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Functional organization of inferior area 6 in the macaque monkey

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Functional organization of inferior area 6 in the macaque monkey

I. Somatotopy and the control of proximal movements

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Summary. Two series of experiments are reported in this paper. The first concerns the movement representation in the macaque inferior area 6, the second the functional properties of neurons located in the caudal part of this area (histochemical area F4). By combining single neuron recording and intracortical microstimulation, we found that inferior area 6 is somatotopically organized. The axio-proximal movements are represented caudally, the distal movements are represented near the arcuate sulcus. The mouth field is located laterally, the hand field medially. There is no leg field. A comparison between neuron properties and histochemical characteristics of inferior area 6 showed that the proximal movements representation includes most of area F4, whereas the distal movements representation corresponds to area F5 and to the rostral part of F4. Neurons located in that part of F4 where proximal movements are represented respond very well to tactile stimuli. They have large receptive fields mostly located on the face and on the upper part of the body. A large number of these neurons respond to visual stimuli. Objects approaching the animal are particularly effective. The tactile and the visual receptive fields are in register. The most represented movements are reaching movements, movements bringing the hand to the mouth or to the body and facial movements. There is a congruence between location of visual fields and preferred arm movements. It is argued that the receptive field arrangement and the response properties are more complex in area F4 than in the primary motor cortex and that area F4 neurons are involved in the control of arm movements towards different space sectors.

Key words: Area 6 – Macaque monkey – Somatotopic map – Proximal movements – Visually responsive neurons

Introduction

The role of area 6 in the control of movement has been matter of debate for years. A central issue of this debate has been the relationship between area 6 and area 4. Broadly speaking, two main points of view have been expressed. According to Fulton (1934) area 6 is an area separate from and functionally higher than area 4. Unlike the primary motor cortex, chiefly involved in movement execution, its functional role is that of programming movement and, in particular, sequences of movements. The concepts of a higher-order motor area located in front of area 4 has been challenged by Woolsey et al. (1952). Using as evidence the results of their stimulation experiments they argued that the rostral part of area 6 is not involved in movement control. According to them the sectors of area 6 that have such a role are the supplementary motor area and the caudal part of area 6 located on the cortical convexity. This last part of area 6, however, is not an independent area but, together with area 4, forms the precentral motor cortex. In it axial and proximal movements are represented.

The ideas of Woolsey have been a dogma in the physiology of the motor system for almost three decades. To be sure, cortical microstimulation experiments showed that the organization of the primary motor cortex was more complex than that resulting from surface stimulation studies (Kwan et al. 1978; Sessle and Wiesendanger 1982), but the basic Woolsey's notion of a single motor area located on the cortical convexity was not challenged. Recently however a convergent series of data coming from ablation experiments (Moll and Kuypers 1977; Halsband and Passingham 1982; Petrides 1982), single neuron recordings (Godschalk et al. 1981; Rizzolatti et al. 1981a, b, c; Weinrich and Wise 1982; see also Wise 1985) as well as from studies of cortico-cortical

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Offprint requests to: G. Rizzolatti (address see above) connections (Matsumura and Kubota 1979; Muakkassa and Strick 1979) provided strong evidence that one or, possibly, several association motor areas exist on the cortical convexity in front of area 4. Furthermore, recording experiments showed that in the rostral part of area 6, near the arcuate sulcus, there are neurons which respond to stimulation of distal parts of the body (Rizzolatti et al. 1981a, b) and become active during distal movements (Kurata and Tanji 1986; Rizzolatti et al. 1981a). Mouth related neurons were found laterally, hand related neurons were found medially near the spur of the arcuate sulcus. These findings and the previously mentioned anatomical data suggest that area 6 is not only involved in motor control but that it is also somatotopically organized.

The first aim of this paper is to investigate the somatotopic organization of inferior area 6 (see Matelli et al. 1986) by combining microelectrode intracortical stimulation and single neuron recordings. This approach allows one to acquire information on the somatotopy of the parts of area 6 which are electrically not excitable, and to compare the functional properties of the parts of areas 4 and 6 from which similar movements are evoked. The second aim of this work is to study the correlations between neuron discharge and active movements during a wide range of natural behavioral acts. This naturalistic approach seems to us the most adequate to obtain information on the specific properties of a motor area, when little is known on its function. In this paper data will be presented concerning the somatotopic organization of inferior area 6 and its control of proximal movements. In the accompanying paper (Rizzolatti et al. 1988) the organization of distal movements will be discussed.

Methods

Surgical preparation and recording procedure

The experiments were carried out on three macaque monkeys (Macaca nemestrina) selected for their docility. A few days before the first recording session a craniotomy over the posterior part of the frontal lobe was performed under general anesthesia (ketamine hydrocloride, 15 mg/kg i. m. repeated every 30 min) and the coordinates of the arcuate sulcus and central sulcus were assessed. A chamber was positioned over the hole and cemented to the skull. A support for the microelectrode advancer and a device which allowed a rigid fixation of the head during the experiments were also implanted. The surgery was made in aseptical conditions.

The recordings were carried out five days a week, for about five hours each day. During the recordings the monkey was seated in a primate chair with its head fixed. Each monkey was recorded for approximately three months. Single neurons were recorded using tungsten microelectrodes (impedence 0.5–2.0 MΩ, measured a 1 kHz frequency) inserted into the cortex through the dura, which was left intact. Neuron activity, after a conventional AC amplification, was monitored on an oscilloscope and individual action potentials isolated with a voltage discriminator. The signal from the voltage discriminator was monitored and fed to a PDP 11-23 computer for histogram construction.

The microelectrode used for recording was also used for electrical intracortical microstimulation. The stimulation was made every 500 μ, by applying trains of cathodal pulses generated by a constant current stimulator. Train duration = 50 ms, pulse duration = 0.2 ms, frequency = 250 Hz, current intensity 3 to 40 μA. The current strength was controlled on an oscilloscope measuring the voltage drop through a 10 KΩ resistor in series with the stimulating electrode.

Testing of active movements

Once a neuron was isolated, we studied its discharge during animal's proximal and distal forelimb movements and during its mouth movements. Proximal movements were evoked by presenting pleasant and annoying. In both cases the animal extended its arm in response to the stimuli. In the case of pleasant stimuli (food, syringe filled with orange juice), the animal reached for the stimulus and brought it towards its mouth, whereas in the case of annoying stimuli (e. g. laboratory gloves, a pair of forceps, objects found at hand in the laboratory) the stimulus was either pushed away or grasped and subsequently thrown away. After an initial informal testing, neurons responding to reaching movements were studied using a plexiglass perimeter which surrounded the monkey at arm's distance. The perimeter had nine holes (diameter of each hole 7 cm) distributed in three vertical rows corresponding respectively to the vertical axis of the body and to positions 40° to the right and 40° to the left of the body midline. In each row the central hole was at the monkey's shoulder level, the other two holes were located 20° above and 20° below it. Pieces of food were presented through the holes and the animal had to extend its arm in order to get them. The test was carried out with either arm and then repeated, without the perimeter, near the animal's body with the same elevation and azimuth as in the first test. With this stimulus presentation the reaching movement was accomplished using a different set of muscles with respect to the perimeter test. To be more precise, it was accomplished with a flexion of the arm and not with an arm extension.

Some neurons discharged during movements that bring the hand to the mouth or to the body. These movements consist of a flexion of the elbow combined with various shoulder displacements. Bringing to the body movements were evoked by touching various parts of the animal's body. Bringing to the mouth movements were examined by allowing the animal to take food presented in various space positions around it. When the food was located in the space contralateral to the tested arm the bringing to the mouth movements consisted of a shoulder abduction plus an elbow flexion, whereas when the stimulus was in the ipsilateral space the bringing to the mouth was achieved by a shoulder adduction plus an elbow flexion. Bringing to the mouth movements were also studied by presenting stimuli near the animal's face. The combined analysis of these various movements allowed us to correlate the neuronal discharge with specific proximal movements or with the global motor act.

Distal movements were evoked by presenting objects of different size and orientation and observing the hand-finger movements made by the animal to grasp them. They were studied when the animal had its arm extended in different positions of the space and repeated with the arm flexed. A detailed description of the tests used for studying distal movements will be presented in the accompanying paper (Rizzolatti et al. 1988). It is important however to stress here that we classified as distal neurons only those neurons that fired consistently during a particular distal movement regardless of whether the arm was flexed, extended, adduced or abduced.

A careful study of distal and proximal movements also allowed us to control axial movements. To give an example, if movements directed towards the same space position were effective in activating a neuron during reaching for some types of objects but not during reaching for other types of objects, axial adjustments can hardly be responsible for the firing of the neuron. This point will be discussed in details after presenting the data on neurons related to distal movements (Rizzolatti et al. 1988).

In addition to forelimb movements, mouth movements were also studied. Buccal movements were observed during reaching for and grasping the food, as well as during chewing and sucking. Buccal and facial movements were also observed in response to emotional stimuli. Leg movements were examined, but less systematically than arm and mouth movements.

In order to relate objectively the neuron discharge to the sequence of movements, the stimuli used for eliciting the various responses, were connected, through a holder, to an electronic circuit which gave a signal every time the animal touched them. This signal was used for constructing peristimulus histograms.

In conclusion, the method of testing a large variety of movements and subtracting progressively those which were ineffective gave precise information on the type of movement which was effective in triggering a given neuron. Although this method has never been systematically applied to the motor areas, it has been successfully used in the study of parietal cortex. The description of "arm projection" neurons and "hand manipulation" neurons by Mountcastle et al. (1975) and the study of area 7b by Hyvärinen and his coworkers (see Hyvärinen 1982) testify on the reliability of this method.

Somatosensory and visual stimulation procedure

After assessing the properties of a neuron during active movements of the animal, its responses were tested with somatosensory and visual stimuli. Somatosensory stimuli consisted of hair bending, touch of the skin, light pressure of the tissue, and slow and fast rotation of the joints. Light pressures on the muscle bellies and tendons were also applied. In order to construct response histograms a metallic probe (diameter 0.1 cm) was used. The probe was connected to an electronic circuit which sent a signal to the computer whenever the tip of it touched the skin of the monkey.

Visual stimuli consisted of three dimensional objects. Geometrical solids, food and various objects found at hand in the laboratory were used. The stimuli were moved by hand towards the animal from different angles. The procedure was repeated again and again until the borders of the visually responding region were delimited. Borders of the visual responding region were considered the parts of space whose crossing gave constant responses. In one monkey the visual receptive fields were also studied by using a mechanical device consisting of a plexiglass rod (length 60 cm) surrounded by a short cylindrical teflon guide (length 10 cm). Metallic rings were attached to the rod at a distance of 10 cm from one another. The rod was moved towards the animal and when the metallic rings touched the center of the cylindrical guide an electric pulse was generated. The pulses were sent to a computer for histogram construction. In order to study the receptive field of the neurons, an object was attached to the tip of the rod and moved towards the animal. The correlation between the electric pulses and the neuron discharge allows us to establish the extension in depth of the receptive field. Furthermore, the preferred trajectory orientation could also be described.

The animal's behavior during testing of active movements and passive stimulation was recorded on one track of a video-tape, the neuron activity was simultaneously recorded on a second track in order to correlate the monkey's behavior to the unit firing.

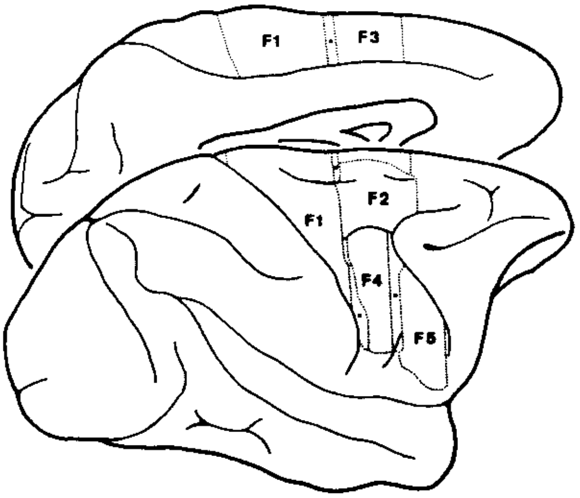

Fig. 1. Cytochrome oxidase map of the agranular frontal cortex. The spur of the arcuate sulcus sets the limit between inferior and superior area 6. Inferior area 6 is constituted by areas F4 and F5. F1 corresponds to area 4. Asterisks indicate transition zones

Histological identification

About 1 week before sacrificing the animal, a series of electrolytic lesions (30 μA cathodal current for 30 s) equally spaced one from another were made at the border of the studied area. After the last experiment the animal was anesthetized with ketamine (15 mg/kg/ i. m., repeated every 30 min), the dura was removed and the stereotaxic coordinates of the arcuate sulcus and central sulcus were assessed. After an additional dose of sodium thiopental (30–40 mg, i. v.) the animal was perfused through the left ventricle with warm buffered saline followed by fixative and the brain was removed (for details see Matelli et al. 1985). The brain was frozen and cut (each section 60 μm) parasagitally in one monkey and coronally in the other two. Alternate sections were stained with the Nissl method and reacted for cytochrome oxidase histochemistry. The locations of the penetrations were reconstructed and related to the various cytochrome oxidase subareas of the frontal agranular cortex (Matelli et al. 1985). For each penetration a reconstruction was made of the depths at which the various peripheral movements had been elicited by the electrical stimulation. Furthermore a systematic comparison was made between the evoked movements and the characteristics of the neurons recorded at the same location. Since the aim of this paper was not the description of the laminar organization of the motor responses in area 6, but the general somatotopic organization of this area, the data concerning differences between superficial and deep layers will be reported only when changes in somatotopic organization were observed.

Results

Somatotopic organization

The agranular frontal cortex (area 4–6 complex) of the monkey is constituted of five histochemical areas

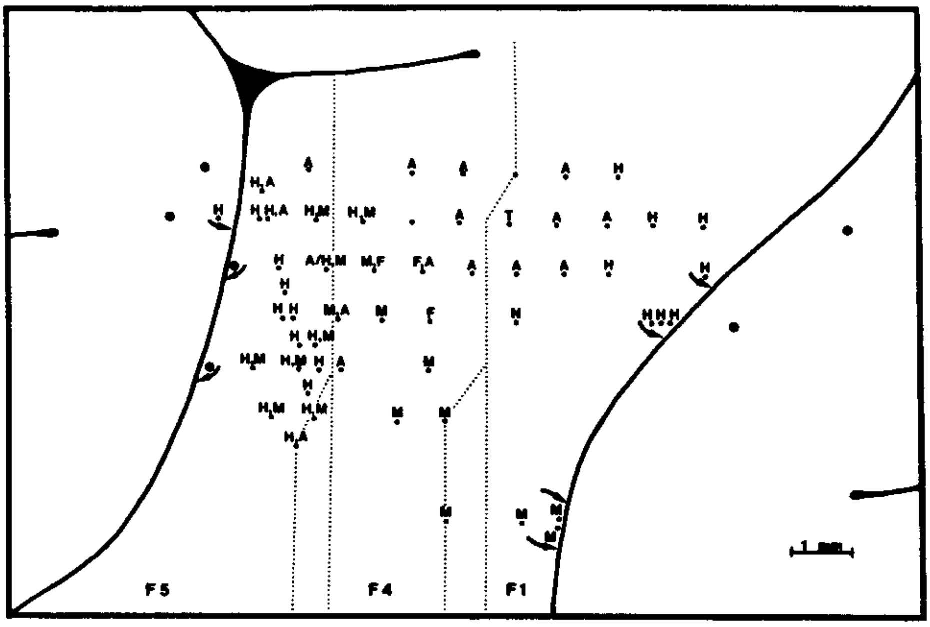

Fig. 2. Somatotopic map based on the neuron responses during active movements. The inferior part of the left frontal agranular cortex is shown (monkey MK2). The dots indicate the microelectrode penetrations. The letters represent the body parts controlled by the neurons encountered in each penetration. Dot without symbols and open circles indicate the penetrations, within agranular cortex and outside it respectively, in which no neurons responding to active body movements were recorded. The histochemical areas (F1, F4 and F5) are separated by dashed lines. Unmarked areas between F1 and F4, and F4 and F5 are transition zones. A = arm; F = face; H = hand; M = mouth; N = neck; T = upper trunk

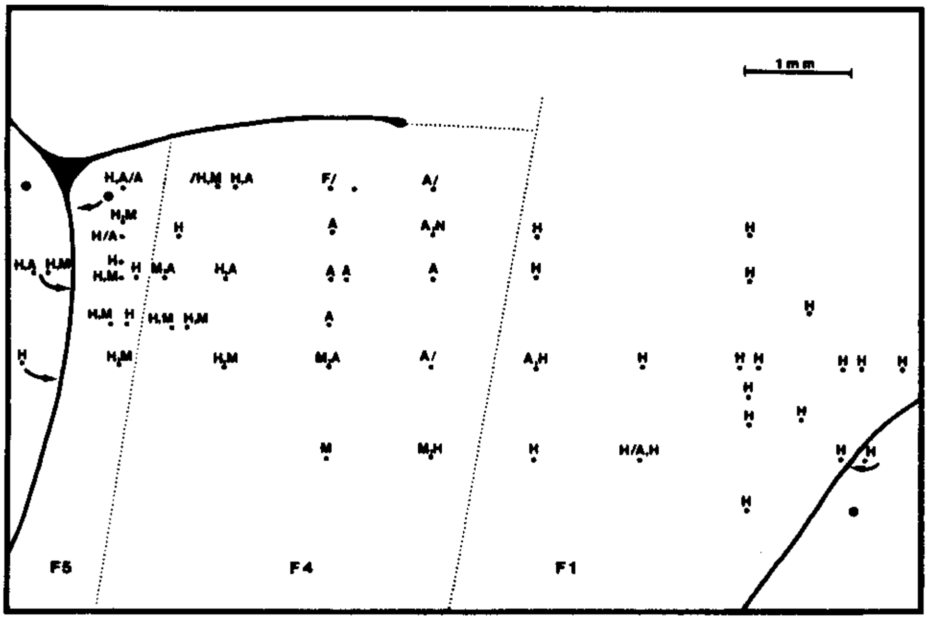

Fig. 3. Somatotopic map based on the neuron responses during active movements. The data are from monkey MK3. For other conventions see Fig. 2.

(Matelli et al. 1985) (Fig. 1). In this study we will describe the somatotopic organization of two of them: F4 and F5, which together form the inferior area 6. Three types of somatotopic maps will be presented: a) maps based on neuron discharge during animal's active movements, b) maps based on neuron responses to somatosensory stimuli, c) maps based on peripheral movements evoked by electrical microstimulation.

Somatotopic maps based on neuron responses during active movements are shown in Figs. 2 and 3. The dots indicate the penetration locations, the symbols the movements represented in a given location. Since in area F4 and F5 the neuron activity is frequently related to movements involving more than one articulation (see below), the maps are expressed in terms of body parts controlled by the neurons encountered in a given penetration and not in terms of joints. Cases in which a shift from one body part to another was found in a same penetration are indicated by a slash. Symbols on the left side of the slash indicate the body part represented in the upper part

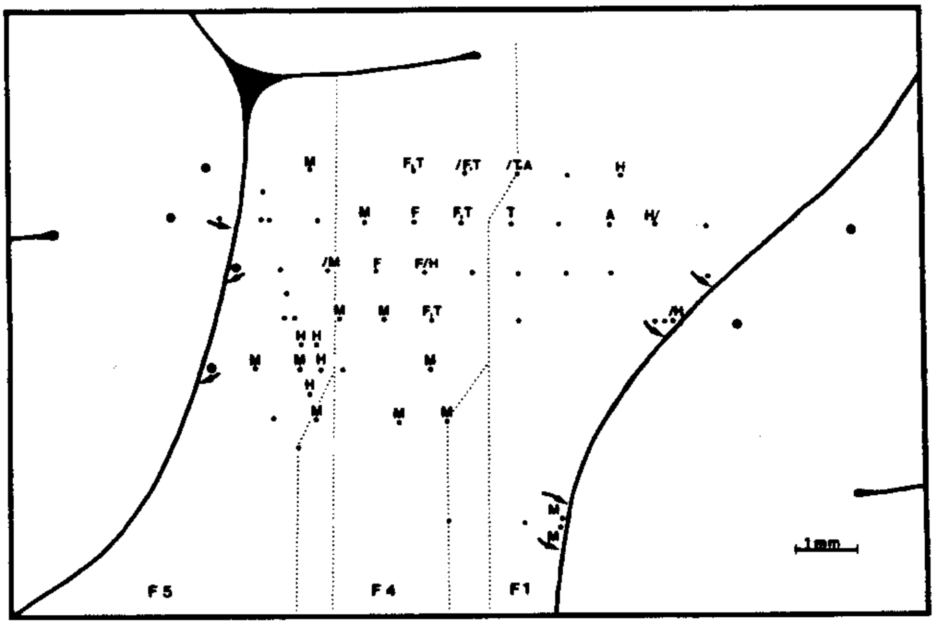

Fig. 4. Spatial distribution of penetrations where neurons responsive to tactile stimuli were recorded. The data are from monkey MK2. Conventions as in Fig. 2

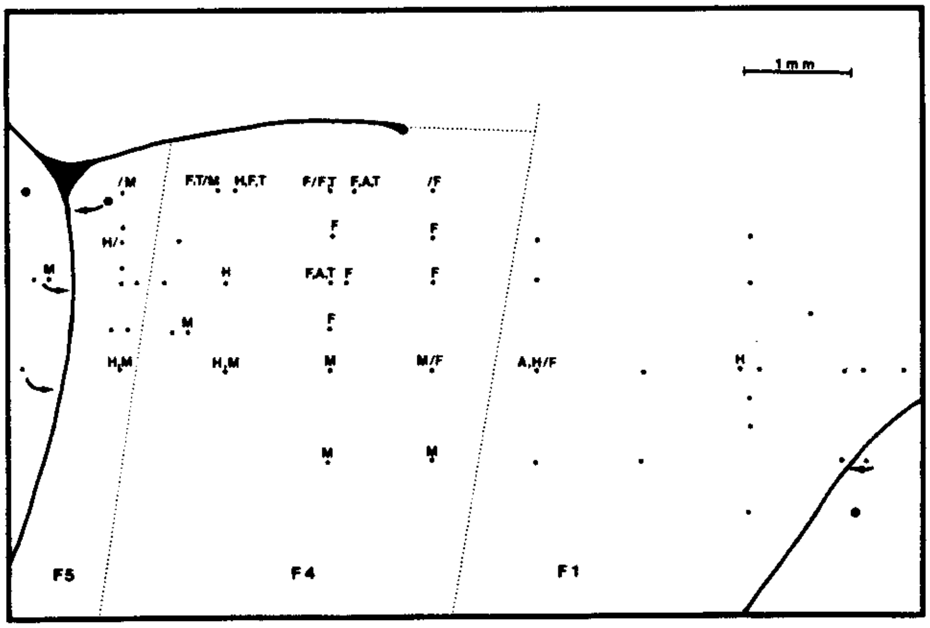

Fig. 5. Spatial distribution of penetrations where neurons responsive to tactile stimuli were recorded. The data are from monkey MK3. Conventions as in Fig. 2

of the penetration, those on the right side of the slash indicate the body part represented in the lower part of the penetration. Omission of symbols indicates the absence of neuron responses during active movements.

It is clear from the figures that there are two somatotopic representations in the cortex lying between the central and arcuate sulcus. The distal parts of the body are represented twice, a first time near the central sulcus and then again near the arcuate sulcus; the proximal parts are represented on the cortical convexity. The border between the two representations corresponds to the border between F1 and F4.

The rostral representation of distal movements roughly coincided with F5. This correspondence however was not perfect since distal movements were found also in the rostral part of F4. An important difference between the distal representation in F1 (area 4) and inferior area 6 was that whereas in F1 there was a clear segregation between the mouth and the hand field, the two representations partially overlapped in inferior area 6. However, also in this area there were points where only the hand or only

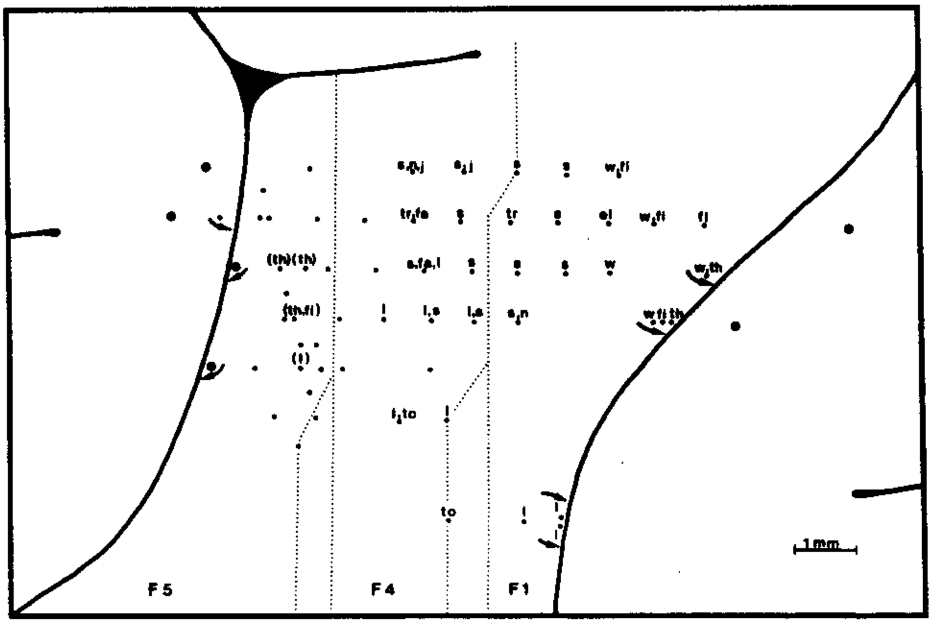

Fig. 6. Distribution of cortical loci responsive to electrical stimulation. The data are from monkey MK2. The letters indicate the jòint about which movement was elicited of face movements. Letters in brackets indicate that the movement was not constantly evoked by a current of 40 μA. El = elbow, fa = face, fi = fingers, j = jaw, l = lips, n = neck, s = shoulder, th = thumb, to = tongue, torsi = trunk, w = wrist. Other conventions as in Fig. 2

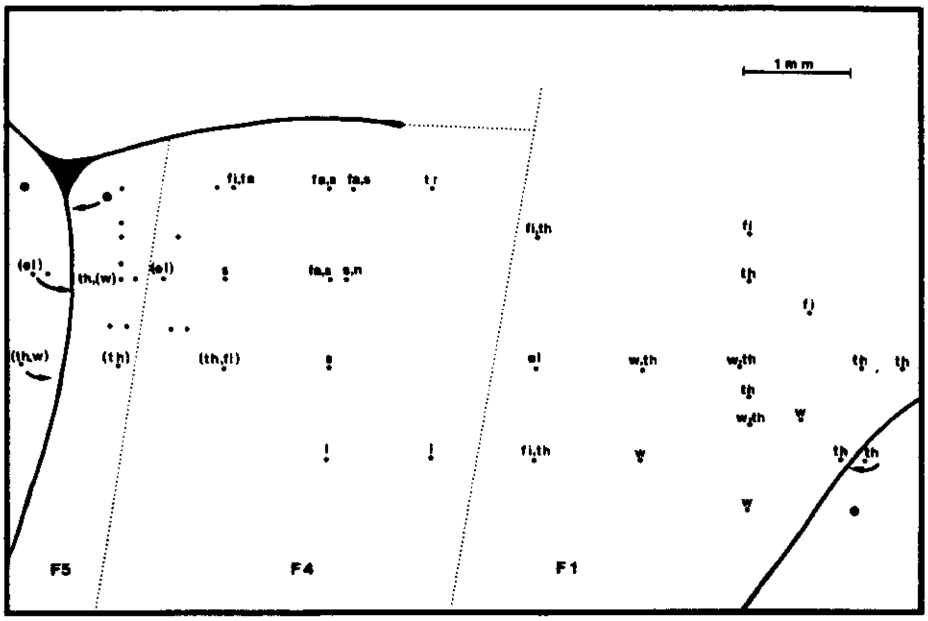

Fig. 7. Distribution of cortical loci responsive to electrical stimulation. The data are from monkey MK3. Other conventions as in Fig. 6

the mouth was represented. Pure mouth penetrations were located in the cortex lateral to that shown in the figures. This region was systematically explored in one monkey (MK1).

Figures 4 and 5 show the somatotopic organization of inferior area 6 as revealed by tactile responses of its neurons. In F1 only a limited number of cells responded to tactile stimuli, most neurons being activated exclusively by proprioceptive stimulation. In contrast, the responses to tactile stimuli were very strong in F4. Furthermore, unlike in F1, in F4 different body parts were frequently represented in the same penetration and at the same depth. For example, face and chest, or face and shoulder could be represented together. This never occured in F1. Finally, as one can see by comparing the maps obtained during active movements (Figs. 2 and 3) with those obtained with tactile stimulation (Figs. 4 and 5), arm is most represented in the former map, whereas face is the body part most represented in the latter map. This is due to the fact that many F4 neurons responded passively to stimulation of the

Table 1. Location of the receptive fields of F4 neurons

	Lip	Face	Face, neck chest and shoulder	Chest and shoulder	Chest and arm	Arm	Hand	Others	Total
Number of neurons	16 (15,5%)	47 (45,6%)	11 (10,7%)	7 (6,8%)	7 (6,8%)	7 (6,8%)	4 (3,9%)	4 (3,9%)	103 (100%)

face and actively to arm movements (see below). Thus the organization of movements representation in F4 is different and more complex than that in F1.

In the rostral part of F4 and in F5 strongly responsive tactile neurons tended to decrease and were substituted by neurons less easly triggerable by passive stimulation. Some of these neurons were activated by tactile stimuli, other by proprioceptive stimuli. In some penetrations only neurons firing during active movements were recorded. The body parts represented were the mouth and the hands.

The results of electrical microstimulation of area 4–6 complex are shown in Figs. 6 and 7. The excitable region included F1 and that part of F4 which responds well to tactile stimulation and where proximal movements are represented. In contrast, the rostral part of F4 as well as F5 were poorly or not at all excited with the currents used in these experiments. Out of 31 penetrations made in F5, only in one movements could be evoked with a current of 30 μA and in additional seven with a current of 40 μA.

The maps obtained with electrical stimulation were congruent with those based on neuron discharge during active movements. There was a clear shift from distal movements represented near the central sulcus to proximal movements represented on the brain convexity. This distal to proximal progression may give the impression of a single somatotopic map including area 4 and a part of area 6. However, the pattern of movements evoked by the electrical stimulation was more complex in F4 than in F1 (see Figs. 6 and 7). For example, in contrast to F1, arm movements were found to be frequently associated in F4 with other movements like face movements or neck movements. These various peripheral movements were obtained with similar or identical currents and were difficult or impossible to dissociate. Since neurons related to arm movements had frequently receptive fields located on the face, and, sometimes, were intermingled with neurons discharging during face movements, the movement pattern observed in F4 cannot be attributed to a spread of current. This pattern undoubtedly reflects the intrinsic organization of this area. Finally, the peripheral responses obtained from F5, although rare and inconstant, concerned distal movements. Thus the presence of a distal representation near the arcuate sulcus was confirmed also by the electrical stimulation.

Location and general characteristics of the recorded neurons

We have studied the functional properties of 542 neurons of area 4–area 6 complex. Of them 122 were related exclusively to the mouth, and 420 to the face, trunk, limbs and their movements. Neurons that responded both to limb and mouth movements were included in this last group. Pure mouth neurons were mostly recorded from one monkey (MK1; 98 cells) and their properties will be not described here. The remaining neurons were recorded from monkeys MK1 (N = 111), MK2 (N = 129) and MK3 (N = 186). 82 neurons were located in F1, 152 in F4 and 186 in F5.

Neurons recorded from area F4

The neurons recorded from area F4 can be subdivided into two main groups. The first is constituted of cells strongly responsive to tactile stimuli and (with few exceptions) related to proximal and facial movements. These neurons represent the great majority of cells encountered in a region of F4 which extends rostrally from the border of F1 almost to the border of F5 and laterally for about 4 mm from the spur of the arcuate sulcus. They will be referred to as F4 neurons. 103 neurons belonged to this group.

The second group is formed by neurons mostly related to distal movements. These neurons fire strongly during specific active movements and are usually less responsive than those of the first group to passive stimulation. They are located in a rostral strip near the border of F5. Twenty-four neurons belonged to this class. Since their properties are

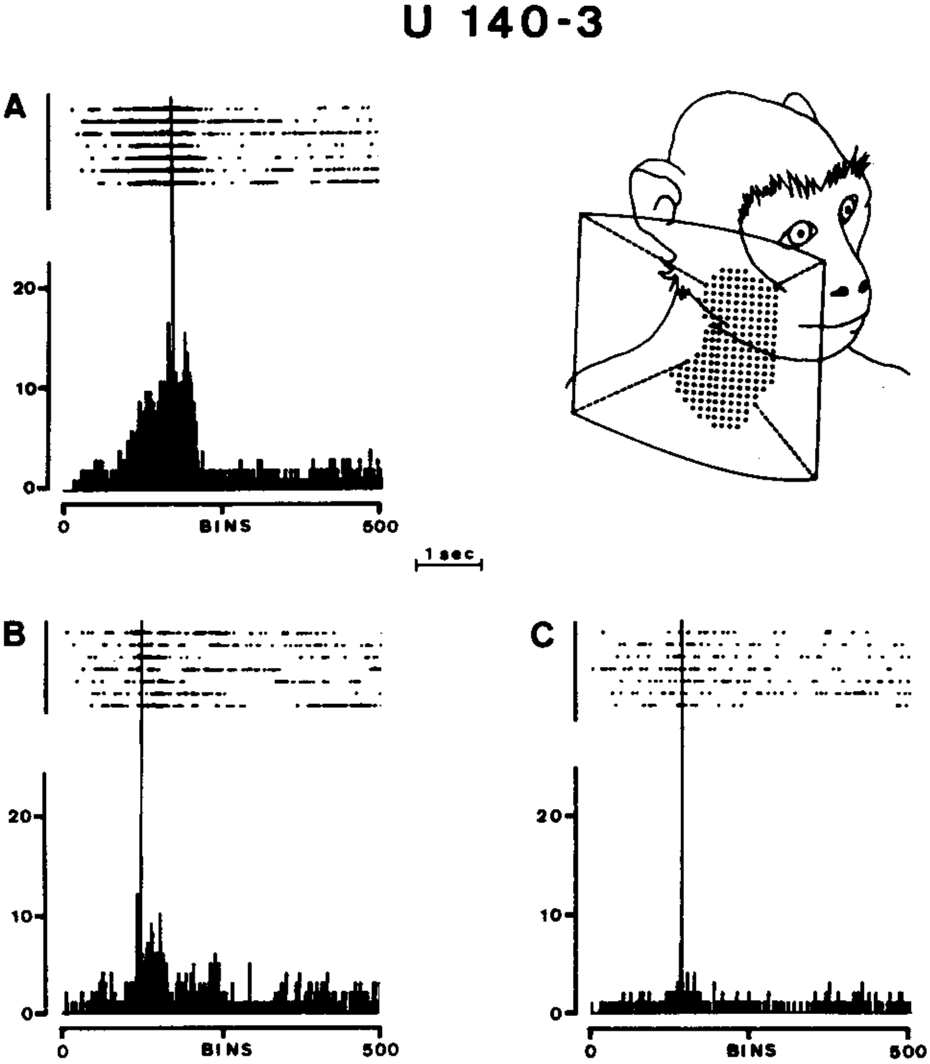

Fig. 8A–C. Study of passive properties of a F4 neuron. The neuron responded to visual and tactile stimuli. The tactile and visual receptive fields are shown on the upper right side of the figure. **A** Visual and tactile responses. The stimulus (a piece of cotton wrapped around the tips of a jeweller's forceps) was moved towards the tactile field. The vertical bar indicates the moment when the skin was touched. **B** Tactile responses of the neuron. The eyes were closed. The small response preceding the synchronization signal is due to the fact that this neuron responded when the stimulus bent the hairs, whereas the signal was triggered by the contact of the stimulus with the skin. **C** Stimulation of the peripersonal space and the face ipsilateral to the recorded side. The histograms are aligned with the moment when the skin was touched. All the histograms are the sum of 7 trials. Individual trials are shown above the histograms. Bin width: 10 ms

indistinguishable from those of F5 neurons they will be dealt with together with these neurons in the accompanying paper (Rizzolatti et al. 1988). In addition 16 neurons had properties similar to those of F1 neurons (see below), and 9 neurons had complex properties.

Passive properties of F4 neurons

F4 neurons responded very well to tactile stimuli. Hair bending, gentle touch of the skin or pressure of the skin evoked vigorous, highly repeatable responses. The receptive fields were usually large and included glabrous and hairy skin. Their size could vary from a few square centimeters to a large sector of the body surface. The location of the receptive fields of F4 neurons is shown in Table 1. Note the predominance of neurons partially or exclusively related to the face. The four cells of the column "other" had large receptive fields. In two of them the field included the face, arm, neck and chest, in one cell the receptive field was located on the neck and torso, and, finally, in one on the torso and legs. The majority of the receptive fields were contralateral (71%), 27% of them were bilateral and 2% ipsilateral. Six neurons were also activated by joint stimulation. These joints were the elbow (4 cells) and shoulder (2 cells). One of the neurons responding to elbow rotation was also activated by passive movements of the wrist.

Most F4 neurons discharged in response to visual stimuli (N = 88; 85%). With few exceptions (N = 4) they belonged to the category of peripersonal neurons. With this term we named (Rizzolatti et al. 1981c) those neurons that require, in order to be

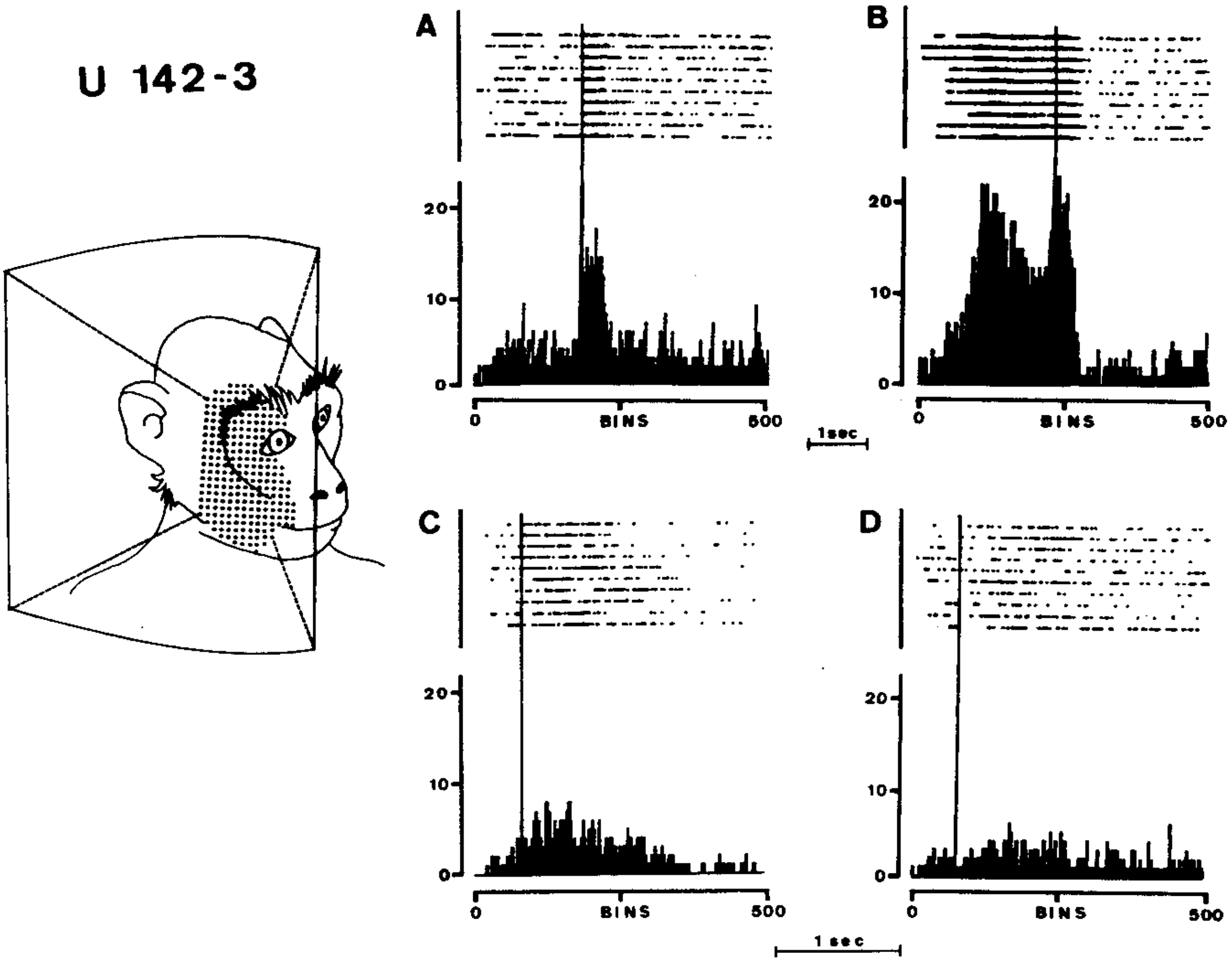

Fig. 9A–D. Study of passive properties of a F4 neuron. The visual and tactile receptive fields are shown on the left side of the figure. **A** Responses to the tactile stimulation of the contralateral face. The eyes were closed. **B** Visual and tactile responses of the neuron. The stimulus (the hand of the experimenter) approached the face of the animal, stopped at the distance of 2–3 cm from the skin for approximately 1 sec, then it touched the face. **C, D** Study of the visual responses of the neuron using the mechanical device described in Methods. **C** The stimulus (a piece of cotton) was moved towards the contralateral hemiface, in **D** towards the ipsilateral hemiface. **C, D** The histograms are aligned with a pulse signalling that the stimulus was 30 cm from the animal. All histograms are the sum of 10 trials. In **A, B**, the bin width was 10 ms; in **C, D** 5 ms

effectively driven, stimuli located in the space near the animal (peripersonal space). Among the peripersonal neurons some responded only to stimuli very close to animal's body (10 cm or less), others were triggered by stimuli located more distantly, but always within the animal's reaching distance.

Figure 8 (right side) shows the tactile and visual receptive field of one F4 neuron. The tactile field extended on face, neck and upper part of the chest. It was contralateral to the recorded side. The visual field was located around the tactile field. Its extension in depth was about 10 cm. The histogram in A shows the neuron responses to an object moved towards the animal. The histogram is aligned with the moment when the object touched the skin. Note the discharge preceding the tactile stimulation. In B the eyes were closed. In this condition only the discharge following the tactile stimulation is present. Finally, C shows that the stimulation of the peripheral space and skin ipsilateral to the recorded side was not effective.

Figure 9 illustrates the receptive field and the responses to tactile and visual stimuli of another F4 neuron. Tactile responses are shown in A, visual and tactile responses in B. In A and B the histograms were aligned with the moment when the skin was

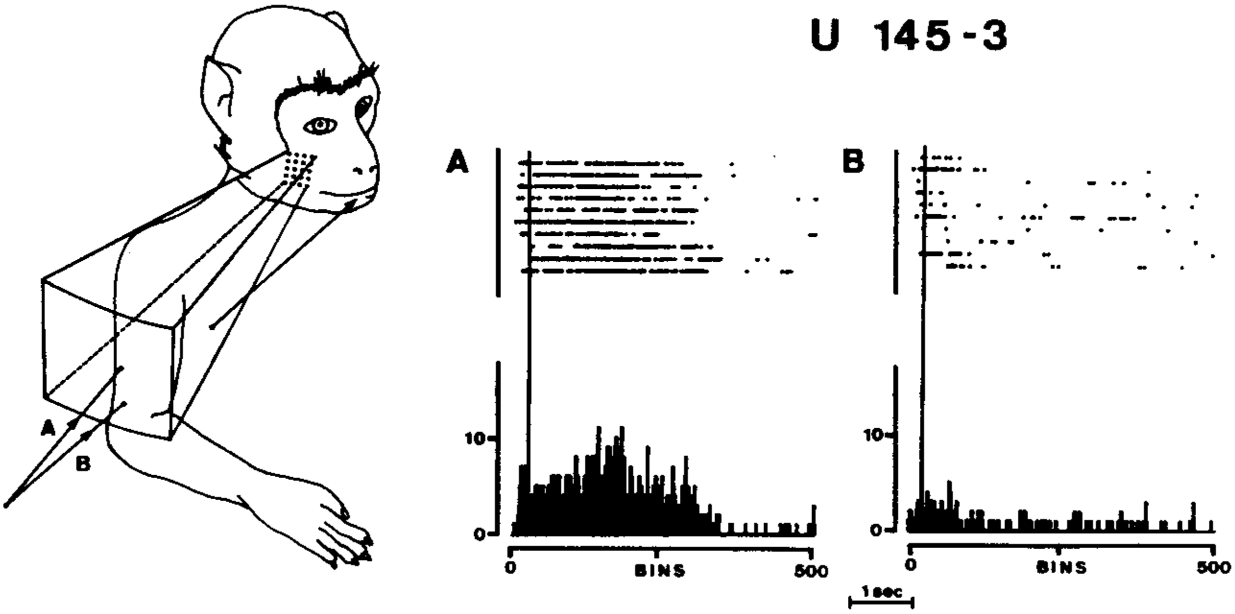

Fig. 10A, B. Study of visual properties of a F4 neuron. The neuron responded to visual and tactile stimuli. Its visual and tactile receptive fields are shown on the left side of the figure. The visual responses of the neuron were studied using the mechanical device described in Methods. **A** Neuron responses to stimuli moved towards the tactile field (trajectory A, left side of the figure). **B** Neuron responses to stimuli moved towards a part of the skin adjacent to the receptive field (trajectory B, left side of the figure). The histograms are aligned with a pulse signalling that the stimulus was 50 cm from the animal. The histograms are the sum of 10 trials. The bin width was 10 ms

touched. In C and D the visual responses of the neuron were studied using the mechanical device described in Methods. The advantage of this device is that it gives a measure of the distance of the stimulus from the monkey. The histograms can be, therefore, aligned with the electric pulse corresponding to the distance that fits best with the discharge onset and the depth of the receptive field can be delimited more objectively. In C the stimulus was moved towards the cutaneous receptive field, in D towards the correspondent part of the face contralaterally. For C the best response alignment corresponded to a distance of 30 cm from the monkey. No consistent response was found in D. Note that in C and D the time scale is different from that in A and B.

F4 neurons did not require particular visual stimuli and could be triggered very easily by any type of visual object. A piece of cotton wrapped around the tips of a jeweller's forceps, a piece of food or even the hand of the experimenter moved towards the animal could activate the neurons. Large stimuli were usually the most effective in the case of large fields. Besides approaching stimuli the wiggling of an object within the field was also usually effective.

Visual receptive fields were in register with tactile receptive fields. When the tactile field was bilateral, the visual field was also bilateral, whereas, when the tactile field was unilateral, visual responses could be elicited only from the correspondent part of the visual space. Furthermore, when the tactile field was located on the face, only stimuli moved towards the face were effective, whereas in the case of large fields including the chest also stimuli moved towards this part of the body triggered the neuron. Small deviations from the effective trajectory could influence dramatically the neuron response. An example is shown in Fig. 10. In A the stimulus was moved towards the tactile receptive field, in B it was moved towards an adjacent part of the skin. Note the marked difference in the intensity of the response in spite of the fact that the distance between the stimulus trajectories was relatively small.

Discharge of F4 neurons during active movements

Forty-eight out of 103 F4 neurons (47%) fired during active movements of the animal. Table 2 summarizes the effective types of movements. A comparison with Table 1 shows that, whereas face was the most represented body part as far as the passive responses are concerned, arm movements predominate among the active movements. Putting together all different types of arm movements, it turned out that 67% of neurons firing during active movements were related

Table 2. Movements represented in F4 neurons

	Arm reaching	Bringing to the mouth	Bringing to the body	Other arm movements	Hand movements	Facial movements	Neck movements	Total
Number of neurons	14 (29,2%)	9 (18,8%)	1 (2%)	8 (16,7%)	3 (6,3%)	12 (25%)	1 (2%)	48 (100%)

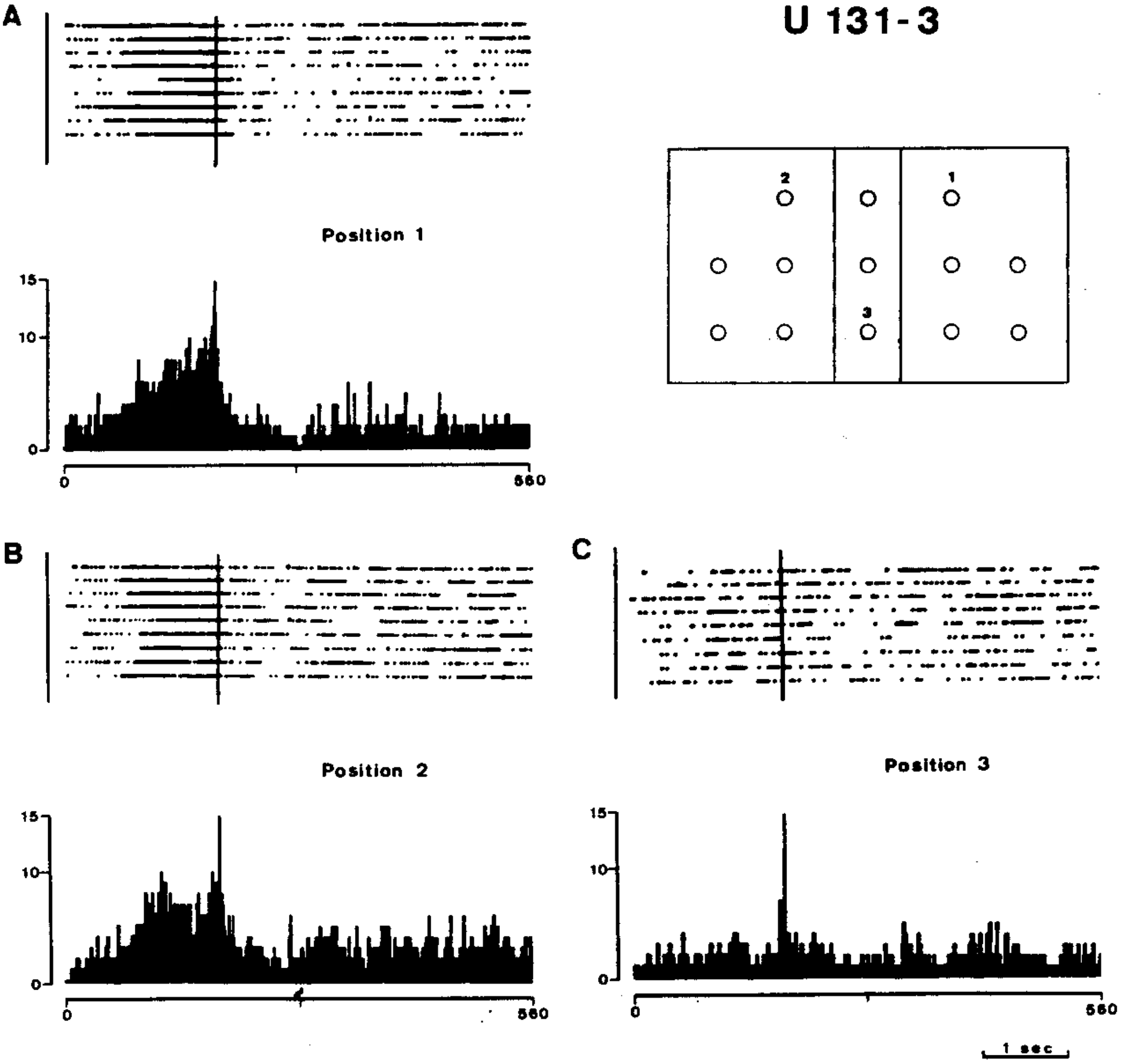

Fig. 11A–C. Study of a F4 "reaching" neuron. **A–C** Neuron responses to reaching movements towards stimuli presented in the position 1, 2 and 3 of the perimeter schematically represented in the upper right side of the figure. The monkey used the contralateral hand. The histograms are aligned with the moment when the hand touched the object. They are the sum of 9 trials. Bin width: 10 ms

to the arm. In contrast very few neurons were related to axial movements.

Figure 11 shows the responses of a typical reaching neuron. On the right side of the figure the testing perimeter is represented. The neuron discharged when the animal projected the arm towards points in the space above its shoulder (upper visual space; positions 1 and 2) whereas there was no response when the animal projected the arm towards points in the space below its shoulder (lower visual space; position 3). The discharge ceased immediately after the animal touched the object. All histograms are aligned with the moment when the animal touched the stimulus. Ten neurons showed a pattern similar to that described in the figure, 2 were activated by movements towards the contralateral upper quadrant, 2 by movements towards a large bilateral space around the body.

It is interesting to note that reaching neurons activated by movements towards the upper space as defined above had tactile receptive fields on the face (N = 9) or lips (N = 3) and visual receptive fields around the tactile ones, that is in the upper space. The two neurons which fired during movements not restricted to the upper visual space, had large tactile receptive fields on the body and large visual fields in register with them. The correlation between position of the tactile and visual receptive fields and direction of the effective movements was confirmed by the fact that, with only one exception, reaching units with bilateral fields (N = 11) were activated by movements towards the right and left space, whereas units with a contralateral field (N = 3) were activated by movements towards the correspondent part of the space. As far as the bilaterality of movement is concerned, 9 reaching neurons were activated by movements of both arms, 1 neuron by contralateral arm. In 4 neurons only the contralateral arm was tested.

A congruence between the position of the receptive field and the direction of the effective movements was present also in those neurons that fired when the animal moved the arm towards the mouth (N = 9) or the body (N = 1). The neurons that responded to movements toward the mouth had receptive fields on the lips and the peribuccal region, the neuron that fired during movements towards the body had a large receptive field which included the chest and the contralateral arm. Although we have not tested the specificity of the bringing to the mouth neurons in great details, nevertheless it was clear that none of them fired when the animal moved the arm towards the head or the body. All neurons of this group, including the one responsive to movements towards the body had visual receptive fields which were in register with the tactile ones. Five neurons fired during movements of either arm, 4 during movements of the contralateral arm and one neuron was tested only with the contralateral arm.

Finally out of 12 neurons triggered by facial movements, 10 had tactile receptive fields on the face and visual fields around the face. The remaining two neurons were inhibited during facial movements; their excitatory tactile receptive field was on the arm.

F4 neurons with complex properties

This is a small, heterogeneous group formed by nine neurons. Two of them were basically similar to the typical F4 neurons. They responded to tactile and visual stimuli and were activated by active proximal movements. However, unlike typical F4 neurons, they required in order to be triggered stimuli moved away from the animal. This was true for tactile stimuli, which evoked an "off" and not an "on" response, and for visual stimuli that were effective only when withdrawn from the animal. These neurons also fired during reaching movements, especially during fast arm projections towards an object.

The remaining neurons, although not identical to each other, had, as their main characteristic, the fact that they fired during specific distal movements provided that the arm was in a certain, usually extended, position. "Conditional neurons" of this type were also found in F5 (Rizzolatti et al. 1988).

Neurons recorded from area F1

Although the aim of this work was to study inferior area 6 neurons, it was of interest to have also a sample of neurons from area F1 (area 4). As far as the active movements are concerned, the large majority of F1 neurons (N = 66) fired in relation to specific simple movements of different parts of the body (see Lemon et al. 1976). Fifty neurons were related to distal movements (finger N = 45, wrist N = 5), 16 were related to axio-proximal movements (elbow N = 3, shoulder N = 8, axial movements N = 5). As far as the passive properties are concerned, in sharp contrast with neurons found in F4, very few F1 neurons could be activated by tactile stimuli. Seventeen neurons (26%) did not respond to any passive stimulation, 45 (68%) responded to rotations of joints and/or pressure on muscles or tendons and, finally, only 4 (6%) responded to the touch of the skin.

A surprising observation was that many F1 neurons fired during movements of either hand. Bilaterality of F1 neurons was systematically tested in monkey MK3. Out of 37 recorded neurons, all related to distal movements, 22 fired during movements of both hands, 15 during those of the contralateral hand. Although bilateral neurons in the rostral part of area 4 have been described (Wannier et al. 1986), the percentage of bilaterral neurons we found in MK3 was remarkably high. However, since our sample is based on a small number of penetrations, located outside the anterior bank of the central sulcus, this percentage should be considered with caution. Neurons with same properties are usually clustered together and the probability of a biased sample is high when the number of penetrations is limited. The fact, however, remains that bilateral neurons are present in area F1 outside the anterior bank of the central sulcus and it is not unlikely that their number in this specific location has been underestimated in the past.

The remaining F1 neurons (N = 16) were characterized by a greater complexity than those described above. Three neurons fired during active hand movements, but responded also to passive stimulation of the mouth; 7 discharged during finger movements but responded also to rotation of proximal joints and finally 6 neurons, beside being activated by proprioceptive stimuli, responded to approaching visual stimuli.

Discussion

According to the classical stimulation experiments there are two movement representations in the agranular frontal cortex, one corresponding to the precentral gyrus, one corresponding to the medial wall of the hemisphere (Penfield and Welch 1951; Woolsey et al. 1952). Our data show that a third map exists in inferior area 6. In this map axio-proximal movements are localized caudally, adjacent to the axio-proximal movements of F1, distal movements are localized rostrally near the arcuate sulcus. The mouth field is represented laterally, the hand field medially. There is no leg field. The segregation, however, between the various movement fields is not so precise as in area 4. For example, in the hand field many neurons discharge also with mouth movements, and in the arm field, the face is also represented. Thus, the movement representation is less discrete in area 6 than in area 4, and the movements represented in it have complex characteristics.

The inferior area 6 map is formed by a proximal movement representation and a distal movement representation. A first argument in favour of a distal representation in area 6 has been presented some years ago by Rizzolatti et al. (1981a, b) on the basis of the somatosensory responses of neurons of the postarcuate cortex (F5 in our present terminology). Since those experiments were carried out in curarized monkeys it has been objected (Weinrich et al. 1984) that the observed neuronal responses could be due to attempts of the animal to withdraw the stimulated arm and therefore to the activity of proximal neurons. This objection is rather weak. Against it there are two observations: first, the cutaneous area (receptive field) from which the neuronal responses were obtained remained constant during the recording of a given neuron, second the position of this area changed when the electrode was placed in a new position. These results could be attributed to the animal's withdrawing movements only if one postulates that the monkey changed movement every time the experimenter changed the recording position. A possibility which does not seem to be very likely.

The correctness of the observations of Rizzolatti et al. was confirmed by Kurata and Tanji (1986). They conditioned two monkeys to move their arms to various preset positions and, when the required position was reached, to press a key. This procedure allowed them to dissociate proximal and distal movements. They found that neurons related to distal movements do exist in area 6 and that they are located in its rostral part. The data presented in the present paper closely agree with these findings.

In addition to pyhsiological evidence, anatomical data also support the notion that distal movements are represented in F5. Injections of tracers in the hand field of area 4 give selective labelling in that part of area 6 where physiologically the hand is represented (Matsumura and Kubota 1979; Muakkassa and Strick 1979; Godschalk et al. 1984; Matelli et al. 1986; Strick 1985). Thus the presence of a distal representation in area 6 is now demonstrated beyond any reasonable doubt.

The problem of a proximal representation in area 6 is quite different. The presence of this representation has always been accepted (see Humphrey 1979), but the general belief was that this representation is an extension of that, mostly related to distal movements, of area 4 (Woolsey et al. 1952).

This conclusion is unavoidable if one uses the electrical excitability of the agranular cortex as the only criterion for the parcellation of the agranular cortex. The representations of proximal movements in F1 and F4 are contiguous and the greater complexity of those evoked from F4 may be considered an insufficient evidence to separate functionally the two areas. This separation, however, becomes obvious when the properties of the neurons of the two areas are taken into consideration.

Typically, F1 neurons, or at least those on brain convexity, respond to proprioceptive stimuli, discharge vigorously during active movements, are not triggered by visual stimuli and their input-output organization concerns one or few adjacent joints (Lemon and Porter 1976; Lemon et al. 1976; Phillips and Porter 1977; Wong et al. 1978). In contrast, F4 neurons respond to tactile stimuli, are activated by visual stimuli (in addition to our data see Godschalk et al. 1981) and their input-output relationship is very complex, frequently involving different body parts. Thus the difference between the two areas is quite clear.

Visual responses in F4 are very peculiar. Unlike classical visual neurons, F4 neurons do not respond or respond poorly to light stimuli (Rizzolatti et al. 1981c). In contrast, they require to be triggered real objects moved near the animal in its peripersonal space (Rizzolatti et al. 1981c; Gentilucci et al. 1983). The visual receptive fields of F4 neurons are in register with their tactile receptive fields and, as shown by Gentilucci et al. (1983), this relation does not change when the eyes change position. Recent data indicate that similar independent-of-eye-position neurons also exist in the cat, in an area, the ventral bank of the cruciate sulcus, which probably corresponds to one of the subareas of the monkey area 6 (Pigarev and Rodionova 1986). Thus, neurons whose visual fields are coded in terms of body coordinates and not in terms of retinal coordinates appear to be a constant feature of the premotor organization in various animal species even phylogenetically distant as carnivores and primates.

The problems of the cues that allow the neurons to recognize the stimulus position in respect to the body is an open question and our data do not add much to their solution. Something however can be said about the function of these bimodal neurons. Our original proposal, based on findings in curarized animals was that their function is essentially predictive (Rizzolatti et al. 1981c). Before a stimulus touches the animal, information is provided on the fact that the stimulus will touch it and an adequate response can be prepared in advance. This hypothesis fits well with the properties of those neurons whose input and output are closely linked as, for example, neurons which fire during active face movements and respond to stimulation of the face and the space around it. For those neurons, however, in which the visual receptive field is anchored to a certain part of the body but where the effective active movement concerns another body part, this simple predictive function does not seem to be sufficient to explain the neuron properties. In this case the prediction of an event appears to change in a more general indication of where the stimulus is located. For example, in the case of reaching neurons that have a tactile field on the face, a visual receptive field in the upper space and that discharge during arm active movements towards the upper space, the neuron response to visual stimuli does not signal only that the stimulus will touch the face, but provides, in addition, spatial information on where the stimulus is located so that the arm movement can be properly organized. In this way a new, spatial dimension is added which is necessary for the organization of proximal movements. These data show also that spatial information is available not only to neurons of posterior parietal lobe (Hyvärinen 1982; Lynch 1980) but is present also in the part of frontal lobe connected with it.

Whereas it is impossible to deny that an independent movement representation exists in inferior area 6, the notion that its two parts – F4 and F5 – form a single functional region can be challenged. It may be argued that, since the part of area 6 where proximal movements are represented is excitable while that where distant movements are represented is not, it is arbitrary to unify them in a single representation. Especially so since according to some anatomical data (Künzle 1978; Murray and Coulter 1981), the posterior bank of the arcuate sulcus (area F5) has little or no cortico-spinal projections, whereas F4 contributes in a substantial way to the cortico-spinal system. Obviously, the choice of criteria for area 6 subdivision is a rather subjective matter, nevertheless some recent anatomical data appear to remove what was the major obstacle for the unification of the two subareas in one functional area, their different output organization. Toyoshima and Sakai (1982) and Martino and Strick (1987) have demonstrated that a projection to the spinal cord originates also from the posterior bank of the arcuate sulcus. Surprisingly enough, however, the hand field is not connected with the cervical enlargement of the spinal cord but with its upper cervical segments, that is with the part of the spinal cord which controls proximal arm movements (Martino and Strick 1987). This paradoxical finding may be explained by postulating that in the monkey there is a proprio-spinal system similar to that described in the cat by Lundberg and his coworkers (Illert et al. 1976, 1977; Alstermark et al. 1981) and that the distal movement commands are conveyed from inferior area 6 to the related spinal motor neurons via a polysynaptic pathway. This hypothesis would explain why area F5 is poorly excitable in spite of direct connections to the spinal cord. Secondly, it would explain why the peripheral movements observed after F5 stimulation concern, when present, the distal segments of the upper extremities and not the proximal segments as one would expect from the anatomical termination of the cortico-spinal-pathway. Regardless of whether this interpretation is correct or not the fact remains that F5 is connected with the spinal cord and, therefore, the argument that F5 has an output organization radically different from F4 looses its strength.

A final point which deserves some comments concerns the global organization of area 6. New data on the cytoarchitecture and myeloarchitecture of this area have recently confirmed the correctness of its subdivision into an inferior and a superior part and showed that the superior part is constituted by two sectors, one rostral (6DR) and one caudal (6DC) (Barbas and Pandya 1987). When the electrical stimulation maps (Woolsey et al. 1952) are matched with these anatomical subdivisions of superior area 6, it turns out that 6DC is electrically excitable whereas 6DR is not. Furthermore, as in inferior area 6, the electrically excitable part is related to proximal movements, although, in the case of superior area 6, of the lower limb. Considering these facts, it is attractive to postulate that the same organization principle is valid for superior and inferior area 6, and that also in superior area 6 and precisely in 6DR there is a representation of distal movements. It is obviously impossible to predict whether this putative movement representation concerns exclusively the foot movements or whether there is in it an integration between movements of the upper and lower extremities as it occurs in inferior area 6 for hand and mouth movements. These speculations, however, may be useful for future experiments aiming to solve the problem of the functional role of superior area 6.

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Experimental Brain Research

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

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Offprint requests to: G. Rizzolatti (address see above) 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 cervial 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).

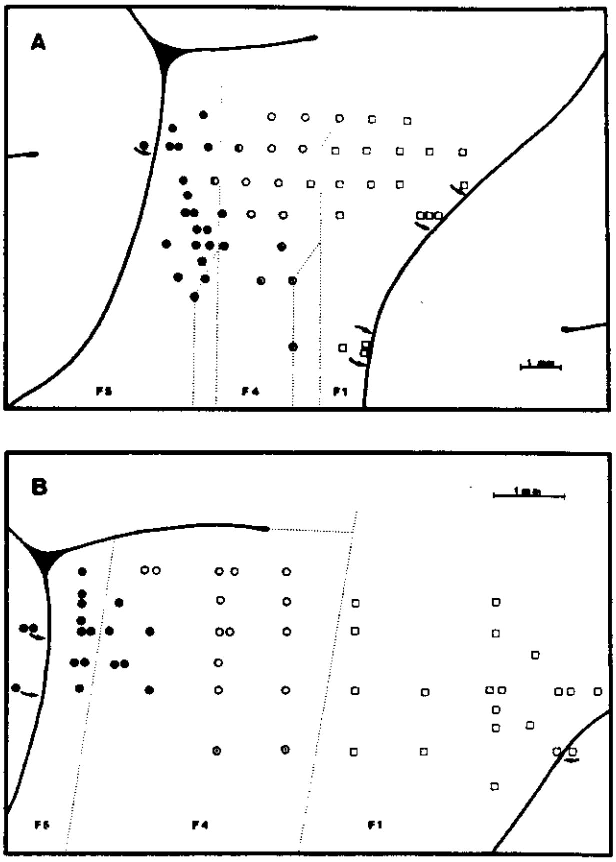


Fig. 1A, B. Spatial distribution of F5, F4 and F1 (primary motor cortex) neurons. **A, B** Show the inferior part of left frontal agranular cortex of monkey MK2 and MK3. The dashed lines separate the histochemical areas F1 (area 4), F4 and F5. Unmarked areas between F1 and F4, and F4 and F5 are transition 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

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 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 majoritiy 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

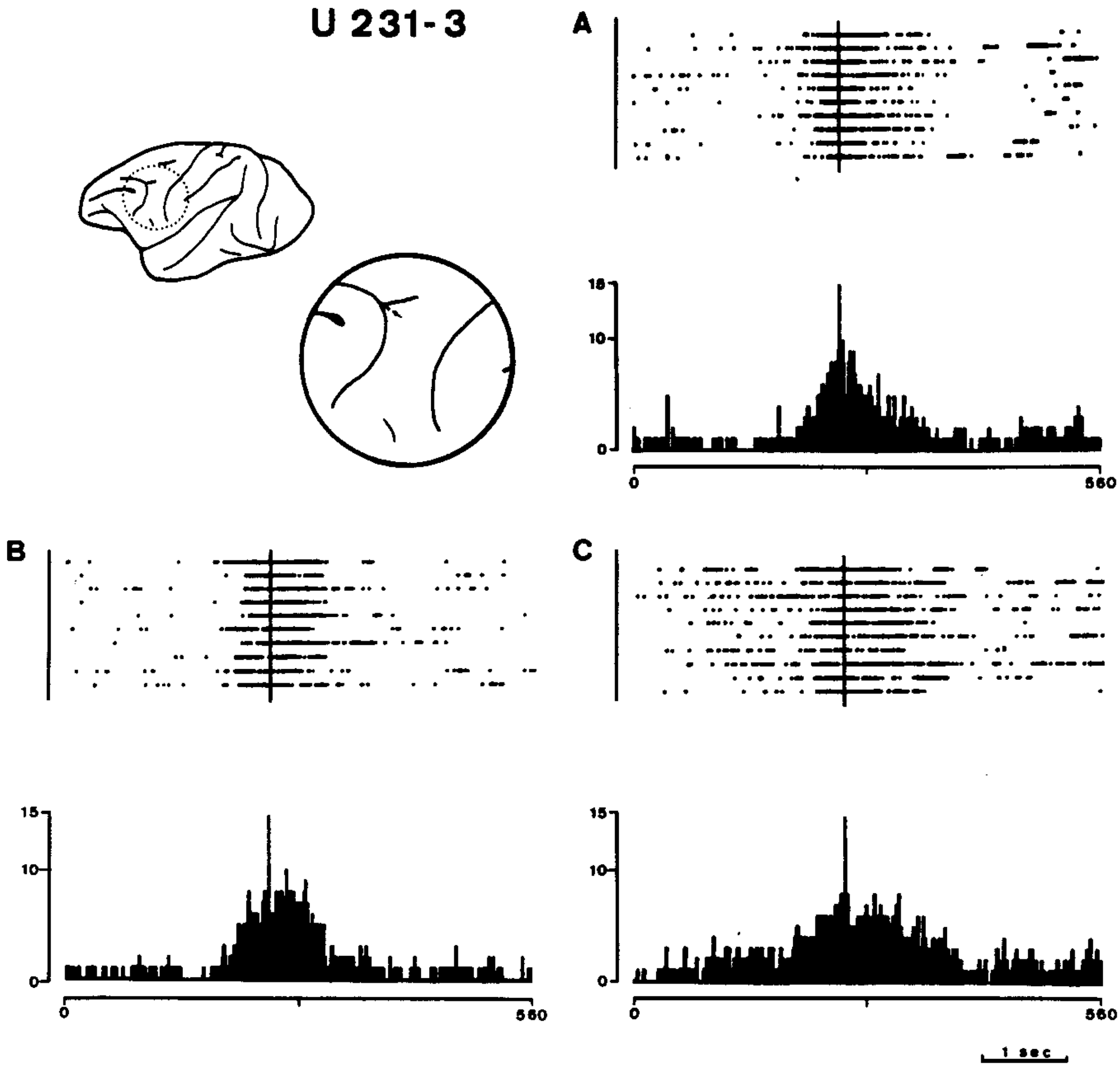


Fig. 2A–C. Study of “Grasping-with-the-hand-and-the-moth” neuron. On the left side of the figure a lateral view of the monkey brain is shown. The arrow indicates the location of the penetration in which the neuron was recorded. **A** Neuron discharge during grasping with the mouth. **B** Neuron discharge 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

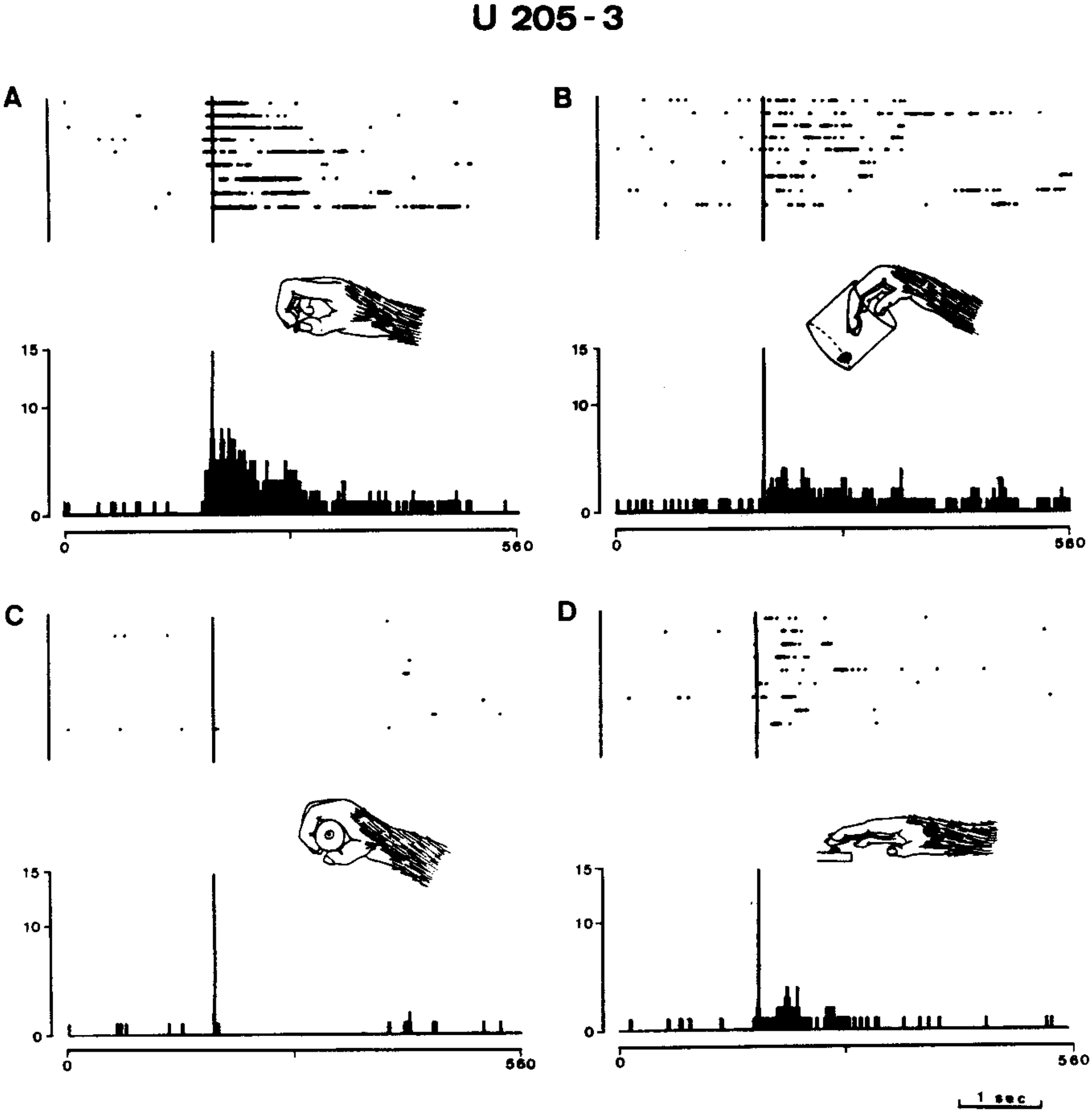


Fig. 3A–D. Study of a "Grasping-with-the-hand" neuron. **A** Neuron discharge during precision grip. **B** Neuron discharge during finger prehension. **C** Neuron discharge during whole hand prehension. **D** Neuron discharge during index flexion. In all trials the contralateral hand was used. The histograms 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

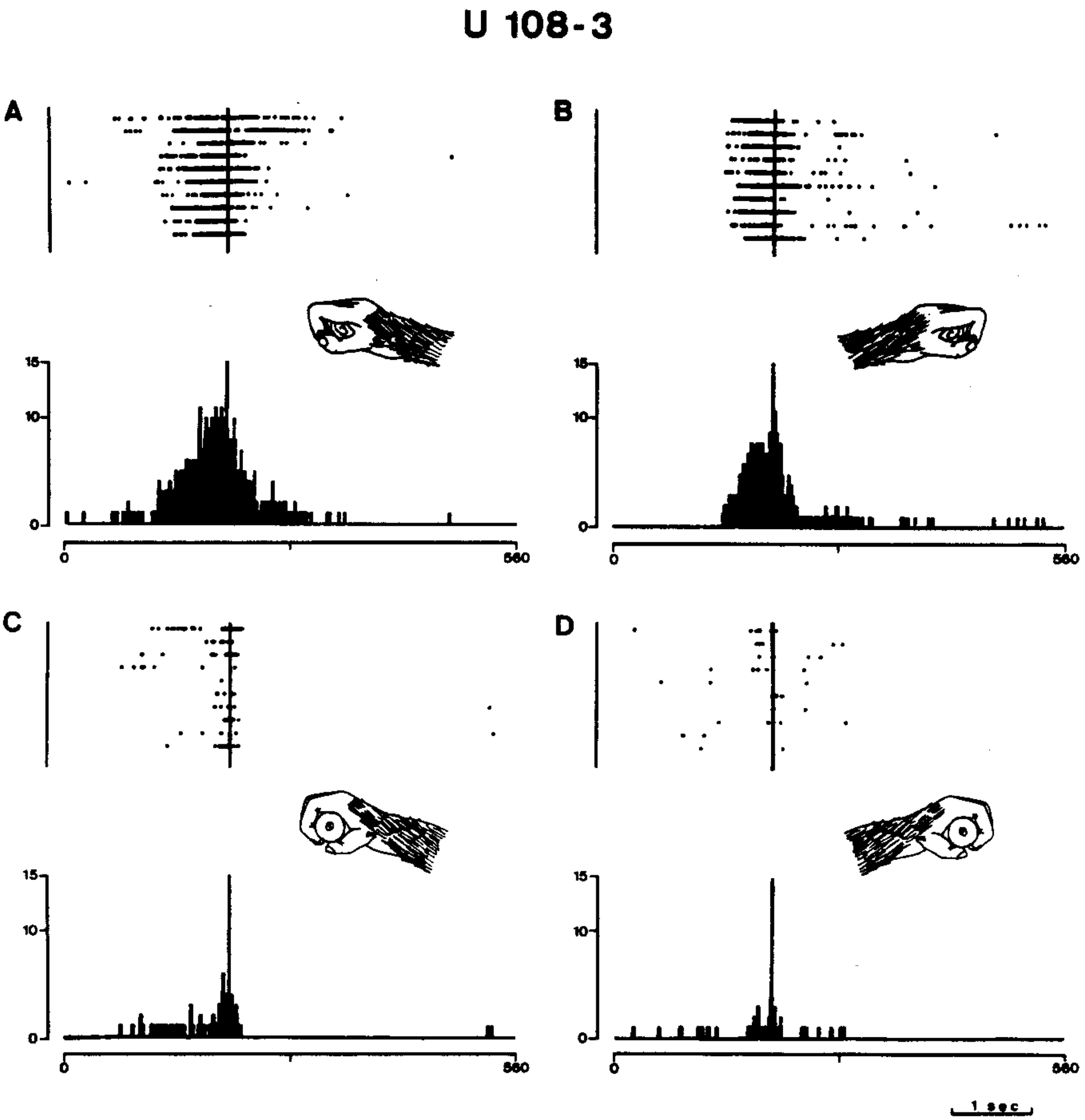


Fig. 4A–D. Study of "Grasping-with-the-hand" neuron. **A, B** Neuron discharge during precision grip. **C, D** Neuron discharge during whole hand prehension. The neuron was tested during contralateral (**A, C**) and ipsilateral (**B, D**) hand movements. The histograms are the sum of 10 trials. Other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

grip neuron whose response was not modified by the wirst 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

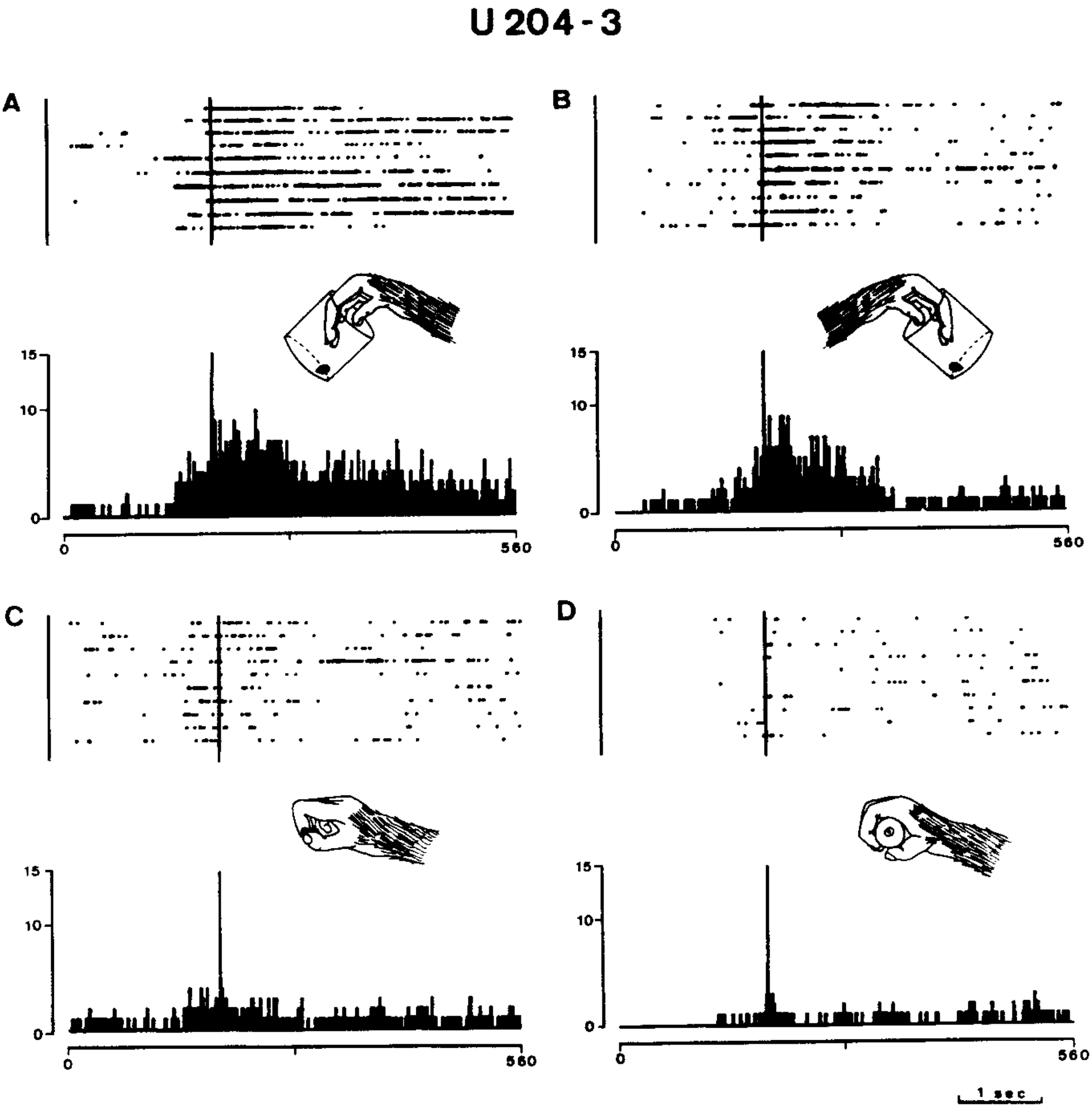


Fig. 5A–D. Study of "Grasping-with-the-hand" neuron. **A, B** Neuron discharge during finger prehension with the contralateral and ipsilateral hand respectively. **C** Neuron discharge during precision grip. **D** Neuron discharge during whole hand prehension. The testing in **C** and **D** was carried 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

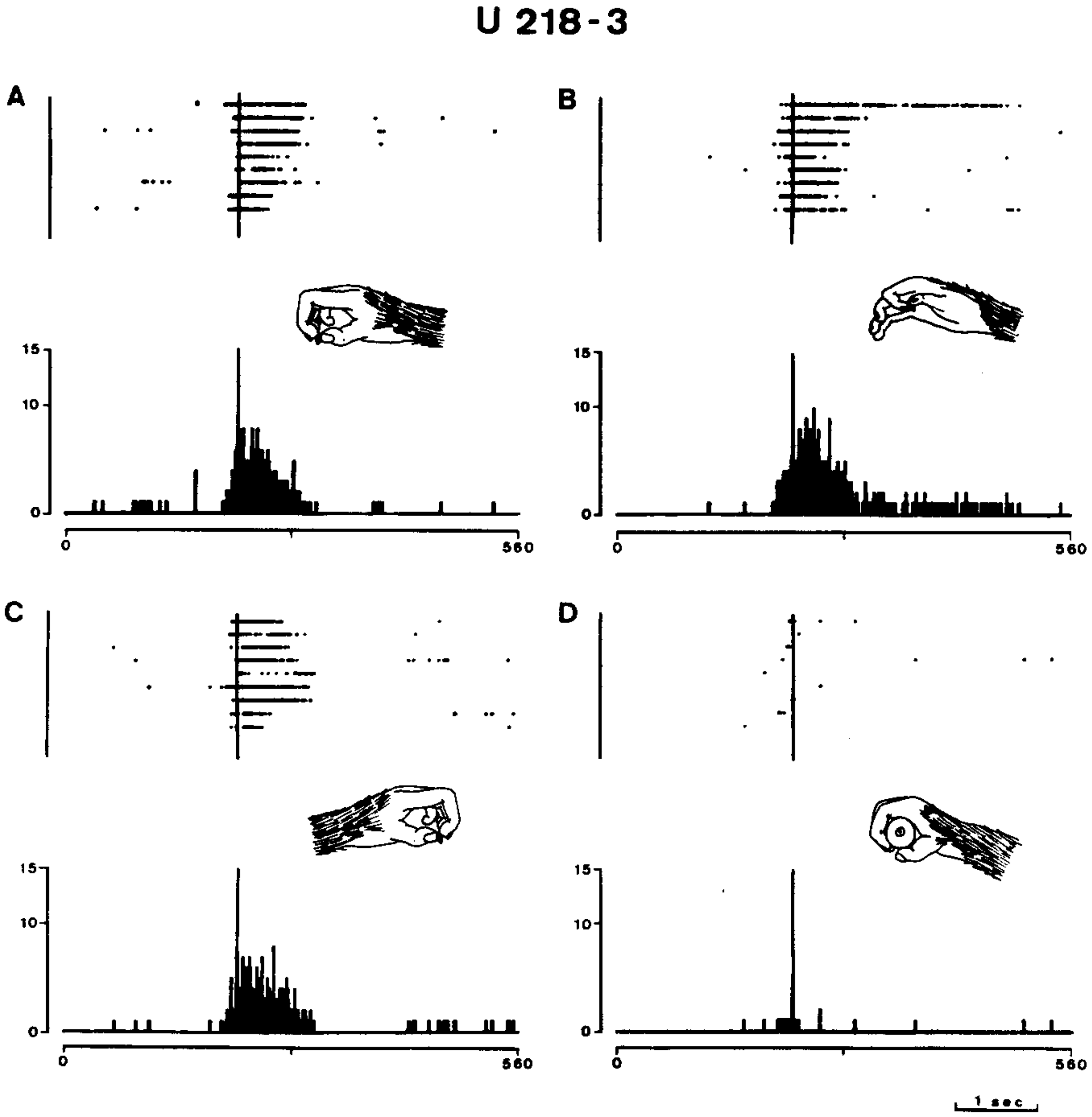


Fig. 6A–D. Study of a "Grasping-with-the-hand" neuron. **A, B** Neuron discharge during precision grip with the contralateral hand. In **B** the wrist was oriented at 90° in respect to **A**. **C** Neuron discharge during precision grip with the ipsilateral hand. **D** Neuron discharge during whole hand 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	
	N	(%)	*N*	(%)	*N*	(%)	*N*	(%)	*N*	(%)
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	
	N	(%)	*N*	(%)	*N*	(%)	*N*	(%)
Grasping-with-the-hand-and-the-mouth-neurons	17	(39)	8	(19)	18	(42)	43	(100)
Grasping-with-he-hand-neurons	18	(29)	29	(48)	14	(23)	61	(100)
Total	35	(34)	37	(35)	32	(31)	104	(100)

movements occured, 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

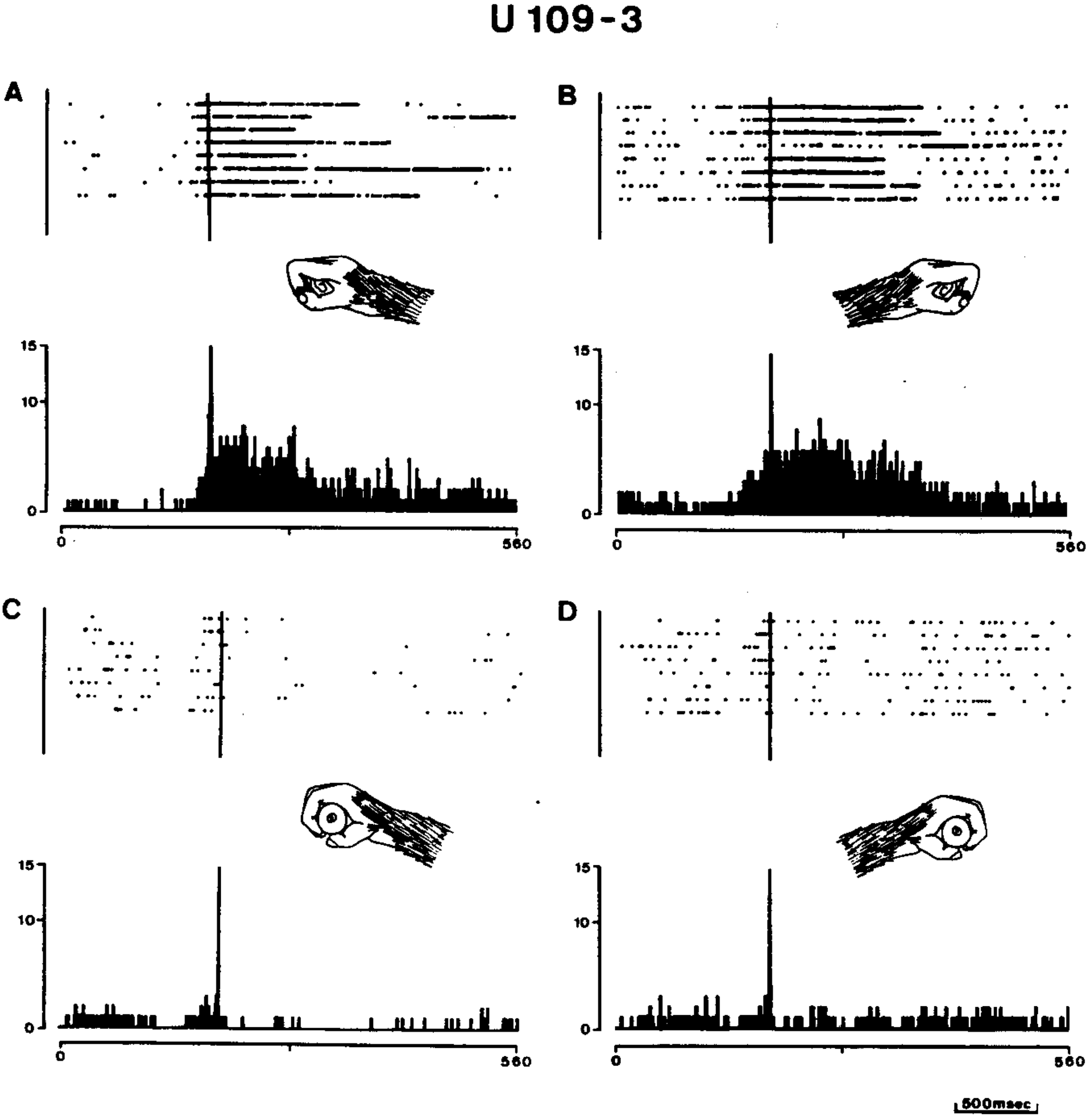


Fig. 7A–D. Study of a "holding" neuron. **A, B** Neuron discharge during holding with the thumb and index finger of the contralateral and ipsilateral hand. **C, D** Neuron discharge during holding with the whole hand. The contralateral hand was used in **C**; the ipsilateral one in **D**. The histograms 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 verly 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; Weinrich 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.

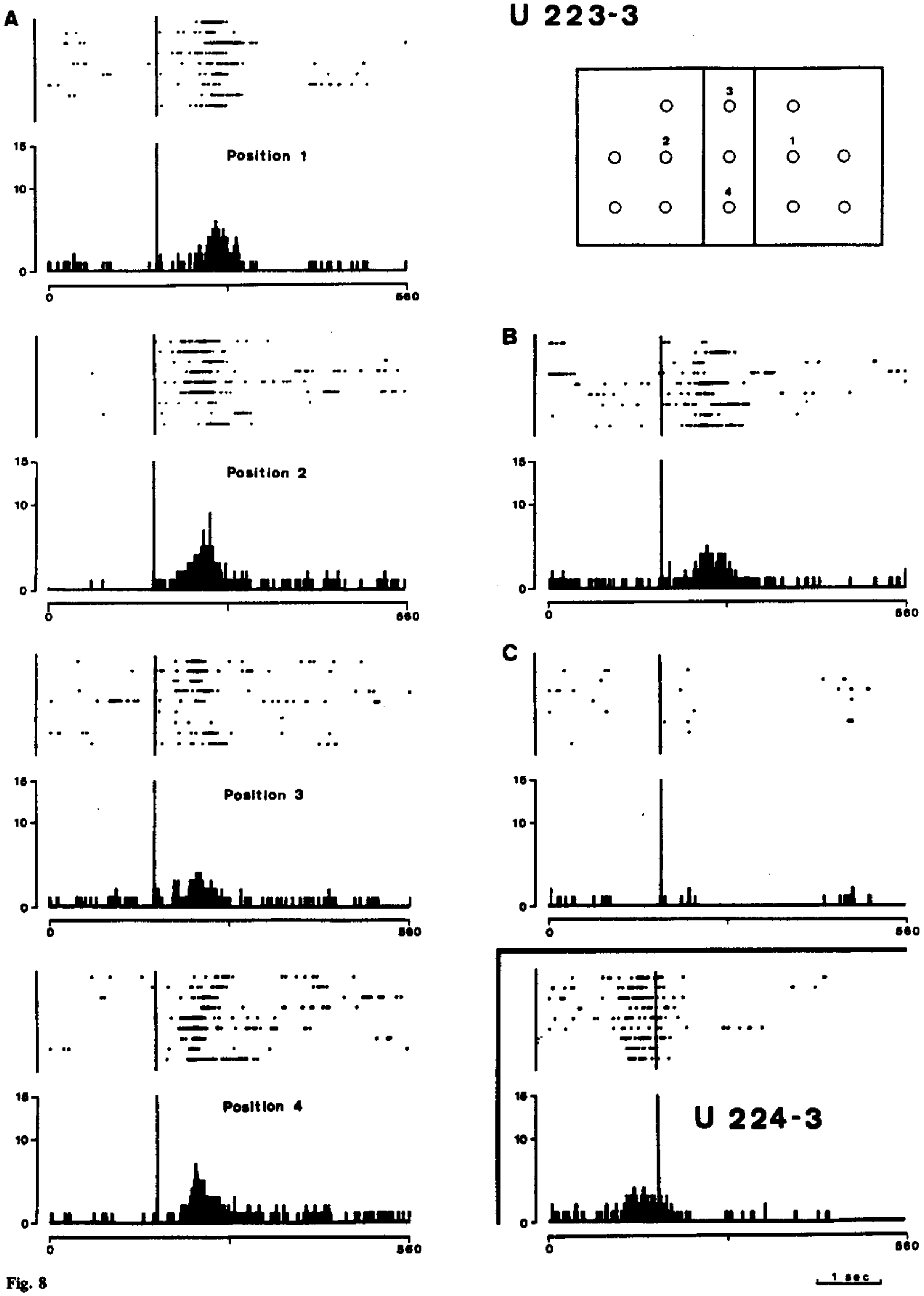
F5 neurons discharging with proximal movements

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


A
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3
2
1
4
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Position 3
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Fig. 8

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 complexitiy 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 cortico-motoneuronal 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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