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FUNCTIONAL PROPERTIES OF MONKEY MOTOR CORTEX NEURONES RECEIVING AFFERENT INPUT FROM THE HAND AND FINGERS

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SUMMARY

1. Records have been made from area 4 of the cerebral cortex in five conscious monkeys. The properties of 216 neurones responsive to natural stimulation of the hand and fingers have been investigated.

2. 46% of these neurones responded only to cutaneous stimulation (especially light brushing across the glabrous skin) and a further 38% responded only to movement of the digits. 4% responded to brief prods of the hand. 12% of the sample responded to more than one stimulus modality.

3. Many hand-input neurones, including pyramidal tract neurones, responded at short-latency (8–15 msec) to light mechanical stimulation of the hand and to weak electrical stimulation of the median nerve.

4. Responsive neurones were found at all depths of the cortical grey matter. Responses of shortest latency were encountered in neurones probably located in layers IV and V.

5. The behaviour of eighty hand-input neurones was analysed during a simple, stereotyped task which involved pulling a lever and collecting a food reward from a small well. For comparison, the activity of 117 neurones with inputs from the wrist, elbow or shoulder was also analysed.

6. Nearly all hand-input neurones modulated their activity either before (48/80) or during (29/80) the retrieval of the reward which required precision grip between index finger and thumb. Many were silent during proximal arm movements and some displayed activity patterns independent of these movements.

7. By contrast, the activity of many neurones with proximal arm (elbow, shoulder) inputs was unrelated to food retrieval and manipulation, but well related to arm movements.

8. Forty-three of the eighty neurones had cutaneous input from the hand. Twenty-seven were active before hand contact. Thirty-five modulated their discharge when contact was made (twenty-one excitation, fourteen inhibition).

9. Most hand-input neurones were more active during fractionated movements of the hand or fingers than during power or ball grips requiring simultaneous flexion of all digits. Neurones with glabrous inputs often showed intense activity during small, precise finger movements and during active tactile exploration without the aid of vision.

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10. Analysis of the discharge frequency of twenty-five hand-input neurones revealed that some (mainly non-pyramidal tract neurones) had a similar mean frequency and range of modulation during both active movement and passive stimulation. Others (mainly pyramidal tract neurones) had a greater frequency range and higher mean frequency during active than during passive movements.

INTRODUCTION

There is now plentiful evidence that the motor cortex in the primate is of fundamental importance for the performance of fine hand and finger movements. Destruction of the motor cortex or pyramidotomy results in a permanent deficit of such movements, while other limb movements recover (Lawrence & Kuypers, 1968; Brinkman & Kuypers, 1973). Infant monkeys subjected to pyramidotomy never develop the capacity to execute relatively independent movements of the fingers (Lawrence & Hopkins, 1976). It is known that there are direct monosynaptic connexions from the motor cortex to spinal motoneurones in monkeys, apes and man, animals which possess the ability to produce fractionated finger movements, while they are lacking in animals such as cat and dog which do not possess the capacity for relatively independent finger movements (Kuypers, 1973). These direct cortico-motoneuronal connexions are preferentially distributed to motoneurones supplying distal motoneurones (Kuypers, 1960) where they exert powerful e.p.s.p.s (Phillips & Porter, 1964; Clough, Kernell & Phillips, 1968; Porter, 1970).

Despite the unique relationship between hand and motor cortex, most chronic studies have concentrated on natural activity in the motor cortex during wrist or elbow movements. Compared to the varied motor repertoire of the hand, the nature of movement at these more proximal joints is restricted and this has enabled controlled analysis of the relationship between activity in the motor cortex and the performance of a simple movement, such as flexion and extension of the wrist or elbow (Evarts, 1968; Conrad, Matsunami, Meyer-Lohman, Wiesendanger & Brooks, 1974; Humphrey, Schmidt & Thomson, 1970). This approach allows an exact description of the events in the motor cortex related to different parameters of the simple movement (Thach, 1978). Such studies are more difficult to apply to the hand and fingers because of the great variety of possible movements and postures. Indeed, the versatility of the movements of the primate hand make it an intriguing possibility that the characteristic features of these different movements may be reflected in the activity of the motor cortex.

The approach employed in the present study extends previous observations (Lemon, Hanby & Porter, 1976) and examines in a semiquantitative manner the 'motor field' of motor cortex neurones by analysis of their activity during a variety of movements. Recent studies have described the powerful peripheral afferent input to the primate motor cortex (Rosén & Asanuma, 1972; Lemon & Porter, 1976; Wong, Kwan, MacKay & Murphy, 1978) and there is a strong relationship between afferent input to a motor cortex neurone and its activity during natural movement (Lemon *et al.* 1976; Evarts & Fromm, 1977). Therefore the natural activity of neurones with identified inputs from the hand and fingers was studied, and compared with that of neurones with inputs from other arm regions.

Preliminary results from this study have been reported elsewhere (Lemon, 1979).

METHODS

Training. Five monkeys (two *Macaca multatta*, one *Macaca nemestrina* and two *Macaca fascicularis*) were used. They were trained to extend the right arm and grasp a knob attached to a horizontal spring-loaded bar and to pull the bar about 15–25 mm into a fixed target zone (see Fig. 4). This required a 4–6 N. force. For convenience, the manipulandum is referred to as a lever. A correct pull of the lever produced an auditory cue and food reward. The monkeys were also trained to accept natural stimulation of their limbs without struggling.

Implant operation. When fully trained, the monkey was deeply anaesthetized with penthrane and thiopentone and a headpiece (Porter, Lewis & Linklater, 1971) was attached to the skull by stainless-steel bolts. A craniotomy was made on the left side and the positions of the central and arcuate sulci measured. A cylinder 22 mm in diameter was mounted over the exposed area, which was protected by a thin silastic membrane. The cylinder was positioned so as to allow electrode penetrations normal to the surface of the motor cortex hand area. Stimulating electrodes were implanted in the upper medullary pyramidal tract in two monkeys. For exact location, the penthrane anaesthesia was lightened until weak reflexes were present. The electrodes were then fixed at loci which yielded flick-movements of the contralateral digits with brief trains of cathodal shocks (5 shocks, 300 Hz, each shock 200–300 μA). E.m.g. wires were implanted in: Biceps, triceps, brachioradialis, flexor carpi ulnaris, extensor carpi ulnaris, extensor digitorum communis and flexor digitorum superficialis. In two monkeys, fine stainless-steel stimulating electrodes in a silastic cuff were implanted on the median nerve at the axilla. All connexions were made subcutaneously to a multipin socket on the headpiece.

Recording. During daily recording sessions, the monkey's head was fixed by three sprung bars screwed on the headpice. No other parts of the body were restrained. Tungsten micro-electrodes were passed through a guide tube the tip of which just touched the silastic covering the dura. The electrode was first advanced with a fine screw drive through the dura until neuronal activity was detected. Dimpling during penetration of the dura was estimated from the distance that the electrode advanced beyond the end of the guide tube; when the dura was soft, dimpling was small. The electrode was then advanced using a hydraulic microdrive and the depth of each neurone carefully noted, the criteria of Bishop, Burke & Davis (1962) being used to discriminate cell soma from axon potentials. Single unit activity, e.m.g.s and lever movement analog signals derived from a potentiometer were recorded on an FM tape recorder. The depth was noted at the transition from grey to white matter (lack of soma responses and presence of axon spikes). The electrode was then advanced a further 1·0 mm to ensure that no further soma responses were detected. This method indicated whether penetrations were within the depth of the central sulcus (soma responses up to 7 mm below the cortical surface) or in the convexity of the precentral gyrus (soma responses for 3·0–3·5 mm). During electrode withdrawal the depth of the last soma response was noted; comparison with the reading for initial penetration usually confirmed a small amount of dimpling (100–300 μm). After several weeks, electrode penetration became difficult and dimpling large (2–3 mm) because of the growth of tough fibrous tissue above the exposed dura. This was overcome by periodic removal of this tissue under full anaesthesia.

PTNs were identified by stimulation of the medullary pyramid. Antidromic thresholds ranged from 30 to 400 μA. All neurones classified as PTNs followed three shocks at 100–500 Hz. The frequency was adjusted to suit the antidromic latency of the pyramidal tract neurone (PTN). These latencies ranged from 0·7 to 4·5 msec. Collision tests were satisfactorily performed on all PTNs. Neurones failing to respond antidromically to shocks of up to 500 μA were classified as non-PTNs. Three shocks at 500 μA strength never disturbed the monkeys, which performed the task normally during periods of pyramidal tract stimulation.

Testing of afferent inputs. The afferent input and input zone for each neurone was examined in the relaxed monkey (cf. Lemon & Porter, 1976). The trunk, upper limbs, face, jaw and neck were investigated. Where possible the response latency was determined by applying a touch-sensitive probe to the centre of the afferent input zone. Each stimulus was a brief, light tap. For neurones with inputs from the hand or forearm, weak electrical shocks were applied to the median nerve via the implanted cuff. Each shock produced a twitch in the forearm muscles via motor axons excited within the cuff. The shock strength of a 50 μsec shock which just produced a palpable twitch in these muscles was determined during each recording session. Its value (T) was usually 1·0–2·5 V. Thresholds for excitation of a given cortical neurone were then expressed as multiples of T. Shocks of up to 2·5 T were tested. These did not perturb the monkeys, and 2·5 T shocks applied percutaneously to human subjects were not painful.

Peri-response histograms were constructed for 50–100 successive stimuli delivered one every 1–3 sec. Response latency was taken from the first post-stimulus occurrence of a change in the probability of discharge that was significantly different at the $P < 0.01$ level from the pre-stimulus activity.

Neuronal activity during movement. The activity of well isolated neurones was analysed during the task with a computer (PD11-03) (cf. Lemon *et al.* 1976). Only those neurones which showed a consistent pattern of activity during the task were studied further. After each successful lever pull, the food reward was presented to the monkey by the experimenter and the approximate instant of food collection signalled by the experimenter with a foot switch. In most trials the food reward was placed close to the lever knob. Peri-response histograms of neurone activity during ten to sixteen successive trials were constructed by the computer for a period up to 750 msec before lever movement and up to 2 sec after it. The food reward was then placed in a different position and a new histogram constructed for a further ten to sixteen trials. This procedure required the monkey to employ a variety of shoulder, elbow and wrist movements to obtain the food reward (Lemon *et al.* 1976). Varying the size, shape and retrievability of the food reward required the monkey to use different hand and finger movements to obtain the reward. In most cases a small piece of apple was placed in a rosette device (Fig. 4) (Haaxma & Kuypers, 1975) with a well between two slots which were just wide enough for the monkey to insert his thumb and index finger and retrieve the food from the well; the three ulnar digits were flexed out of the way. This highly fractionated movement of the digits was contrasted with the ball grip (Griffiths, 1943; Napier, 1956) in which all digits are flexed around the object. This grip was elicited either by presenting the monkey with a large cube of apple or by training the monkey to squeeze an inflated rubber bulb. This bulb (3 cm diameter) fitted neatly into the monkey's hand and he was trained to squeeze it within fixed pressure limits in order to obtain a food reward.

Frequency analysis. Off-line analysis was carried out on discharges of uninjured area 4 neurones with large, stable signal-to-noise ratios. Sample periods (10–30 sec) were selected, during which the monkey performed a voluntary movement which was associated with optimal activity in the neurone. Prior examination of the neurone's behaviour using the tests described above usually revealed one particular movement of this kind (e.g. repeated precision grip movements for many hand or finger neurones). The computer calculated the total number of discharges for each sample period and the discharge frequency of the sample was calculated by dividing this number by the sample duration. A mean value for the five to six separate samples was determined. The computer also displayed the distribution of the intervals between successive discharges expressed as an instantaneous or interval frequency. The frequency range of each neurone was determined from this data. Results from samples taken during active, voluntary movement were compared with those from periods during which the most effective peripheral stimulus (e.g. joint motion or light touch) was repeatedly applied in the relaxed monkey. The discharge of the neurone was also analysed for periods when the monkey was not moving and received no extraneous stimulus. In this manner, five to six samples were analysed for each of the three conditions, namely 'active', 'passive' and 'rest'.

Histology. Histological re-construction of electrode tracks, including those in the pyramidal tract, was carried out at the end of each chronic experiment. Details are given in the succeeding paper (Lemon, 1980).

RESULTS

Location of motor cortex neurones with hand inputs

749 neurones were recorded from 241 electrode penetrations made in five monkeys. All neurones were located within the cytoarchitectonic area 4. 216 of these neurones exhibited clear and reproducible responses to natural stimulation of the hand or fingers while the monkey was fully relaxed and in the absence of any significant e.m.g. activity. Fig. 1 shows the surface topography of the left pre-central gyrus in two monkeys, together with the surface location of micro-electrode penetrations. Those penetrations which encountered neurones with hand or finger inputs are marked with a square; penetrations made close to the central sulcus have a greater chance of detecting such neurones, although neurones with hand or finger inputs are scattered

throughout the arm area and some lie well rostral to the central sulcus (cf. Lemon & Porter, 1976). A more detailed analysis of the distribution of these neurones is given in the succeeding paper (Lemon, 1981).

Afferent input from the hand and fingers

Of the 216 neurones with this input, thirty-eight were identified as pyramidal tract neurones (PTNs), fifty-nine as non-PTNs and the remaining 119 neurones were unidentified. 210 neurones had their input zones restricted to the contralateral hand; six had bilateral hand input zones. The principal effect of natural stimulation was excitation in 207 cases and inhibition in nine cases.

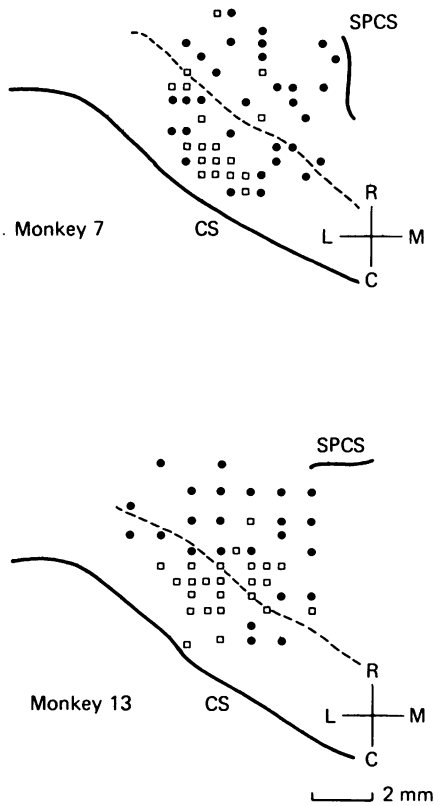

Fig. 1. Surface location of micro-electrode penetrations in two monkeys (*M. fascicularis*). Diagram shows left hemisphere with the central sulcus (CS) and superior precentral sulcus (SPCS) marked by continuous lines. The dotted line represents the extent of the rostral bank of the central sulcus. Penetrations marked with a square (□) encountered neurones with hand and finger afferent input zones; other penetrations, in which no hand input neurones were found, are marked with a filled circle (●).

Table 1 shows the effective stimuli for the 216 neurones. Eighty-two neurones (38 %) responded only to joint movement; nearly all responded in one direction only and most tonically discharging neurones were excited in one direction and inhibited in the other. Nineteen neurones responded to movement of a single joint on one digit and thirty-four neurones received their input from a single digit. Neurones responsive to movement of the thumb were usually not influenced by movement of the other digits.

A further ninety-nine neurones (46%) responded to cutaneous stimuli; eighty-four (39%) of them were excited by light brushing of the skin, usually the glabrous skin. Responses were very phasic and only lasted while the tactile stimulus moved across the input zone; the smallest input zones were located on the tips of single digits, and especially the thumb (less than 2 cm^2) while the largest zones included the whole hand (greater than 5 cm^2). The distribution of skin input zones by size is shown in Table 2. The majority of neurones had zones which covered either part of the palm of the hand or the ventral surface of several digits. Hair motion and deep pressure (maintained indentation of the skin) excited twelve (6%) and four (2%) neurones respectively, and the sizes of the effective input zones are also included in Table 2.

TABLE 1. Effective stimuli for neurones with afferent input from hand and fingers

Stimulus	All neurones	PTN	non-PTN
Movement of single phalangeal joint	19	2	8
Movement of joints on one digit	15	4	3
Movement of joints on two digits	19	4	5
Movement of joints on > two digits	29	5	4
Hair movement	12	2	1
Brushing skin	84	13	20
Deep pressure	3	1	1
Brief taps to hand	9	3	4
Mixed: brushing skin and joint motion	16	3	7
Mixed: deep pressure and joint motion	1	1	0
Mixed: brief taps and joint motion	9	0	6
Total	216	38	59

TABLE 2. Size of cutaneous afferent input zone for neurones responding to brushing the skin alone (84), brushing skin and joint movement (16) hair movement (12) and deep pressure (four neurones)

	All neurones	PTN	non-PTN
< 2 cm^2	26	4	8
2–5 cm^2	51	9	12
> 5 cm^2	39	7	9
Total	116	20	29

Eighteen neurones (8%) were excited by brief prods applied to the thenar and hypothenar eminence. They were not influenced by gentle touch but nine were responsive to movement of finger joints (cf. Lemon & Porter, 1976).

Cutaneous modalities were therefore well represented in this population of motor cortex neurones; by contrast most neurones with inputs from the elbow and shoulder were influenced by joint movement or muscle palpation. The majority of hand-input neurones responsive to tactile stimuli were not influenced by joint motion, and vice versa for joint-sensitive neurones. However the input to twenty-six neurones (12%) revealed convergence of modality including sixteen that were excited by cutaneous stimulation of the immobilized digits and by passive motion of the same digits. The size of input zone for these sixteen neurones is also included in Table 2.

There appeared to be no clear differences between PTNs as a group and non-PTNs with respect to their responses to peripheral stimuli. PTNs responding to either deep or superficial modalities from the hand were equally common. PTNs with large axons (short antidromic latencies) were often phasic in their discharge (Evarts. 1965) and

unresponsive to passive stimuli. This was reflected in the shorter mean antidromic latencies of unresponsive PTNs (0·95 S.D. ±0·20 msec) compared to PTNs with clearly defined input zones (1·46±0·56 msec).

Latency of afferent input from hand to motor cortex

Since inputs from the hand may provide continuous afferent feed-back to motor cortex neurones during certain voluntary movements, the latency of responses of these neurones to stimulation of the hand was determined, using either mechanical or electrical stimuli.

Mechanial stimulation. Latencies were determined with a touch-sensitive probe for fifty-seven neurones (including ten PTNs) responding to cutaneous stimulation of the hand/fingers. Many responded very rapidly to the applied stimulus (Fig. 2*B*);

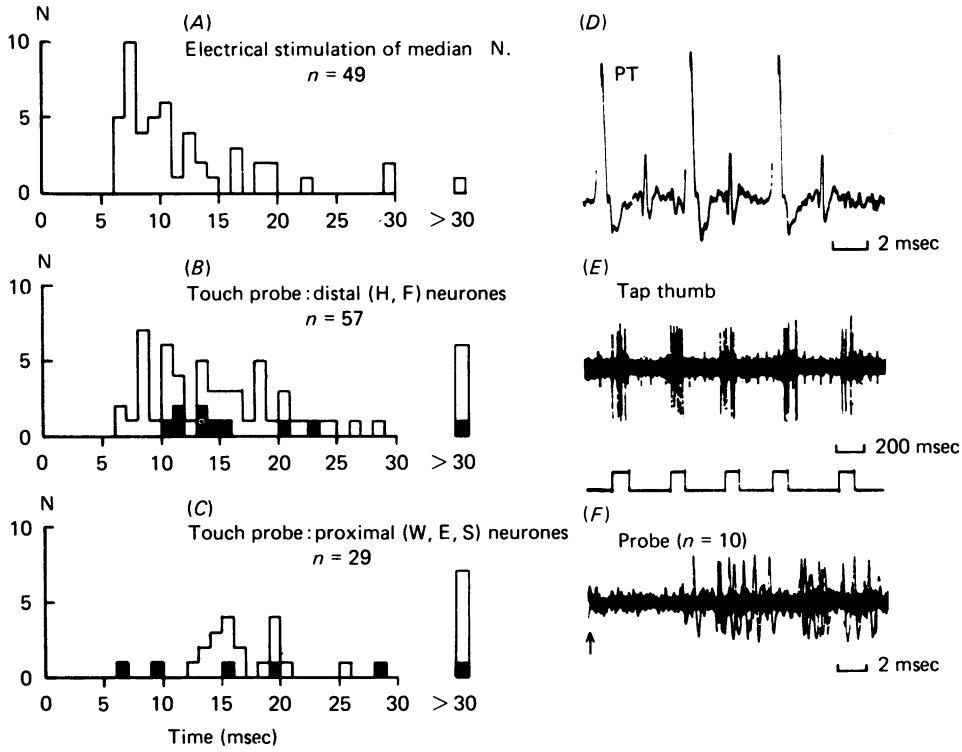

Fig. 2. Latency of afferent input to area 4. *A*, distribution of response latency for forty-nine area 4 neurones responsive to weak stimulation (< 2·0 *T*) of the contralateral median nerve at the axilla. Neurones with latencies of 30 msec or longer are shown in the column on the extreme right of the histogram. *B*, latency distribution for fifty-seven neurones with input zones confined to the hand (H) and fingers (F) and responsive to light taps with a touch-sensitive probe (see text). Identified PTNs are shown by filled columns. *C*, latency distribution of twenty-nine neurones responding to light taps in the wrist (W), elbow (E) and shoulder (S) regions. *D–E*, short-latency input to a hand PTN. *D* shows antidromic response of the PTN at 2·7 msec to three successive shocks each 100 μA strength (frequency: 200 Hz). *E*, bursts of discharges from the PTN evoked by light taps to the tip of the immobilized thumb. Each tap is signalled by an upward deflexion in the signal record. *F*, ten superimposed sweeps triggered by application of the touch probe (arrow) to the tip of the thumb. The PTN responded repeatedly within 10–12 msec.

forty-three neurones (75%) responded in under 20 msec and eleven (19%) in under 10 msec. This sample probably represents the strongest input from hand to motor cortex since only those neurones with marked responses to the gentle taps produced by the probe were analysed. Taps applied to the bellies of muscles acting at the shoulder, elbow or wrist excited a further twenty-nine neurones and their latencies are shown in Fig. 2*C*. In this proximal' group 19/29 (65%) responded in less than 20 msec but only two neurones (7%) had latencies of under 10 msec. This suggests that some of the most rapid inputs to the motor cortex come from the hand and fingers.

Short-latency inputs to PTNs were also detected and an example is shown in Fig. 2. Sample responses to a light probe tap of the thumb (Fig. 2*F*) show the PTN responding with a latency of about 10 msec. Many neurones responding to the probe stimulus showed early facilitation followed by inhibition.

Electrical stimulation. In two monkeys these short latency inputs from the hand were confirmed by weak median nerve shocks. Fig. 2*A* shows the latency data of forty-nine responsive neurones. A prominent short-latency group (45/49 neurones (92%)) responded in less than 20 msec and twenty-four neurones in less than 10 msec (49%). Even when the conduction time from hand to axilla (2·5–3·0 msec for the fastest median nerve afferents) is added to the latencies shown in Fig. 2*A*, they still suggest a very rapid input pathway. These forty-nine neurones included thirty that responded only to passive movements of the digits and not to cutaneous stimuli. Thirty-two neurones had thresholds of less than 1·2 times the muscle twitch threshold, *T* (see Methods). There was no clear distinction between the thresholds of neurones responding respectively to joint motion and tactile stimuli.

Depth of responsive neurones

Recent studies on the motor cortex show considerable differences in afferent and efferent connexions of various cortical laminae (Jones & Wise, 1977; Sloper & Powell, 1979) and even within one lamina (Catsman-Berrevoets & Kuypers, 1978; Catsman-Berrevoets, Kuypers & Lemon, 1979). An attempt was therefore made to determine the depth within the cortex of neurones with afferent inputs from the hand. Only those neurones recorded in micro-electrode penetrations with a minimum amount of dimpling (100–300 μm; see Methods) were included. In addition, only penetrations made normal to the cortical surface and which could be identified in subsequent histological material as being confined to the convexity of the gyrus were included.

Fig. 3*A* shows the distribution by cortical depth of 132 hand-input neurones which met the above criteria. They were found at all depths although the great majority of neurones lay in the upper 2·0 mm of the cortex with a clear peak at about 1·5 mm. The distribution of PTNs with hand inputs is also shown (filled columns). The depth distribution of a further ninety-one neurones which did not appear to have any afferent input is also shown (Fig. 3*B*). As can be seen, there was no clear difference in the depth profile of the responsive and non-responsive populations, and it is more likely that both represent a sampling bias towards the neurones with large somata, and particularly the large pyramidal neurones of lamina V (Humphrey & Corrie, 1978). Fig. 3*C* plots the cortical depth of forty-nine neurones with hand inputs for which the response latency was determined by touch-sensitive probe. All the shortest

latency responses (< 10 msec) were found in neurones located between 1·4 and 2·0 mm deep. Responses in less than 20 msec were found in neurones lying in all the upper cortical layers, but neurones lying below 2·5 mm only had long latency responses (25 msec or more).

There was no clear difference in the depth distribution of neurones responsive respectively to joint motion and cutaneous stimuli.

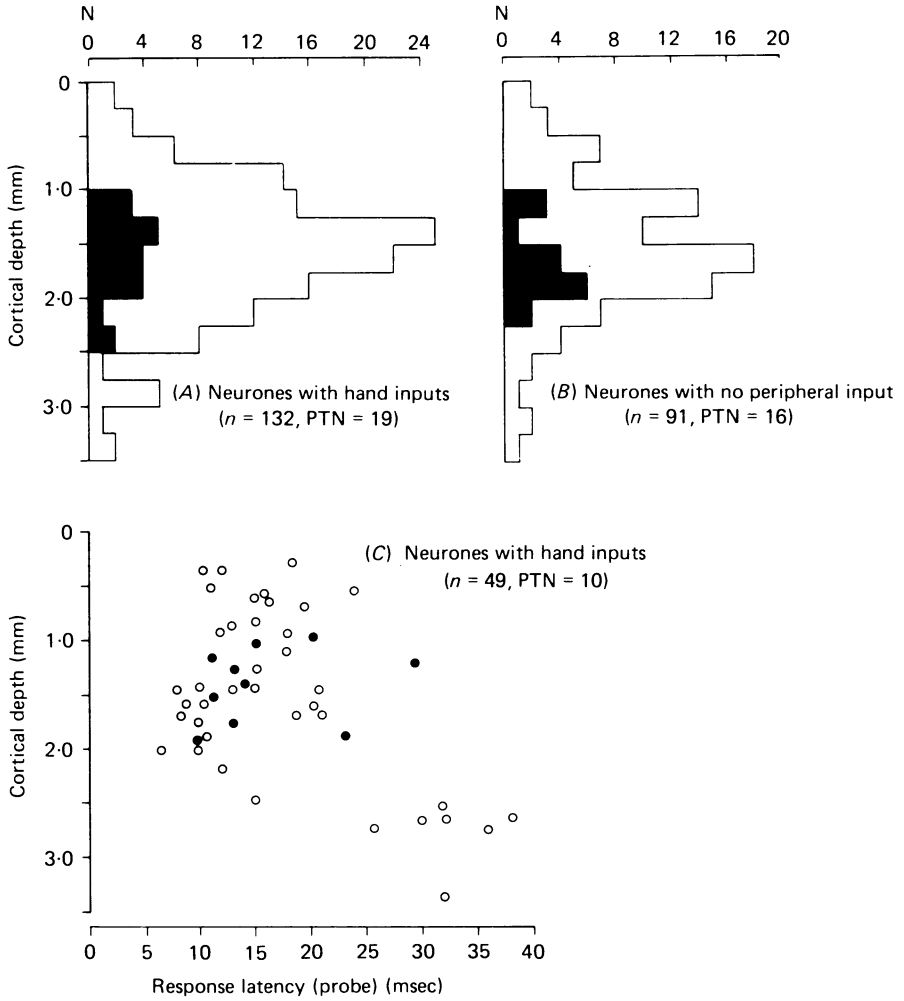

Fig. 3*A*, depth distribution of 132 neurones responsive to stimuli applied to the hand. The depth distribution of ninety-one unresponsive neurones is shown in *B*. In *C* the response latency of 49 hand-input neurones has been plotted as a function of their cortical depth. Latencies determined with a touch-sensitive probe. PTNs are represented by filled columns in *A* and *B* and by filled circles in *C*.

Activity of hand-input neurones during voluntary movements

The activity of eighty hand-input neurones was analysed (*a*) during the trained task (lever pull and food collection). Discharge patterns obtained were compared in a semiquantitative manner with those of 117 neurones having wrist, elbow or shoulder input zones. Forty-five neurones with no apparent afferent input were also analysed.

The behaviour of the hand-input cells was also investigated (*b*) during reaching

movements to collect the reward from different positions (32/80 neurones), (*c*) before and after hand contact with the reward, (*d*) during a variety of hand grips: power, ball and precision (17/80 neurones), (*e*) during small exploratory movements and during natural movements (grooming, scratching etc.).

Activity during the trained task. The task employed required the use of many different muscles and movements (Fig. 4). However, preliminary analysis revealed that many hand-input neurones were particularly active before and during the hand and finger movements associated with food retrieval. In order to quantify this difference in activity during different phases of the task, and to determine whether hand-input neurones were active during proximal arm movements, a comparison was made of activity during two phases of the task, the *lever* and *pick-up* phases (Fig. 4). The rosette containing the reward was positioned only 5–8 cm from the lever knob.

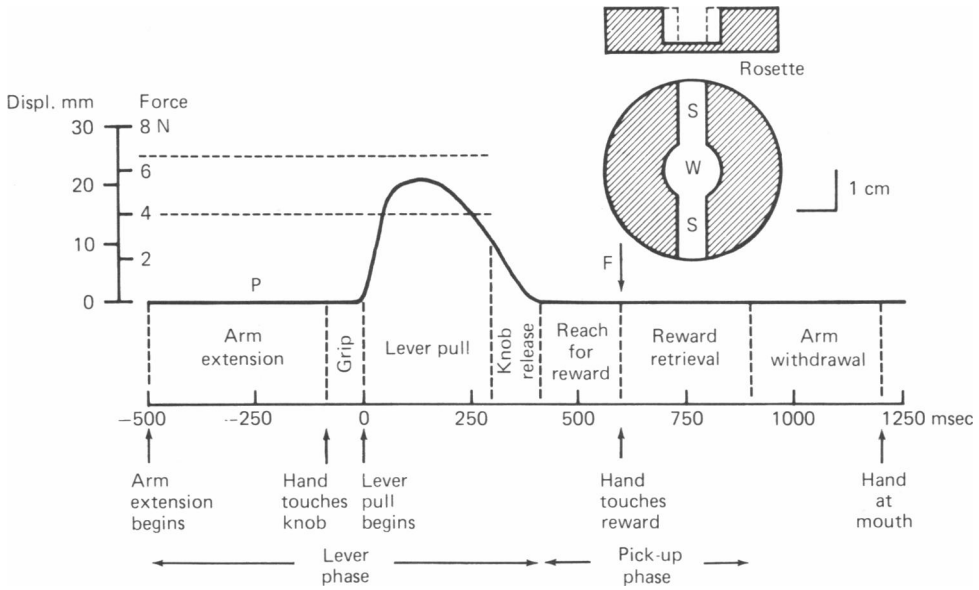

Fig. 4. Events occurring during the performance of the trained task. The monkey extended his right arm 500 msec before beginning of lever movement (time zero). He reached out and grasped a knob positioned about 25 cm in front of him at chest level. He then pulled the knob, which was mounted on a horizontal spring-loaded bar, into a target zone (dashed lines) between 15 and 25 mm from the rest position. This required a force of 4–6 N. Displacement of the lever (P) lasted for about 400 msec. A correct pull was rewarded by a piece of apple, placed in the well (W) of the rosette device illustrated (section above, plan below). This device was positioned close to the lever knob. After releasing the knob, he reached for the food, contacting it about 600 msec after time zero (F). He inserted his index finger and thumb into the slots (S), retrieved the food, withdrew his arm and ate the reward. This sequence of events is based on measurements made in three of the five monkeys which performed the task.

Thus the arm movement required to reach for the reward was much smaller than that observed during extension of the arm before the lever pull or during arm withdrawal after food collection (Lemon *et al.* 1976). During the *pick-up phase*, which lasted 300–500 msec (Fig. 4), both e.m.g. and cine-film evidence demonstrated that movements were largely confined to the hand and fingers. Independent movements of the index finger and thumb to remove the food reward from the rosette device (see Methods) were particularly evident in this phase.

Modulation of neuronal activity immediately before and during the pick-up period was therefore considered to be broadly related to hand and finger movements.

The *lever phase* consisted of arm extension, grip of the knob and the pull (Fig. 4). From the present study and from previous work with this task (Porter & Lewis, 1975) it was clear that this phase involved many different proximal muscles. The knob was gripped in a power grip described by Napier (1956) as a coal-hammer grip. This contrasted strongly with the precision grip used by the monkey to extract his food reward. Differences in neuronal activity for different types of grip are described below.

Thus comparison of activity for the pick-up with that for the lever phase indicated a neurone's behaviour during a period characterized by hand and finger movements compared to that during a phase dominated by movements at the shoulder, elbow and wrist joints. Neurones analysed were placed into four groups. Group 1 showed clear changes in discharge frequency for the pick-up phase, but none for the lever phase. Group 2 neurones showed modulation for both phases but that occuring for the pick-up was greater than that for the lever phase. The reverse was true for group 3 neurones, while those in group 4 only showed modulation for the lever phase.

Peri-response histograms for four neurones drawn from these groups are shown in Fig. 5*A–D*. The averaged lever movement (*P*) and moment of contact of the monkey's hand with the reward (*F*) are also shown. Each monkey retrieved the food in a consistent fashion so that the interval between the beginning of lever movement and *F* varied only slightly (± 100 msec) from trial to trial.

The neurones in Fig. 5*A* and *B* received cutaneous inputs from the hand as shown. Neurone 5*A* showed a clear increase in activity before the food pick-up from the rosette. It showed little modulation during the lever phase, including the power grip of the knob. Such a neurone was therefore classified as group 1. Neurone 5*B* showed a burst of activity during the grip of the knob; this discharge did not continue into the pull phase, and virtually none of the neurones with hand or finger inputs were active during this phase. Neurone 5*B* was more active during the pick-up than the lever phase, and therefore this neurone was classified as group 2.

For comparison, the neurones illustrated in Fig. 5*C* and *D* received inputs from the elbow and shoulder respectively. One neurone (5*D*) discharged during arm extension and was quiescent during the lever pull (arm withdrawal); 5*C* had a pattern of excitation well-related to the pull together with inhibition during arm extension. It did not modulate its activity during the pick-up phase (i.e. a group 4 neurone). Neurone 5*D* did show some modulation after the pick-up, but this was much less than that of the lever phase (i.e. group 3 neurone).

Fig. 6 shows the distribution within the four groups of neurones with inputs from different regions of the monkey's arm. Out of eighty neurones with hand/digit inputs, sixty-one (76 %) were classified as groups 1 and 2 (pick-up activity greater than lever activity) with twenty-six neurones (32 %) active only for the food pick-up. Only 3/80 neurones (4 %) did not modulate their discharge during the pick-up phase (group 4) and only nineteen neurones (24 %) showed more activity for the lever than for the pick-up phase (groups 3 and 4).

By contrast, of the seventy-two neurones with inputs from the elbow or shoulder, fifty-eight (77 %) showed a greater discharge for the lever phase than for the pick-up (groups 3 and 4). Only eight neurones (11 %) were active during the pick-up phase

alone (group 1). A total of seventeen neurones (23 %) with proximal inputs were more active for the pick-up phase then the lever phase (groups 1 and 2) and many of these began to alter their discharge 200–300 msec after the pick-up (cf. Fig. 5*D*) and this change in activity may therefore have been related to proximal movements occurring during transfer of the food reward from rosette to mouth (Fig. 4).

The general relationship of peripheral afferent input to a neurone and its natural activity was further supported by results for neurones with inputs from the wrist (Fig. 6). These neurones were distributed between the pattern seen for neurones with proximal elbow or shoulder inputs and those with distal hand or finger inputs. Wrist-input neurones were equally divided between groups 1 and 2 (twenty-one neurones; 47 %) and groups 3 and 4 (twenty-four neurones; 53 %). About half of the wrist-input neurones in groups 1 and 2 had cutaneous input zones, while none of those in group 3 and 4 had cutaneous inputs. Neurones with no apparent input (*N*) were equally distributed among the four groups.

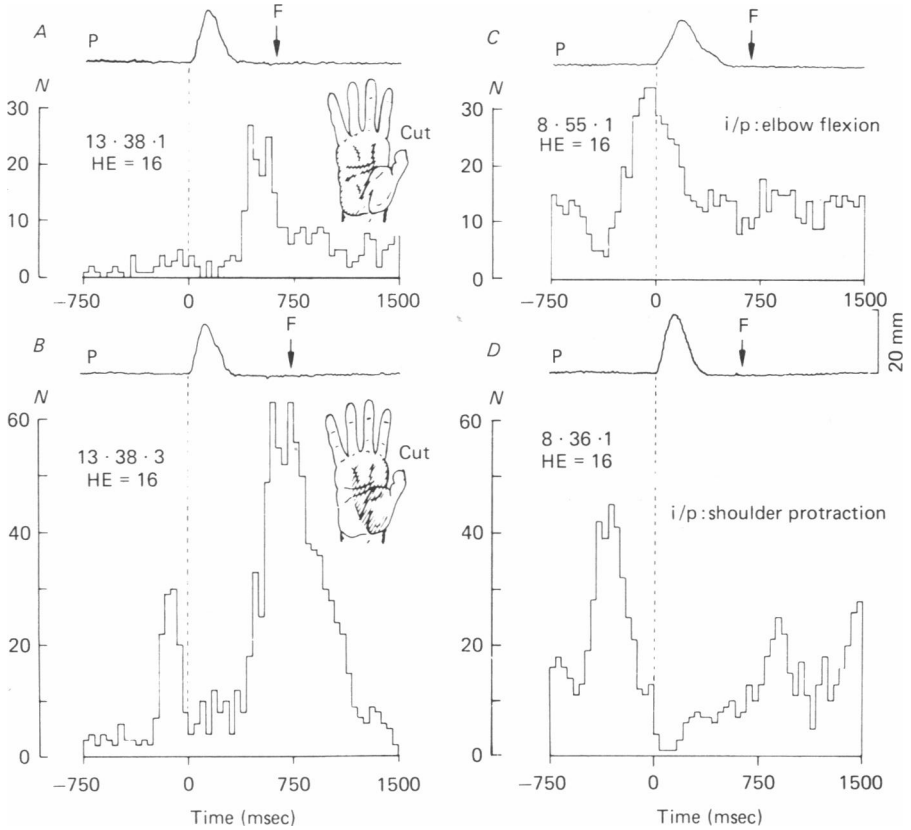

Fig. 5. Examples of activity in area 4 neurones during voluntary movement. Histograms show number (*N*) of discharges accumulated for 16 successive lever pulls (histogram events, HE). Discharges occurring in a period 750 msec before and 1500 msec after the beginning of lever movement (time 0 and dashed line) were analysed. Averaged lever position (P) for the 16 pulls is shown above each histogram, as is the mean time of contact of the monkey's hand with the food reward (arrow, F). *A* and *B*, activity of two neurones responding to tactile stimulation of the area indicated by shading on the hand figurine. *C* and *D*, activity of two neurones responding to passive elbow flexion and shoulder protraction respectively.

Only six neurones with hand inputs showed a clear modulation during collection of food with the ipsilateral hand.

Dependence of activity on arm position. The results above suggest that many hand-input neurones show little or no activity during proximal movement. Another method of assessing the independence from proximal movements for these neurones was to offer the food reward in a number of different positions. Neuronal activity was analysed by the computer for sixteen trials in six different positions. These six positions exploited the full range of arm movement within the visual field of the monkey. For instance, the reward was presented at full arm's length; to the left or

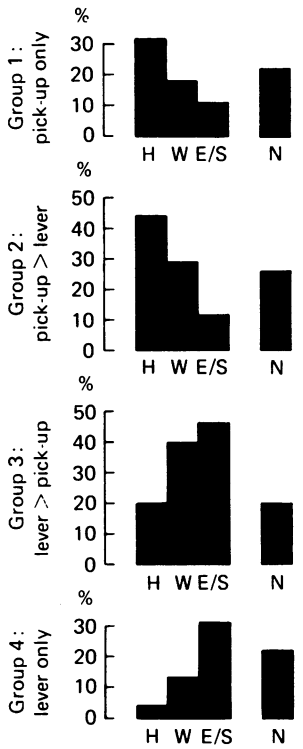

Fig. 6. Distribution of area 4 neurones into four different groups based on their activity during one phase of the movement task characterized by hand and finger movements (pick-up phase) compared to the activity during a phase characterized by proximal movements (lever phase). Neurones showing modulation of activity confined to the pick-up or lever phases were classified as group 1 or group 4 respectively. Those showing a greater modulation of activity in one phase than the other were classified into groups 2 and 3. The Figure shows the percentage distribution of eighty neurones with inputs from the hand or fingers (H), forty-five from the wrist (W), seventy-two from the elbow/shoulder (E/S) and forty-five neurones which did not respond to peripheral stimulation (N).

right of the monkey; at waist or eye level, etc. These different positions prompted the monkey to use a wide variety of shoulder, elbow and wrist movements to reach the reward (cf. Lemon *et al.* 1976). A total of thirteen neurones with hand inputs that showed a clear modulation of discharge during the pick-up were fully analysed in this way; eighteen of these neurones showed no alteration in their activity when the food reward was placed in different positions. A further fourteen neurones did show a clear

variation in their discharge with spatial position. Of fifty neurones with proximal inputs (wrist, elbow and shoulder), forty-six showed position-dependent activity.

Behaviour before and after hand contact. Of the seventy-seven hand-input neurones showing a clear change in activity for the pick-up phase (i.e. groups 1, 2 and 3), forty-eight (62%) clearly modulated their activity before any contact with the food reward was made. Twenty-seven of these cells responded to passive tactile stimulation of the hand; one of them is shown in Fig. 5*A* and it clearly became more active before contact (*F*). The remaining 29/77 neurones, showed no modulation until after contact with the reward.

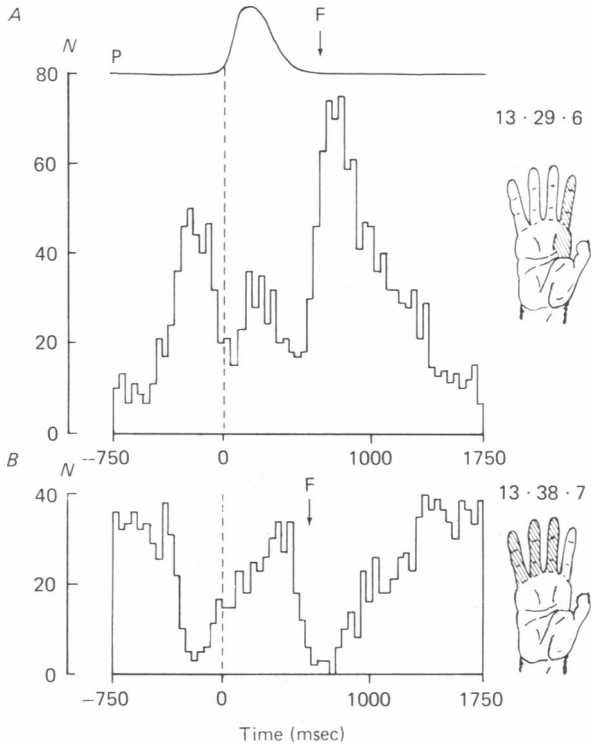

Fig. 7. Activity histograms for two neurones with different cutaneous input zones. One neurone (*A*) was excited by light touch of the index finger and of a small adjoining area of the hand (see figurine); this neurone showed maximum activity after contact with the food reward (F). The other neurone (*B*) was excited by light touch of the three ulnar digits, but showed pronounced inhibition during contact with the lever knob before the pull and with the food reward after the pull.

Of the 43/77 hand neurones with cutaneous inputs, thirty-five clearly altered their discharge when contact was made. 21/35 showed excitation by active touch (e.g. cells in Fig. 5*A*, 7*A*), while fourteen showed inhibition (e.g. Fig. 7*B*) despite the fact that they were *excited* by passive tactile stimuli. Four of these inhibited neurones had input zones restricted to the ulnar digits (e.g. Fig. 7*B*) whereas most of the neurones with input zones on the thumb or index finger showed increases in activity on contact with the food (e.g. Fig. 7*A*). However, there were many cases in which there was no obvious difference in the input to neurones respectively inhibited or excited by active touch.

Activity during varied hand grips. The majority of neurones with hand or finger

showed a greater modulation of discharge frequency during the food pick-up, using a precision grip, than during the coal-hammer variant of the power grip used to grasp the lever knob (Fig. 6, groups 1 and 2).

Different grips were further investigated in a monkey trained to squeeze an inflated rubber bulb with a ball grip in which all the digits were flexed around the bulb. A similar grip was used by the monkey to grasp a large cube of apple (12 mm side) presented on a flat surface. Neuronal activity during this type of grip was compared with that observed during precision grip between index finger and thumb employed by the monkey with the rosette device or while collecting a sunflower seed held between the experimenter's thumb and index finger. Seventeen PTNs with hand inputs were investigated in this monkey. All seventeen showed large modulation of their activity during the precision grip, and for fourteen of them, this modulation was significantly greater than that seen during the ball grip task. Several phasic PTNs failed to discharge at all during the bulb squeeze but discharged vigorously for precision grip (Fig. 8*A*). One PTN showed the opposite behaviour and two PTNs showed no difference in activity between the two grips. In the same monkey 7/9 neurones with proximal inputs showed no difference for the two types of grip.

Activity during small and exploratory movements. For many neurones with hand inputs it was apparent that they exhibited a powerful discharge during relatively small movements of the fingers. If the monkey was offered a seed gripped firmly between the experimenter's fingers, these neurones showed little or no modulation of their discharge activity when the monkey gripped the seed isometrically between index and thumb, but the small digit movements used for adjusting the precision grip were accompanied by a marked discharge. Again this was most noticeable for phasic neurones, such as the PTN shown in Fig. 8*B*. Only 9/80 neurones showed a clearly augmented response during maintained precision grip.

Many neurones displayed intense activity during small exploratory movements without the aid of vision (e.g. seeking a sunflower seed concealed between the experimenter's digits) (Fig. 8*C*). This property was particularly striking for neurones with cutaneous inputs from the glabrous skin of the fingers or thumb. These discharges often occurred at higher frequencies than were ever seen during the more stereotyped phases of the learned task. Certain 'natural' movements (scratching, grooming, picking) were also associated with high frequency discharge in these neurones.

Discharge frequency of hand-input neurones

This was investigated under three different conditions: during the 'best' active movement for the neurone in question; during passive, natural stimulation, and during rest (see Methods). The activity of twenty-five hand-input neurones was analysed and the results from two representative neurones are shown in Fig. 9*C* and *D*. These histograms show the distribution of discharge frequencies collected during 20 sec samples recorded under the three different behavioural conditions. The PTN in Fig. 9*C* showed very little rest activity, but discharged vigorously during precision grip between the thumb and index finger. Discharge frequencies during active movement were considerably higher than those elicited by passive stimulation. The mean discharge frequencies for this PTN during rest, passive and active conditions

were 4, 11 and 22 Hz respectively. Superimposed traces on the right of Fig. 9*C* show that the same PTN was analysed under all three conditions.

A quite different frequency distribution was found for the second neurone (Fig. 9*D*). This unidentified neurone showed tonic activity during rest, and discharged at up to 200 Hz during active precision grip. The neurone showed a similar frequency distribution during passive digit flexion. There was little difference between active (29 Hz) and passive (28 Hz) mean frequencies. The rest value was 10 Hz.

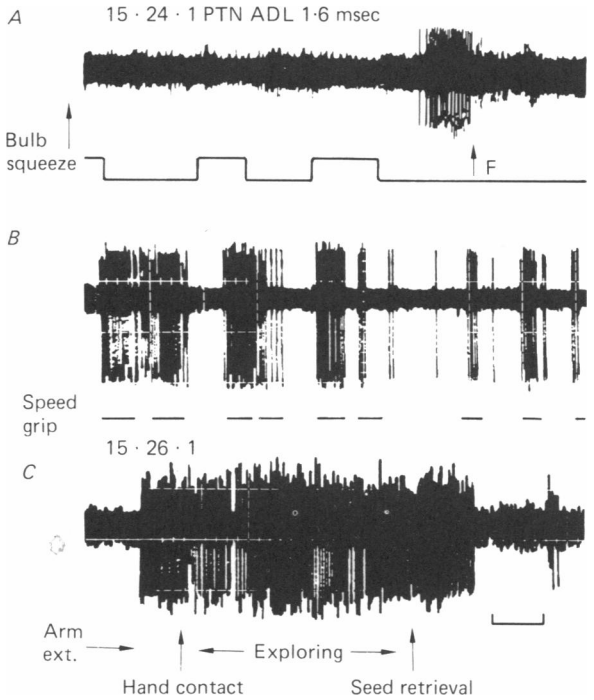

Fig. 8. Activity of hand-input neurones. *A*, record of a PTN with a short antidromic latency (ADL) showing no activity during three successive bulb squeezes performed by the monkey with a ball grip. Onset and duration of squeeze indicated by signal. The PTN fired vigorously just before the monkey used a precision grip between index finger and thumb to retrieve a small seed from a rosette device. Contact with the seed marked by arrow, F. This neurone responded to passive flexion of middle and index finger; *B*, high-frequency bursts of discharges from the same PTN as in *A* during repeated gripping movements of a small seed between index and thumb. Adjustments of grip indicated by signal line. Note absence of activity during periods (indicated by breaks in signal line) when the monkey held the seed in a steady grip without overt movement. *C*, activity of a neurone during active tactile exploration without the aid of vision. The monkey extended his arm until he made contact with the experimenter's hand and then searched about with his fingers until he found and retrieved a hidden seed. This neurone responded to passive tactile stimulation of the glabrous hand. Time calibration: 1 sec for *A*, *B*, 0·5 sec for *C*.

The variation in mean discharge frequency under the three different conditions for all twenty-five neurones is shown in Fig. 9*A*. Many had similar rest (R)-passive (P) slopes, which gave a measure of the efficacy of the passive stimulus. Six neurones showed much higher active than passive frequencies (cf. Fig. 9*C*) and steeper passive-active slopes than rest-passive slopes; this behaviour was found both in phasic

and in tonic neurones (rest frequencies 10–12 Hz). For a further nine neurones, the active mean frequency was either the same or lower than that seen during passive stimulation (cf. Fig. 9*D*). Three of these neurones employed a higher maximum frequency during passive than during active conditions. These observations emphasize the powerful peripheral input to some area 4 neurones.

The differences in active-passive behaviour of the sample presented in Fig. 9*A* did not correlate with either location of input zone on the hand or the modality of the

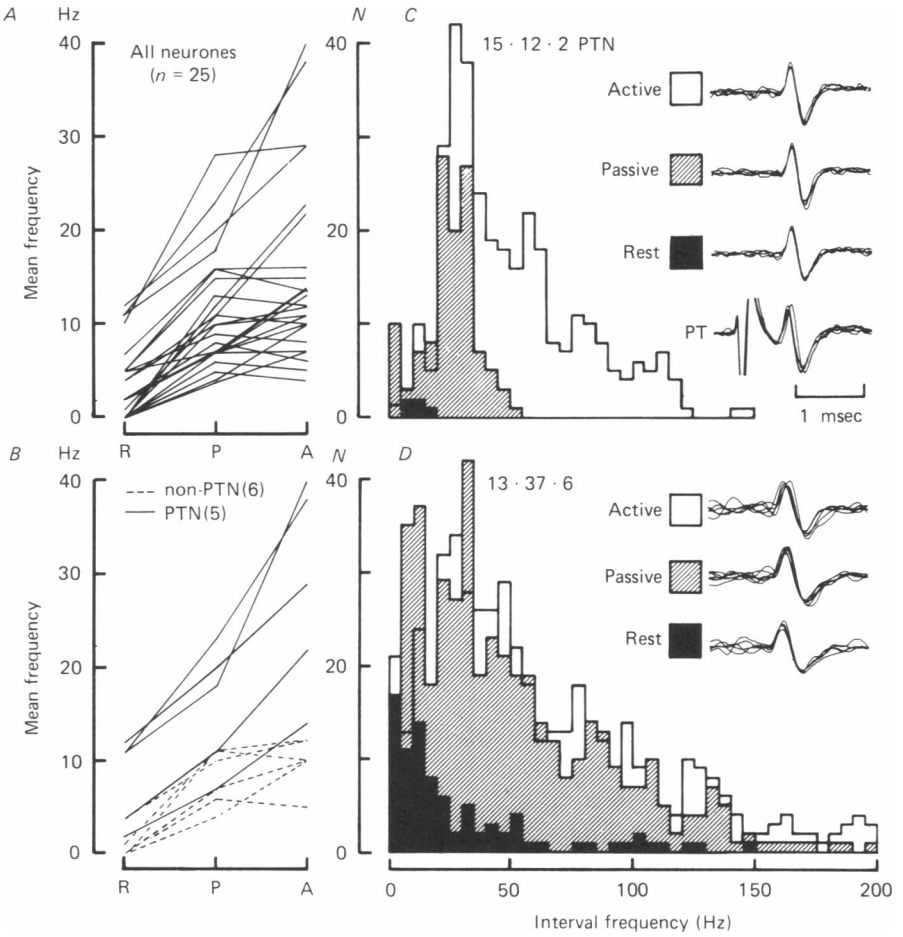

Fig. 9. Discharge frequency of hand input neurones. *A*, mean discharge frequency derived from five to six samples of activity during rest (R), during repeated passive (P) stimulation and during repeated active (A) performance of the 'best' movement for twenty-five neurones with hand and finger afferent input. *B*, mean discharge frequency for five identified PTNs and six non-PTNs. *C* and *D*, distribution of discharge frequency for two neurones. Histograms plot the number (*N*) of intervals against the duration of the interspike interval expressed as a frequency. 'Active' samples for both neurones were taken from periods when the monkey made repeated thumb-index precision grips. 'Passive' samples were taken during repeated flexion of the index finger (*A*) and index and middle fingers (*B*). The inset records were derived from a transient recorder triggered by pulses from a spike-height window discriminator. Each record is of five superimposed sweeps taken at random during the sample period shown. Records demonstrate that action potential from one and the same neurone were sampled throughout.

effective stimulus. However, there were differences between PTNs and non-PTNs (Fig. 9*B*). The five PTNs in the sample all showed higher active than passive mean frequencies and all displayed a steeper passive-active than rest-passive slope. Only the non-PTN showed this latter property, and some non-PTNs had rather similar or lower active than passive frequencies.

DISCUSSION

Afferent input from the hand. As might be expected, cutaneous modalities are particularly well represented among motor cortex neurones with inputs from the hand or fingers (Rosén & Asanuma, 1972; Lemon & Porter, 1976; Wong *et al.* 1978). From previous samples of area 4 neurones representing input from all parts of the monkey's forelimb, Lemon & Porter (1976) found only 10·6 % of neurones sensitive to cutaneous stimuli, and Wong *et al.* (1978), 17·8 %. This emphasizes the importance of the deep proprioceptive input to area 4 as a whole. However, for the selective population of hand input neurones studied here, 46 % were responsive to stimulation of the skin or hairs, compared to 38 % sensitive to joint motion. Since most of the cutaneous neurones were not influenced by joint motion it would appear that modality of afferent input from the hand remains separate within the motor cortex. However 12 % of the present sample showed convergent responses to both cutaneous and joint motion stimuli, as reported previously (Wiesendanger, 1973; Wong *et al.* 1978).

The latency measurements demonstrate the rapid nature of the input from hand to motor cortex; even PTNs may respond within 10–15 msec. The rapidity of these responses suggests that a direct thalamic pathway to the motor cortex is responsible (Kievit & Kuypers, 1977; Horne & Tracey, 1979; Lemon & van der Burg, 1979; Asanuma, Larsen & Yumiya, 1979). Short-latency inputs to motor cortex from the hand have been confirmed using electrical stimulation of peripheral nerve (Lemon, 1979) and these results demonstrate that low-threshold peripheral afferent fibres are implicated, and that the rapid input pathway is available to both deep and cutaneous stimuli. Although neurones responsive to peripheral inputs were found at all depths, the shortest input latencies were detected at 1·4–2·0 mm. In monkey motor cortex, this corresponds approximately to layer IV and layer V (Humphrey & Corrie, 1978; Sloper, Hiorns & Powell, 1979) and overlaps with the region (lower part of layer III and layer IV) in which thalamocortical axons terminate (Strick & Sterling, 1974; Sloper, 1973; Sloper & Powell, 1979). This finding gives some further support for a direct thalamic input to the motor cortex being responsible for the shortest latency responses.

Activity of hand-input neurones during movement. The tasks employed in this study allowed a 'clinical' examination of the behaviour of each neurone during a variety of movements. This approach illuminates the characteristic movement(s) associated with the natural activity of any one neurone in the motor cortex. It demonstrates that most hand-input neurones are clearly active during hand and finger movements, and that in addition, some of them (group 1, Fig. 6) are not recruited at all during proximal arm movements. These neurones may also show patterns of activity during hand movements that are quite independent of arm movement or posture.

Therefore, these neurones have a simple motor field restricted to muscles acting on the hand and fingers. However, a proportion of neurones, in addition to their pick-up

phase activity, also modulated during the lever phase (groups 2 and 3, Fig. 6). This may have been associated with the power hand grip of the lever knob, but it could equally well have been associated with activity in more proximal muscles. Clearly, groups 2 and 3 neurones have a different, wider motor field than those in group 1. Variation in the size of motor fields for area 4 neurones is to be expected from the work of Fetz and colleagues who have shown both with operant conditioning and cross-correlation techniques that the discharge of a single cortical neurone may result in the co-activation of just one or of several different forelimb muscles (Fetz & Finnochio, 1975; Fetz, Cheney & German, 1976). The size of motor fields for corticospinal neurones probably depends on the degree to which their axons branch within the spinal cord (Shinoda, Zarzecki & Asanuma, 1979; Asanuma, Zarzecki, Jankowska, Hongo & Marcus, 1979).

It is clearly necessary to study more than one simple movement to assess the motor field of a given neurone. There appear to be certain characteristic hand movements which are repeatedly represented in the motor fields of hand-input neurones. This applies particularly to fractionated movements of the digits as seen during precision opposition of index finger and thumb and during small exploratory movements. Some hand-input neurones did not modulate their activity during the power grip, in which fractionation of the digits plays a less significant role. These findings are in keeping with the effects of either pyramidotomy or selective lesions of the motor cortex in monkeys (Lawrence & Kuypers, 1968; Brinkman & Kuypers, 1973; Passingham, Perry & Wilkinson, 1978) in which fractionation of movements by the digits remains permanently impaired, so that independent movements of the fingers necessary for the precision grip and fine, manipulatory movements become impossible.

Relationship between afferent input and natural activity. A clear functional feature of neurones in the motor cortex is the correlation between their afferent input and motor field (Lemon *et al.* 1976; Rosén & Asanuma, 1972; Murphy, Kwan, MacKay & Wong, 1978). This relationship clearly applies to neurones with hand inputs, and is particularly striking for those with cutaneous afferent-input zones. However, neurones with apparently similar cutaneous input zones may show either excitation or inhibition following active touch. Neurones with input from the glabrous skin of the digits may discharge during flexion of the digits (thus advancing the input zone towards an object) or in the opposite direction (Lemon *et al.* 1976; Murphy *et al.* 1978). Thus the nature of the afferent input cannot always be used to predict the pattern of activity shown by the neurone during active movement.

Motor cortex activity in the absence of peripheral input. Neurones without demonstrable responses to natural stimulation have patterns of activity during movement which resemble those of responsive neurones. Lewis & Porter (1974) found no marked changes in PTN activity after monkeys were deprived of input from the contralateral hand by means of local anaesthesia. 'Normal' patterns of activity in area 4 neurones have also been observed in monkeys subjected either to dorsal rhizotomy (Lamarre, Bioulac & Jacks, 1978) or section of the dorsal columns (Brinkman, Bush & Porter, 1978). However, all of these experiments have tested a monkey's ability to perform a stereotyped task without peripheral feed-back, and there has been no systematic study either of their performance of novel or demanding tasks or of motor cortex activity during such tasks.

Transmission of afferent input during movement. A further argument against a

feed-back role for peripheral input comes from experiments showing that transmission of this input to the motor cortex and other areas of the C.N.S. is suppressed before and during movement (Ghez & Pisa, 1972; Tsumoto, Nakamura & Iwama, 1975; Coquery, 1978; Dyre-Poulsen, 1978). Horne & Porter (1980) recorded from ventrobasal thalamic neurones which were responsive to natural stimulation in the relaxed monkey but not when the monkey was moving. In the motor cortex itself, responses to weak stimulation of the median nerve are diminished or abolished during active movement of the stimulated limb (Lemon, 1979).

However, in all the above experiments, afferent transmission has been tested using a stimulus unrelated to the voluntary task performed. It therefore remains possible that afferent input directly related to the task may still exert a powerful influence on the motor cortex and other structures. Thus, Evarts & Fromm (1977) showed that small perturbations of the wrist joint produce very powerful responses in motor cortex neurones when a monkey is making a small precise movement of the wrist, compared to very weak responses during a rapid, uncontrolled wrist movement. A similar observation was made by Porter & Rack (1976) for controlled finger movements. Increase of transmission of relevant inputs to the motor cortex might also explain the vigorous discharge seen in some neurones during small exploratory movements of the fingers, in which both deep and cutaneous inputs from the digits may play a role. In contrast, many of the same neurones showed little activity during stereotyped grasping of a knob, a trained task for which afferent feed-back may be of little importance. Finally, operant conditioning of precentral neurone discharge rate by conscious monkeys is more accurate for neurones with small input zones than for those with no input or with large input zones (Wyler & Burchiel, 1978*a*; Wyler & Finch, 1978). Operant conditioning accuracy was greatly reduced when PTNs lost their peripheral input following dorsal column lesions (Wyler & Burchiel, 1978*b*).

Significance of afferent input during movement. Thus under certain conditions, for instance during the acquisition and refinement of novel movements, peripheral input may play a useful and significant role which may not apply to the performance of tasks of a more stereotyped nature. A new motor experience may occur at any time; presumably afferent inputs to the motor cortex are used in the construction of motor programs which in time will ensure accurate performance of the new motor strategy in a manner less dependent on peripheral feed-back. The powerful possibilities of such feed-back are indicated by the fact that some area 4 neurones operate within the same frequency range during the application of peripheral stimuli as during voluntary movement. This finding did not apply to the small sample of PTNs with hand inputs, and may emphasize the importance of additional synaptic inputs for these neurones.

The influence of peripheral afferent input may be more significant for movements of the distal musculature, since peripheral inputs exert effects on rapid ballistic movements of the thumb (Hallett & Marsden, 1979) while ballistic movements of the elbow and shoulder are not sensitive to these inputs (Angel, 1975; Hallett, Shahani & Young, 1975). Monkeys can control neurones with input zones on the distal arm more accurately than those with proximal inputs (Wyler & Burchiel, 1978*a*). The skin is clearly an important source of input for control of finger movements (Marsden, Merton & Morton, 1977; Paillard, Brouchon-Viton & Jordan, 1978; Gandevia & McCloskey, 1977*a*, *b*; Roland, 1978) and this is reflected in the greater significance of cutaneous inputs for hand neurones in the motor cortex.

The results described here, albeit derived from a broad, clinical examination of the monkey's performance, do clearly demonstrate that the behaviour of neurones in the motor cortex is particularly well related to certain types of hand and finger movements and poorly correlated with others. Further examination of these 'best' movements (Smith, Hepp-Reymond & Wyss, 1975; Hepp-Reymond, Wyss & Anner, 1978; Lemon & Kuypers, 1979 and in preparation) should reveal not only how different parametric functions of hand and finger movements are coded in the motor cortex but should give further insights into the special relationship that exists between hand and motor cortex.

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