or whole hand grasping were ineffective in triggering the neuron (B and C).

Figure 4 shows another precision grip neuron. A strong discharge was present when the animal

grasped an object with the index finger and thumb of the right hand (A) or with the same fingers of the left hand (B). In contrast, practically no movement-related discharge was present during prehension with the whole hand (C and D).

Figure 5 illustrates a finger prehension neuron. A and B show the neuron's discharge during finger prehension executed with the hand contralateral and

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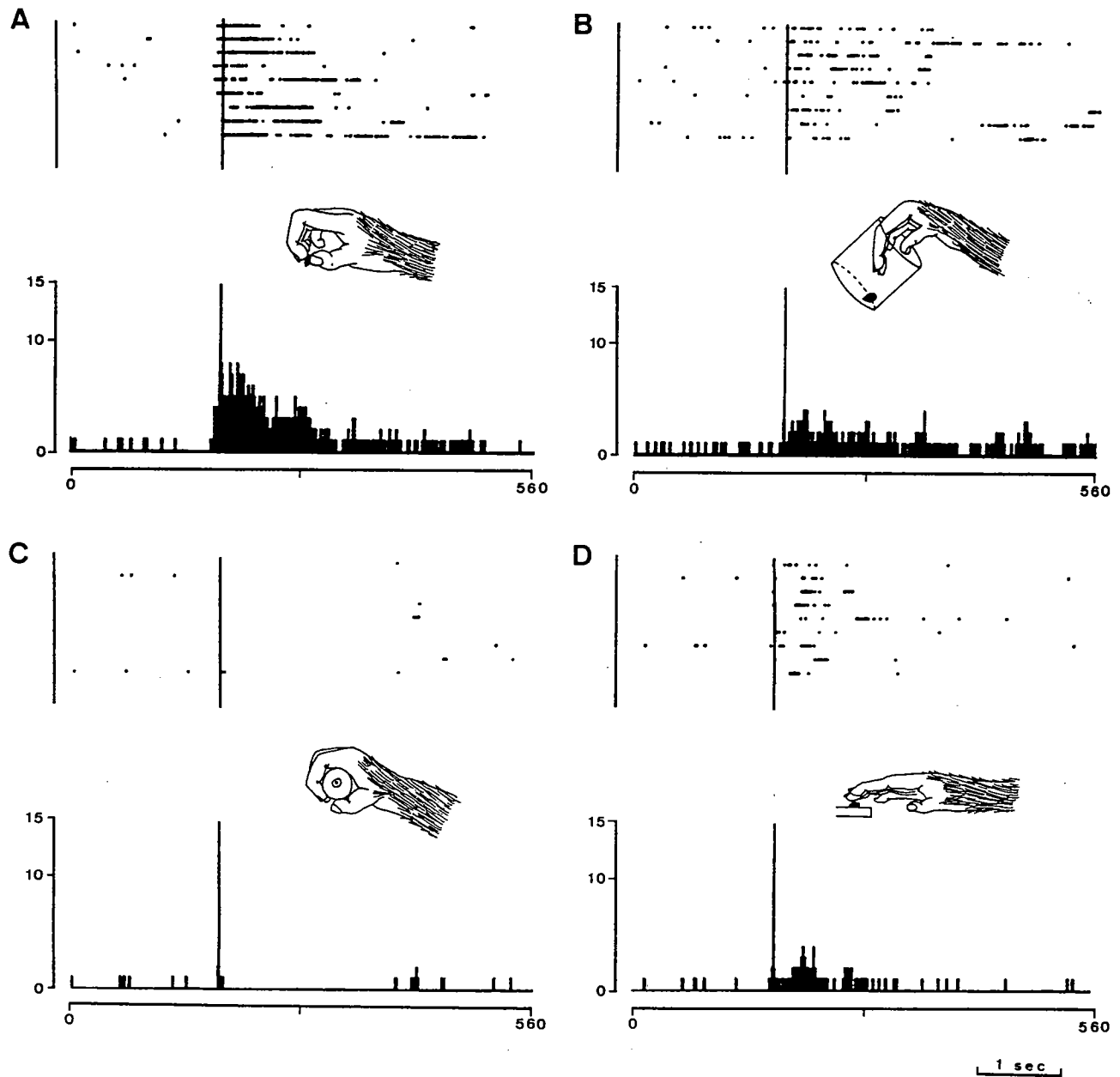


Fig. 3A-D. Study of a "Grasping-with-the-hand" neuron. A Neuron discharge during precision grip. B Neuron discharge during finger prehension. C Neuron discharge during whole hand prehension. D Neuron discharge during index flexion. In all trials the contralateral hand was used. The histograms are the sum of 9 trials. Other conventions as in Fig. 2

ipsilateral to the recorded side respectively; C and D show the neuron's activity during precision grip and whole hand prehension. The selectivity for finger prehension is very marked.

All neurons were tested by presenting stimuli in different space positions, so that the animal had to make different types of proximal movements in order

to reach for and to grasp them. No difference in neuron response was noticed, provided that the distal movement remained unmodified. The influence of wrist orientation was studied less systematically. However, with few exceptions (see below), the wrist position did not appear to influence the neuron activity. Figure 6 shows an example of a precision

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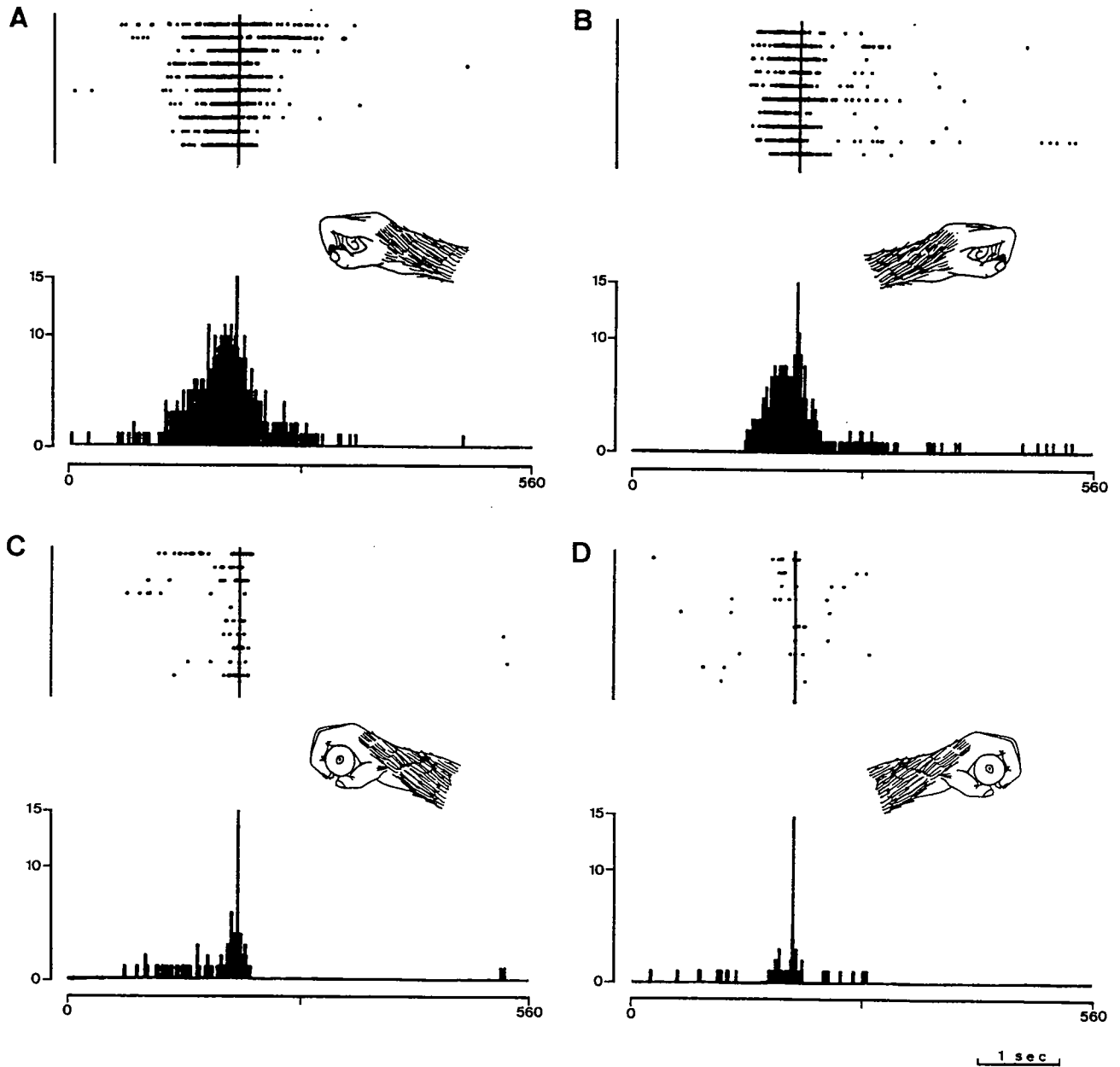


Fig. 4A-D. Study of "Grasping-with-the-hand" neuron. A, B Neuron discharge during precision grip. C, D Neuron discharge during whole hand prehension. The neuron was tested during contralateral (A, C) and ipsilateral (B, D) hand movements. The histograms are the sum of 10 trials. Other conventions as in Fig. 2

grip neuron whose response was not modified by the wrist orientation.

Table 2 shows the number of neurons related to the various types of grasping. It is interesting to note that the most represented prehension types are those which involve delicate finger movements. Whole

hand neurons represented only 7% of grasping-with-the-hand neurons. However, unspecific neurons, which can mediate also this type of prehension, were frequently encountered. Twelve neurons of the precision grip group were tested during primitive precision grip and during advanced precision grip (see

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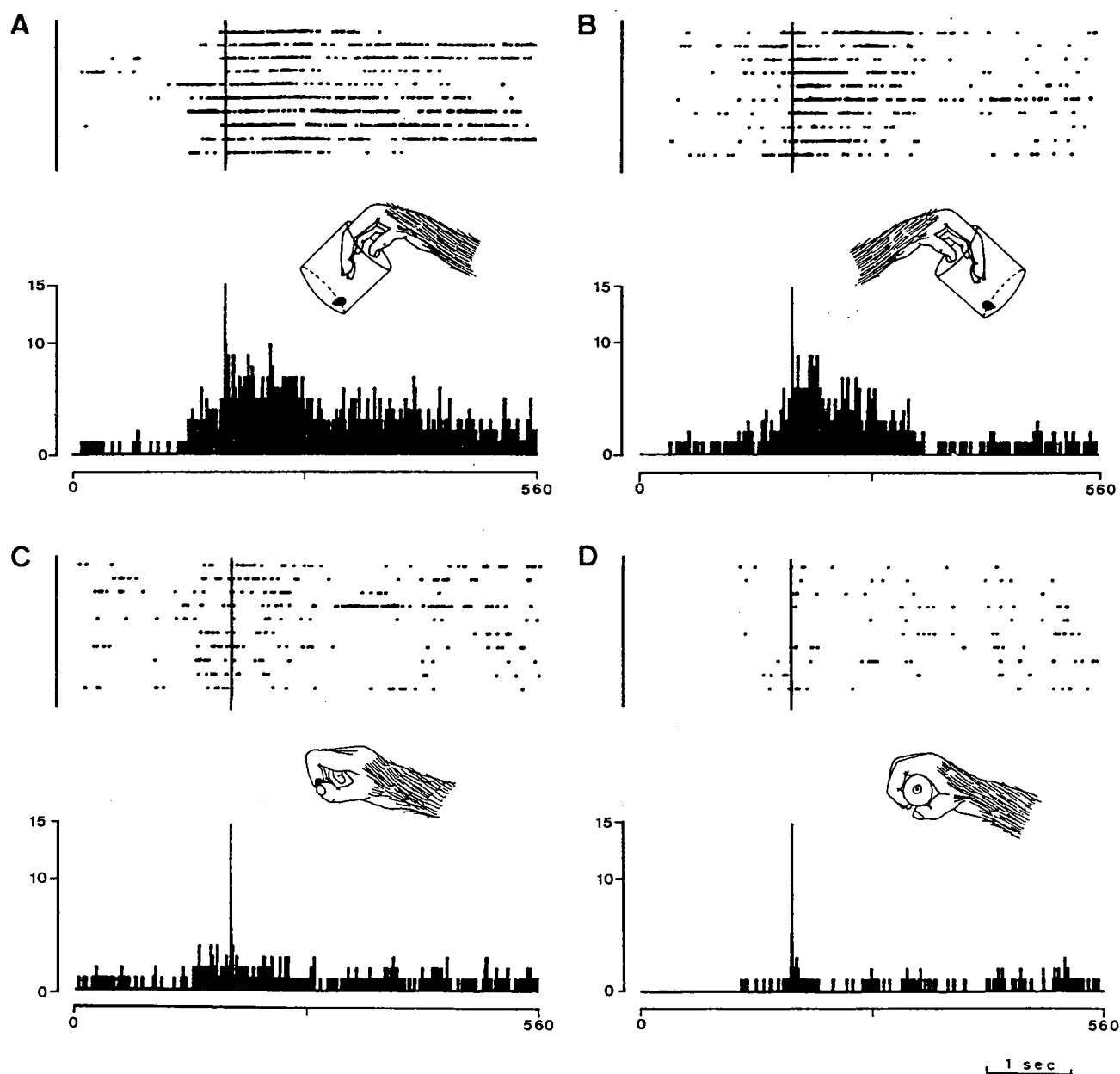


Fig. 5A-D. Study of "Grasping-with-the-hand" neuron. A, B Neuron discharge during finger prehension with the contralateral and ipsilateral hand respectively. C Neuron discharge during precision grip. D Neuron discharge during whole hand prehension. The testing in C and D was carried out with the contralateral hand. The histograms are the sum of 10 trials. Other conventions as in Fig. 2

Methods). Six responded better to the advanced precision grip, 1 to primitive precision grip, and 5 equally well to both types of grasping.

Discharge during grasping movements of the right and left hand were studied in 41 neurons. Thirty-six of them responded to both hands, 5 to the contralateral hand only.

In our standard testing situation the monkey kept its hand on the horizontal plane of the monkey chair. At the food presentation the arm was projected towards it, the fingers were extended and prepared according to the size of the object and, finally, they were flexed and the food grasped. The onset of grasping neurons discharge varied from one neuron

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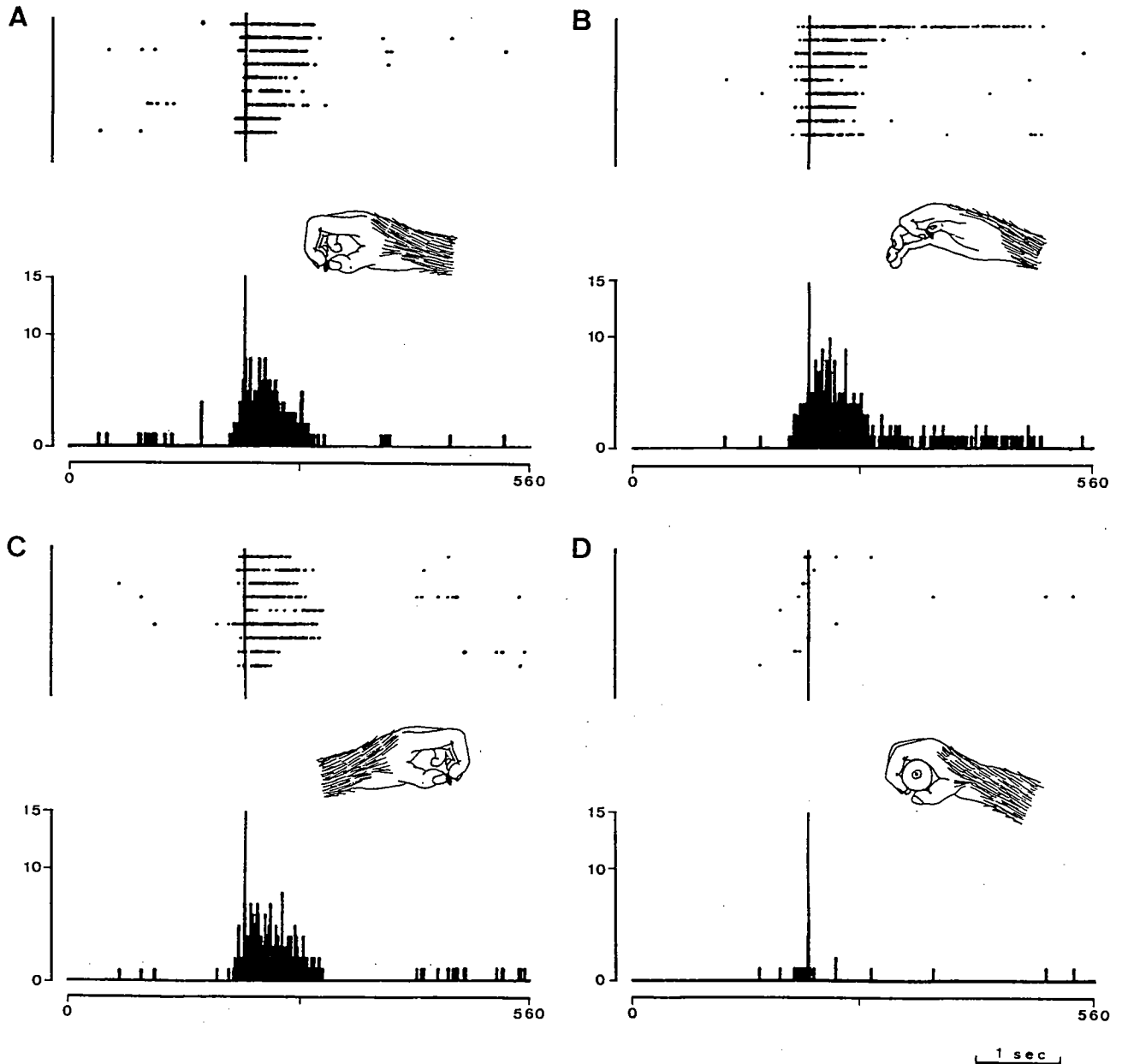


Fig. 6A-D. Study of a "Grasping-with-the-hand" neuron. A, B Neuron discharge during precision grip with the contralateral hand. In B the wrist was oriented at 90° in respect to A. C Neuron discharge during precision grip with the ipsilateral hand. D Neuron discharge during whole hand prehension. The testing in D was carried out with the contralateral hand. The histograms are the sum of 9 trials. Other conventions as in Fig. 2

to another. According to the phase of the movement sequence in which the neuron started to fire we subdivided them into three main categories: a) neurons that began to fire before the appearance of distal movements; b) neurons that began to fire with finger extension; c) neurons that began to fire with

finger flexion. All neurons ceased to fire with or immediately after grasping.

Table 3 indicates the number of neurons falling in each category. The neurons of the first category were classed with the other neurons for the following reasons: a) their discharge increased when the distal

Table 2. Number of neurons related to the various types of grasping

	Precision grip		Finger prehension		Whole hand grasping		Unspecific		Total	
	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)
Grasping-with-the-hand-and-the-mouth-neurons	20	(39)	8	(15)	0		24	(46)	52	(100)
Grasping-with-the-hand-neurons	36	(40)	34	(38)	6	(7)	14	(15)	90	(100)
Total	56	(39)	42	(30)	6	(4)	38	(27)	142	(100)

Table 3. Relation between the beginning of neuron discharge and hand movements

	Before distal movements		With finger extension		With finger flexion		Total	
	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)	<i>N</i>	(%)
Grasping-with-the-hand-and-the-mouth-neurons	17	(39)	8	(19)	18	(42)	43	(100)
Grasping-with-the-hand-neurons	18	(29)	29	(48)	14	(23)	61	(100)
Total	35	(34)	37	(35)	32	(31)	104	(100)

movements occurred, b) the direction of proximal movement was irrelevant in determining the neuron firing, c) about half of these neurons ($N = 8$) showed grasping specificity. Thus, although the discharge preceded the appearance of distal movements, it correlated better with distal movements than with the proximal ones.

An example of a neuron of the first category is shown in Fig. 4. Its discharge started about 1 sec before contact with the object and ended soon after the object had been grasped. Video-tape analysis of the temporal relation between the onset of the neuron's discharge and the animal's movement showed that the neuron started to fire before any observable movement, increased its discharge during hand shaping, characterized by an extension of the first two fingers, and reached the maximal firing during the final phase of grasping, characterized by finger flexion. Thus there was a correlation between neuron's discharge and the motor act (grasping), but not between the firing of the neuron and any individual movement. Examples of neurons which started to discharge with the beginning of finger flexion are shown in Figs. 3, 5, and 6. A comparison with Fig. 4 shows the marked difference in the behavior of these neurons with the former one.

c) Holding neurons. Holding neurons were less numerous than grasping neurons. Unlike grasping neurons, which stopped firing when the object was grasped, holding neurons continued to discharge for the entire time during which the object was held. The specificity for different types of prehension was present in this class of neurons as in the class of grasping neurons. Thirty percent of neurons discharged during precision grip, 15% during finger prehension, 15% during whole hand prehension and 40% were unspecific. Figure 7 shows an example of a holding neuron. Note the long discharge after the grasping. Some holding neurons (26%) started to fire at the moment in which the monkey touched the object, others, as the one in the figure, slightly before. This fact and the observation that there was a large variability among the grasping neurons as far as the end of their discharge is concerned indicate that although, for sake of simplicity, we distinguished two broad classes of cells, in reality there is "continuum" of pure grasping, grasping-holding and holding neurons.

d) Tearing neurons. Neurons of this class became active when the animal made movements of the

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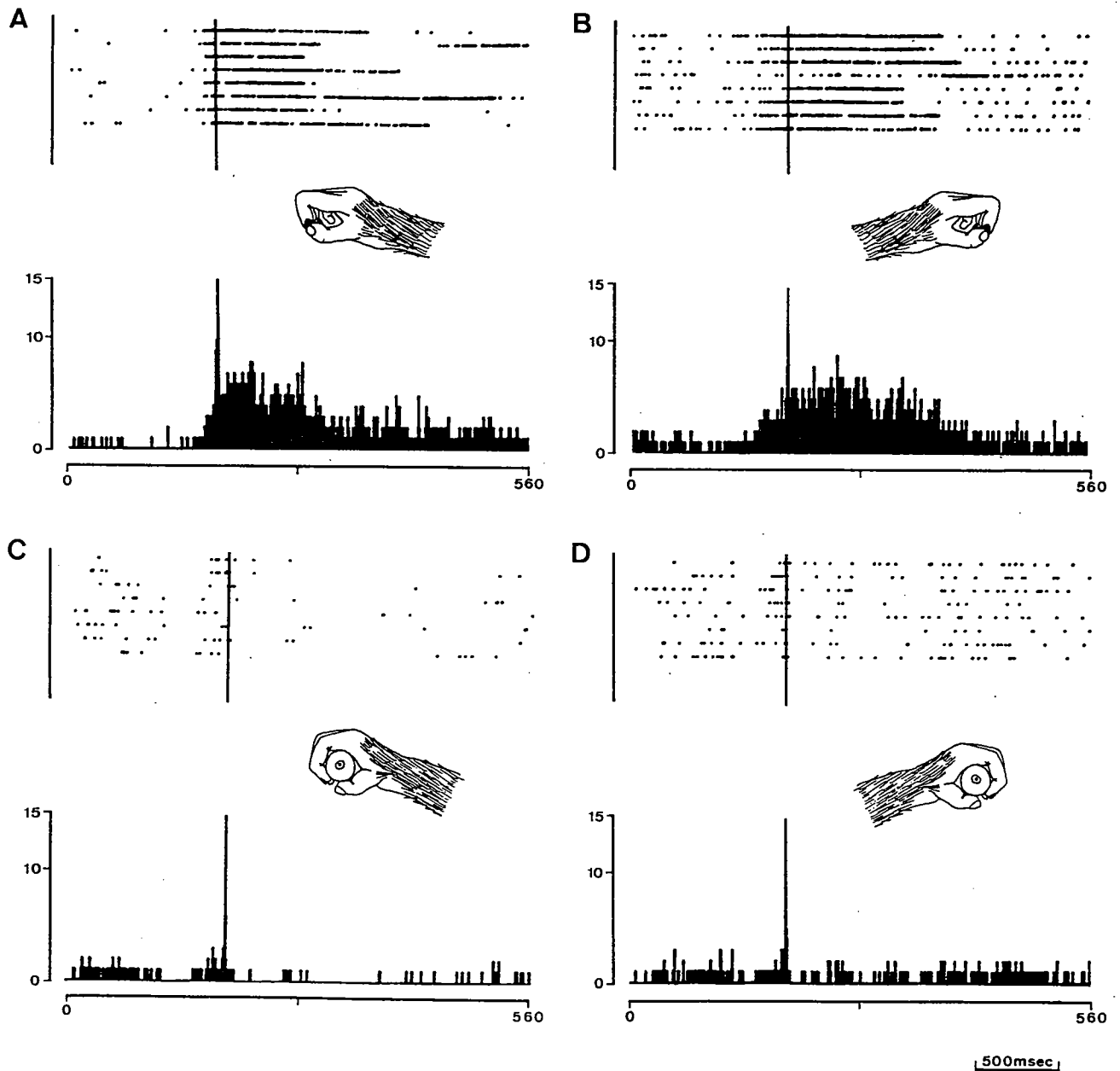


Fig. 7A-D. Study of a "holding" neuron. A, B Neuron discharge during holding with the thumb and index finger of the contralateral and ipsilateral hand. C, D Neuron discharge during holding with the whole hand. The contralateral hand was used in C; the ipsilateral one in D. The histograms are the sum of 8 trials. Bin width 5 ms. Other conventions as in Fig. 2

fingers, hand and wrist suitable for tearing or breaking objects. In these neurons the discharge started at the moment when the hand touched the stimulus. Thirty-six percent of neurons responded to breaking movements executed with the index finger and thumb, 36% to movements of all fingers as for scratching, 28% were unspecific. Tearing neurons

were the only F5 neurons whose discharge was possibly related to force. However the type of movement required for motor acts as tearing or breaking is not the same as for grasping. It may therefore be that the firing of these neurons was related to the distinctive features of the movements which require force rather than to force *per se*.

Responses of distal F5 neurons to somatosensory and visual stimuli

Seventy-three distal F5 neurons could be activated by somatosensory stimuli. The percentage of passively triggered neurons (42%) was approximately the same in the various classes. Thirty-two neurons (44%) responded to superficial tactile stimuli, 9 (12%) to joint movements and 32 (44%) to deep stimulation. The neurons of this last group were the most difficult to trigger giving often inconstant responses. Some of them responded to tapping of the muscles, other to deep pressure. The location of the receptive fields was on the hands for the neurons discharging with hand movements, it was on the hands, mouth or hands and mouth for the neurons activated by both hand and mouth movements. A good correlation was found between the location of the receptive field and the type of prehension effective in triggering the neurons. 18 out of 56 precision grip neurons responded to passive stimulation of the hand. Of them 15 had the receptive field on the thumb, extending either to the index finger or to the thenar eminence; the remaining three neurons were sensitive to wrist rotation. Similarly, the majority of finger prehension neurons activated by passive stimulation of the hand responded when passive stimuli were applied to the fingers (9 neurons out of 12); the remainders had their receptive field on the palm.

Thirty distal neurons (17%) responded to visual stimuli. A neuron was considered visual only if visual responses were present in the absence of any movement. It is very likely that with this strict definition of a visual neuron we have underestimated the real number of cells sensitive to visual stimuli, since neurons whose response is time-locked to the stimulus but which require in addition a subsequent movement in order to fire were not counted as visual neurons. These neurons, which could not be differentiated from other non-visual cells with our procedure, have been described in the premotor areas of conditioned monkeys (Godschalk et al. 1981; Weirich and Wise 1982).

Visual neurons of F5 were more difficult to trigger than F4 neurons. Unlike the latter, they required motivationally meaningful stimuli (for example food) and for some of them the size of the stimulus was also critical. Only 5 neurons showed clear receptive fields, always located around the mouth. For the remaining cells there was no well defined responding area, although stimuli within reaching distance produced stronger and more constant responses than those far from the animal.

With the exception of one cell, all neurons responding to visual stimuli belonged to the classes of

grasping-with-the-hand or grasping-with-the-hand-and-the-mouth neurons. Some of them were selective for precision grip ($N = 8$), some for finger prehension ($N = 6$), others were unspecific ($N = 12$). There was a relation between the type of prehension coded by the cell and the size of the stimulus effective in triggering the neurons. Precision grip neurons were activated only by small visual stimuli, whereas unspecific neurons fired in response to large and small stimuli. Unfortunately, we have not recorded from any visually responsive whole-hand prehension neuron, so we do not know if there are cells firing only in response to large stimuli.

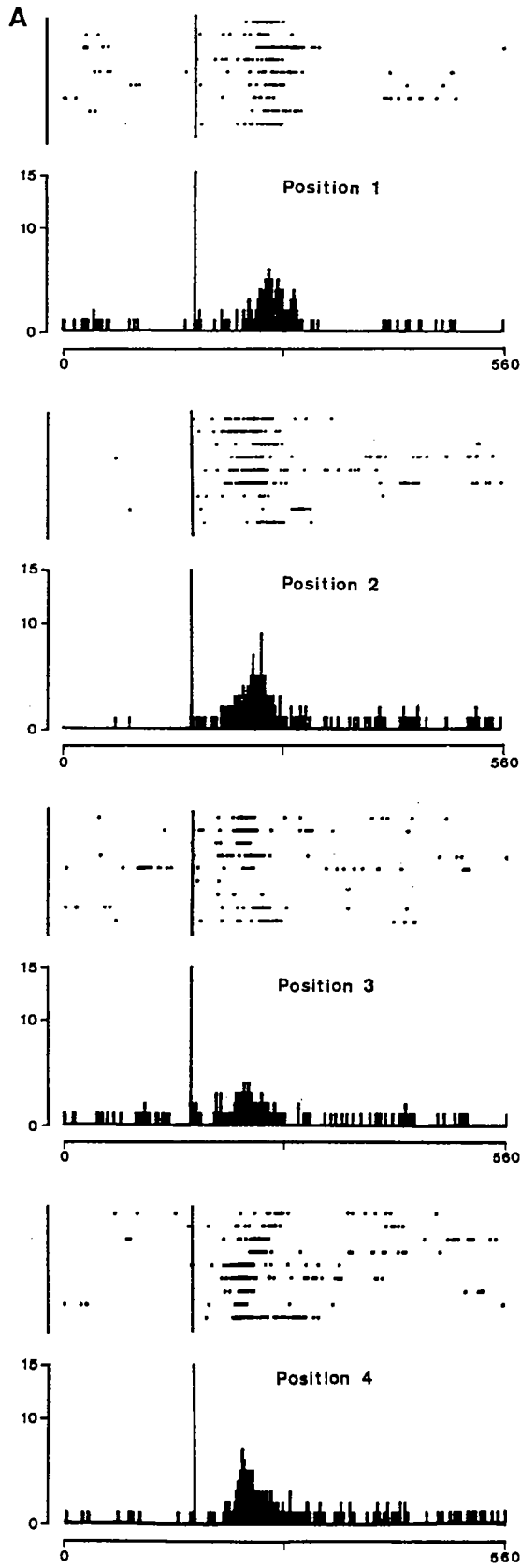
F5 neurons discharging with proximal movements

Two classes of neurons were related to proximal movements. The first class was formed by neurons active during reaching movements ($N = 11$), the second by neurons which fired during arm movements towards the mouth ($N = 9$) or the body ($N = 2$).

Reaching neurons discharged during arm projection to any part of space ($N = 4$) or during movements towards a particular, although large, space sector like the upper visual space, lower visual space, contralateral hemifield, contralateral upper quadrant ($N = 7$). They did not respond to somatosensory stimuli but, in many cases (50%), they could be activated by visual stimuli. There was a good correspondence between the preferred movement direction and the space sector from which visual responses could be evoked. Those neurons which were activated by movements towards any part of space responded to visual stimuli presented anywhere; in contrast, those neurons which responded to movements directed towards a particular space sector were activated by visual stimuli presented in that sector. Half of reaching neurons fired during movements of both arms, half during contralateral arm movements only.

Bringing-to-the-mouth neurons represented a rather homogeneous group of cells which fired during arm movements directed towards the mouth. Figure 8 illustrates the behavior of one of these neurons. The histograms are aligned with the moment in which the monkey grasped the food. Regardless of the arm starting position a discharge was always present during arm movements towards the mouth (A).

In B a piece of food was located near the animal's face and the monkey in order to pick it up, had to flex its elbow instead of extending it as in A. It is interesting to note that, in spite of the similarity of



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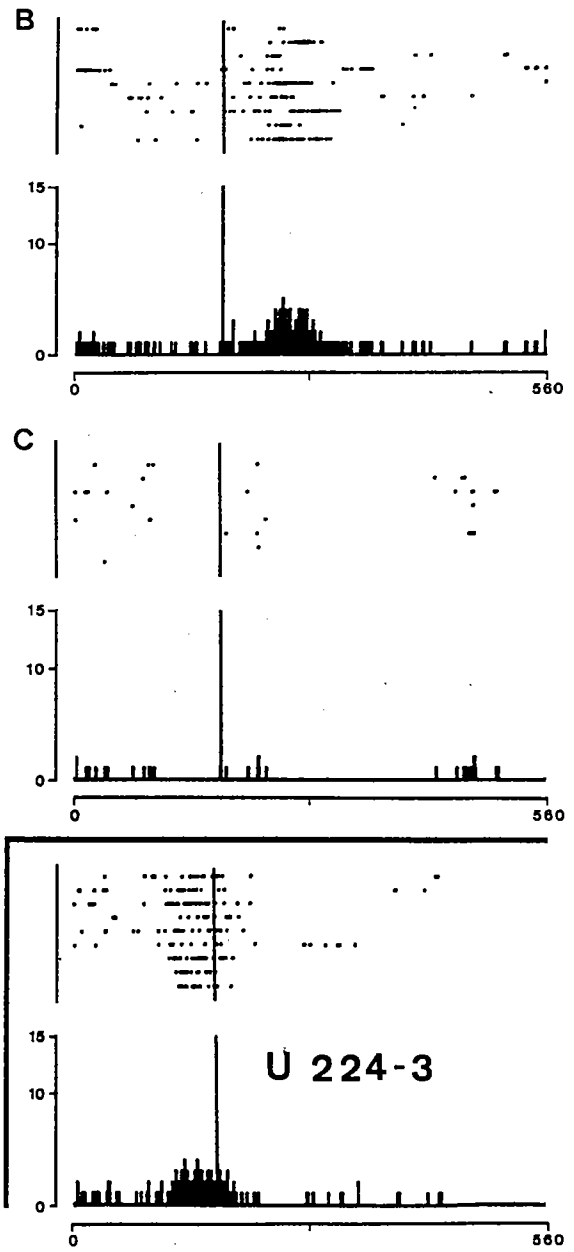
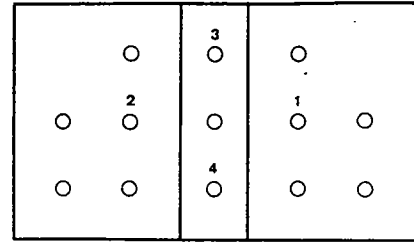


Fig. 8

1 sec

elbow movements (flexion), the discharge was absent during the reaching movement (discharge on the left of the vertical bar) but present during the bringing to the mouth movement (discharge on the right of the bar). C shows that the neuron's discharge was not due to the opening of the mouth or to a peribuccal visual response. In the trials represented in C a piece of food was moved towards the monkey which grasped it with the mouth. No response was present in this condition.

The majority of bringing-to-the-mouth neurons did not respond to visual and tactile stimuli. However, when visual responses could be evoked ($N = 3$), they were obtained with stimuli moved towards and around the mouth. Similarly, tactile fields, when present ($N = 2$), were located on the mouth and the perioral region. The fact that bringing-to-the-mouth neurons relate arm movements to mouth movements was shown not only by this receptive field arrangement, but also by the presence of pure mouth neurons intermixed with bringing-to-the-mouth cells. An example is shown in Fig. 8. Unit 224-3 was recorded at the same electrode location as unit 223-3. Unlike this last unit, it did not fire during arm movements. It became active, however, when the animal opened the mouth, and its receptive visual field was around the mouth. The two bringing-to-the-body neurons had properties similar to those of the previous group, except for the direction of the effective movements. None of them responded to tactile and visual stimuli.

F5 neurons with complex properties

This is a heterogeneous category of neurons whose activity could not be exclusively attributed to a particular motor act. We distinguished a few subgroups among them. The first was formed by neurons which became active during hand grasping movements but on condition that the arm was kept in an extended position ($N = 7$). For most of these neurons ($N = 5$) the position in space of the extended arm was irrelevant; two discharged only if the grasping movements occurred when the arm was extended and lifted in the upper space. Arm position apart, the properties of these neurons were indistinguishable

from those of grasping-with-the-hand neurons. Three cells fired during precision grip, 4 were unspecific.

The second subgroup ($N = 5$) was also formed by grasping-with-the-hand neurons. Unlike, however, the common grasping neurons, the discharge of these cells was inhibited during proximal movements ($N = 5$). For two neurons the movement towards the mouth was inhibitory, for three neurons both reaching movements and movements towards the mouth produced an inhibition.

A third subgroup ($N = 6$) was constituted of neurons which were not related to a specific motor act, but which fired during the various phases of the action which eventually allowed the monkey to introduce the food into the mouth. Although the firing of these cells was constantly evoked during testing, we are not sure whether we really discovered their triggering movement.

Finally, a few neurons fired during motor acts as those described in the previous sections, but, in addition, required other movements in order to be activated or were peculiar as far as their passive properties were concerned. For example, one cell was active only if grasping movements were accompanied by wrist rotations. This neuron responded also to visual and tactile stimuli, provided that the stimuli were rotated in space or on the skin in a particular direction. This direction was the same in both modalities.

Discussion

Functional properties of inferior area 6 neurons

Action may be defined as a sequence of movements which, when executed, allows one to reach his goal. Although the action is unitary in terms of its final aim, from the motor point of view it appears to be formed by various segments, each having its own limited aim. These action segments are the motor acts. Reaching, grasping with the hand, holding, bringing to the mouth, grasping with the mouth are the various motor acts which together form the action the final goal of which is to ingest food. The main finding of our experiments is that inferior area 6 neurons discharge in relation of these various motor acts.

Fig. 8A-C. Study of a "bringing-to-the-mouth" neuron. A Neuron discharge during bringing to the mouth of a piece of food presented in the four positions of the perimeter schematically represented on the upper right side of the figure. B Neuron discharge during bringing to the mouth of a piece of food presented near the animal's face. C Neuron discharge when the

monkey grasped a piece of food with its mouth. Lower right side of the figure: study of a "grasping-with-the-mouth" neuron. The neuron discharged when a piece of food was moved towards the mouth and the monkey grasped it with its mouth. The histograms are the sum of 9 trials. Other conventions as in Fig. 2

Considering the widespread preconception that area 6 is chiefly involved in the control of posture, one possible objection to this conclusion is that axial and proximal adjustments which accompany all these motor acts, are responsible for the firing of F5 neurons and that what we described as an activity related to specific motor acts is simply a consequence of these postural adjustments. Evidence against this interpretation has been presented with the data description. It may be important however to summarize it again before discussing the significance of our findings. *First*, neurons classified as distal neurons were activated by distal motor acts regardless of the position of the arms and body during their execution. *Second*, distal neurons did not fire during axial and proximal movements which were not accompanied by a specific distal motor act (e.g. grasping, holding etc.). *Third*, many neurons showed a marked specificity for the type of grasping effective in triggering them (precision grip, finger prehension, whole hand prehension). These neurons fired when an object, located in a certain space position, was taken with one type of grip, but not with another. In both cases the contribution of proximal and axial musculature to the movement was the same. Yet the discharge changed according to the distal motor act. *Fourth*, in those cases in which the electrical stimulation of F5 was effective, distal movements were observed. *Fifth*, Tanji and his coworkers (Kurata et al. 1985; Kurata and Tanji 1986) have shown a distal movement representation in rostral area 6 using animals conditioned to make specific, well controlled distal movements. The location of distal movement representation found in our experiments corresponds to that described in their experiments.

Whereas it is easy to dismiss the idea that postural adjustments are responsible for the activity of F5 neurons, serious consideration must be given to the possibility that F5 neurons fire in relation to single movements and not in relation to motor acts. To discuss this point let us examine separately the behavior of those neurons which discharge during the execution of a single motor act, e.g. grasping-with-the-hand neuron, and the activity of those neurons which discharge during the execution of more motor acts, e.g. grasping-with-the-hand-and-the-mouth neurons.

In the case of neurons firing during one motor act, there are two findings that point against a simple relation between neuron discharge and single movements. First, movements having same characteristics but executed in two different situations activated the neuron in one case, but failed to do it in another. For example, in the case of grasping neurons the flexion of the fingers made in order to grasp an object was

effective, whereas the same flexion made in order to push it away was not effective. Similar observations were made for proximal movements, where also the discharge depended upon the type of the motor act (e.g. reaching vs. pushing away).

A second, and stronger argument against the single movement hypothesis, derives from the analysis of the temporal relationship between the neuron discharge and the sequence of movements forming a motor act. In the case of grasping with the hand, most neurons that fired during this motor act, discharged not only during actual grasping, characterized by a finger flexion, but also during hand shaping which precedes the actual grasping and is characterized by a finger extension. In addition, some neurons started to fire even before the appearance of distal movements and continued to fire until the motor act was completed. Thus, these neurons and those previously described were active during the whole motor act irrespective of the individual movements forming it and of their temporal occurrence. The correlation was therefore with the entire motor act and not with individual movements.

One may argue that the discharge of grasping neurons, rather than being related to the motor act, was a command for a finger flexion, and that the lack of a strict correlation between the neuron discharge and the flexion was due to the preparatory character of the discharge which, therefore, started in advance of the flexion and was superimposed on other types of movements. If this objection were true, neurons should have been encountered in area F5 which fire during and were correlated with finger extension, adduction and abduction, since all these types of movements concur in forming the grasping. This was not found. The absence of these neurons renders very difficult to consider the "grasping" neurons as cells whose discharge is related in a simple way to finger flexion.

The strongest evidence that something more abstract than a single movement is coded by F5 neurons derives from the behavior of those neurons that fired in relation to two motor acts. In the case of grasping-with-the-hand-and-the-mouth neurons the discharge was present during grasping movements of the hand in the absence of mouth movements and during grasping movements of the mouth in the absence of hand movements. Since two completely different sets of muscles were used in the two motor acts, any explanation of their activity in terms of individual movements can be ruled out.

The definition of motor act includes the concept of aim. A motor act terminates when its aim has been achieved. In this sense inferior area 6 neurons, both those active during one motor act as well as those

active during two or more motor acts, are goal-related neurons. They start to fire at the beginning or during a certain phase of a motor act and stop firing at its completion. There is however a difference between neurons related to one motor act and those related to two motor acts. Whereas the former indicate only the aim intrinsic to the motor act, the latter, in addition to this, signal the aim of the behavior irrespective (within certain limits) of how this can be achieved. In this last case the concept of aim acquires a broader sense, for many aspects similar to that commonly used when one describes the animal's behavior. Obviously, one may object that this generalization is not necessary and that is more adherent to the facts to describe the neurons such as grasping-with-the-hand-and-the-mouth neurons, simply as neurons whose firing is related to two motor acts without postulating for them any purposive character. This may be true. However, the fact remains that the motor acts coded by the same neurons have the same aim. It is hard to believe that this occurs by chance. Thus the description of these neurons in terms of aim stresses an organizational fact and, for this reason, it may be useful for a better understanding of area 6 functions.

The presence of complex relations between neuron discharge and movements (in broad sense) in area 6 is not surprising. This complexity is consistent with the organization trend observed in the nervous system in general and in the motor system in particular as one goes away from the periphery. In the motor system this trend is clear when one compares alpha motor neurons with pyramidal tract neurons. The former project to fibers of one and only one skeletal muscle, the latter send axons to several motor neurons and interneurons of the spinal cord (Fetz and Cheney 1980; Shinoda et al. 1981). This widespread projection of pyramidal tract neurons allows the motor cortex to select populations of motoneurons, whose simultaneous firing ultimately produces elementary movements. Thus as a consequence of this arrangement a new motor property emerges: muscle contractions are transformed in movements (see Evarts 1984). Furthermore, the data of Muir and Lemon (1983; see also Buys et al. 1986; Lemon et al. 1986) indicate that some corticomotoneuronal cells fire during specific types of grasping (e. g. precision grip) but not during others (e. g. whole hand prehension) in spite of a similar EMG activity of finger flexor muscles. This suggests that already in area 4 there is a segregation between neurons which participate in different motor acts. The next step in this organization trend is the emergence of neurons related to motor acts. The complexity of movements controlled by these

neurons is not difficult to explain. It is sufficient to postulate that area 6 neurons control functionally different precentral units. If, for example, a set of area 6 neurons innervates both area 4 neurons controlling flexion of the thumb and area 4 neurons controlling flexion of the index finger, its discharge will ultimately lead to a precision grip movement. It is more difficult to provide an anatomical model which may account for the temporal relationship between neuron discharge and motor acts. A discussion of this point would be however outside the scope of this paper. The interested reader will find some speculations on this point in our review article on premotor cortex (Rizzolatti and Gentilucci, in press).

The role of area 6 in movement

Among the various proposals that have been advanced on the functional role of area 6 in the control of movement, three are particularly interesting: preparation for movements, sensory guidance of movements, control of movement sequencing.

Preparation-for-movements is a rather vague concept. In its broadest sense it indicates all those processes that take place before movement execution and are causally related to it. According to this definition all premotor areas and most association areas should have this functional role. Preparation-for-movement, however, has been used also in more restricted, specific way. According to some authors the main role of area 6 should be that of stabilizing the trunk and limbs in order to render possible the execution of distal movements (for a discussion of this concept see Humphrey 1979). The area 6 "preparation" of movement should consist therefore of an action of axial and proximal movements. The presence in area 6, as well as in supplementary motor area, of a rich representation of distal movements makes this version clearly insufficient.

A new version of preparation-for-movement hypothesis employs this term to signify readiness to move (Weinrich and Wise 1982). Empirical evidence in its favour has been considered the presence in area 6 of neurons that fire in the absence of any movement when an animal, that is instructed to emit a motor response, expects a "go" signal (Godschalk et al. 1981; Weinrich and Wise 1982). Many of these neurons (set-related neurons) show specificity for the direction of the upcoming movements, making it unlikely that they reflect a general increase of arousal (see Wise 1985).

Psychological studies on reaction time have demonstrated that when a subject knows in advance the effectors which he has to use, the direction of an

impending movement, its distance or other relevant movement parameters, his responses are faster than when information on them is given simultaneously with the "go" signal (Rosenbaum 1980). It is clear from this that a motor plan or parts of it may be internally constructed once the necessary information is available. The set-related neurons may represent the neural counterpart of this phenomenon. This, however, does not imply that their primary function is that of increasing the speed of the response. It is more likely that they specify some aspects of the motor plan, and that the increase of response speed is a consequence of this elaboration. However, even if one admits that the primary function of set-related neurons is that of increasing the speed of the response to a stimulus, this does not allow one to conclude also that the primary function of area 6 is to "modify" the excitability of area 4 or of other motor centers in order to obtain fast responses. There are at least three sets of evidence pointing against this point of view: a) Anatomical connections between parietal and frontal lobe (see ref. in Petrides and Pandya 1984) show that area 6 has a crucial role in conveying visual information necessary for movement organization from the posterior association areas to motor cortex (Haaxma and Kuypers 1975; Moll and Kuypers 1977); b) The properties of neurons described in this and in the accompanying paper (Gentilucci et al. 1988) indicate that area 6 represents a more complex stage in movement preparation than that represented in area 4 and that these properties are, for many aspects, similar to those of area 7b (Leinonen et al. 1979; Leinonen and Nyman 1979); c) Set-related cells are present in many cortical areas outside area 6 (see Evarts et al. 1984). This points out that movement preparation is a distributed function which is not specifically proper of area 6.

A second proposal is that area 6 plays a role in sensory and especially visually guided movements (Haaxma and Kuypers 1975; Godschalk et al. 1981; Rizzolatti et al. 1981c). The data of the present experiments clearly support this hypothesis. Furthermore, they give some hints on how sensory information is translated into movements. As it has been shown in the previous section, inferior area 6 neurons code motor acts. All together these neurons form a *vocabulary* where proximal and distal movement necessary for reaching, grasping, holding and bringing the food to the mouth are represented. The various motor acts can be accessed via somatosensory and visual inputs. Particularly interesting is the relationship between visual responses and active movements. Neurons which control proximal movements (those located in area F4) are triggered by

stimuli presented in the animal's peripersonal space. Their receptive fields are anchored to the body and do not change position with eye movements. Thus, an object presented in a particular spatial position activates the neurons controlling the motor act "reach" and, if the motivation is sufficient, these neurons will bring the arm in the space position where the stimulus is located. Somewhat different is the organization of distal movements. In this case the crucial factor is not where the stimulus is located but its size. The great majority of distal neurons, regardless of the category they belong to, specify the motor patterns necessary to take or hold an object according to its size. Most of F5 neurons which respond to visual stimuli are visually activated only if the stimulus matches the type of coded movement. Thus for distal neurons, if the motivational factors are sufficient, the visual stimulus of an appropriate size will trigger the motor act that allows the animal to take possession and hold the stimulus.

It is important to stress that the idea of a vocabulary of motor acts suggests a function for area 6 broader than that related to sensory-motor transformation. Somatosensory and visual stimuli are two of the possible ways in which motor acts located in area 6 can be elicited. Other ways however are conceivable even not related to the actual presence of stimuli. Some recent data by Okano and Tanji (1987) fit well with this point of view. They found that about two-thirds of the inferior area 6 neurons they recorded from, fired both when the monkey pressed a key in response to visual stimuli and when it did the same movement without a triggering stimulus in a self-paced movement paradigm. Thus, although inferior area 6 vocabulary can be addressed by visual stimuli, it is by no means completely dependent on this or other sensory modalities.

The hypothesis that area 6 controls movement sequencing can be interpreted in several ways. The most interesting is probably that a sequence of motor acts or even an entire motor action (e. g. reach-grasp-hold-bring to the mouth) is coded by single neurons. Although some of our neurons with complex properties may suggest something of this kind, the overall evidence is against this type of coding in area 6. This high order vocabulary, if it exists, is located in areas outside area 6.

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