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RESPONSES OF PRECENTRAL CELLS DURING COOLING OF POST-CENTRAL CORTEX IN CONSCIOUS MONKEYS

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SUMMARY

1. A cooling plate was implanted over the forelimb representation in area 2 of the post-central region of cerebral cortex in two monkeys.

2. Recordings were made of the discharges of thirty-seven movement-related neurones (thirty-four precentral and three post-central) in the forelimb motor representation of the cerebral cortex during active and passively imposed limb movements before, during and after cooling area 2 and local surrounding regions.

3. Perfusion of the cooling plate with ice-cooled water for 3–5 min caused marked clumsiness of the conscious animal's forelimb movement and anaesthesia of the contralateral hand.

4. Cooling of area 2 did not reduce the responses of area 4 cells to passive joint movements, nor did it alter the over-all pattern of activity of these cells during self-initiated lever pulling while that could still be performed.

5. Cooling of area 2 did cause a significant increase in background cellular discharge in area 4 while the animal was at rest.

6. Afferent impulses which are generated by passive joint movement and which have been shown to influence cells in area 4 of the conscious monkey at short latencies are probably not transmitted through cortico–cortical connexions from area 2.

INTRODUCTION

Woolsey, Marshall & Bard (1942) and Woolsey, Chang & Bard (1947) showed that evoked responses to stimulation of cutaneous receptors in monkeys were limited to the post-central region of the cerebral cortex but that stimulation of dorsal roots produced responses over a wider area which extended rostrally to include the motor cortex. Albe-Fessard & Liebeskind (1966) demonstrated that, not only was electrical stimulation of peripheral nerves an adequate method of activating cells in area 4 of monkeys, but imposed limb movement which necessarily activated 'deep' muscle and joint receptors was also a very effective stimulus. Since then it has been shown that 75–90% of single neurones recorded in the arm representation of area 4 in

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conscious monkeys are influenced by natural stimulation of the contralateral limb, the majority by passive movement of one or more joints (Fetz & Baker, 1969; Lemon & Porter, 1976; Fetz, Finocchio, Baker & Soso, 1980). These effects occur at short latencies, some less than 10 ms following the forelimb stimulus (Lemon & Porter, 1976).

While the effects upon area 4 cells from stimulation of peripheral receptors are well documented, the pathway by which they reach the motor cortex remains unclear. Early evidence, using evoked potential recordings, showed that the effects on the motor cortex of peripheral stimuli were not abolished by ablation of the somatosensory cortex (Malis, Pribram & Kruger, 1953; Adey, Porter & Carter, 1954). There is also evidence that the fibres responsible ascend in the dorsal columns (Brinkman, Bush & Porter, 1978; Asanuma, Larsen & Yumiya, 1980), a result consistent with the short latencies of the effects. The nucleus ventralis posterolateralis, pars oralis (v.p.l.o.) has been shown both to project to area 4 and to receive input from the contralateral limb at short latency (Horne & Tracey, 1979; Lemon & Van der Burg, 1979; Jones, Wise & Coulter, 1979; Horne & Porter, 1980). However, the failure to demonstrate a projection to v.p.l.o. from the cuneate nucleus using modern retrograde and orthograde anatomical techniques (Tracey, Asanuma, Jones & Porter, 1980) has led to consideration of alternative pathways. Area 2 of the somatosensory cortex receives input from receptors activated by joint movement (Powell & Mountcastle, 1959*b*), projects to area 4 (Jones, Coulter & Hendry, 1978) and receives input from the dorsal columns. It has therefore been reasoned that cortico–cortical efferents from area 2 could mediate the short latency effects occurring in area 4 following natural stimulation of the limb (Friedman & Jones, 1981; Asanuma, Thach & Jones, 1983). The apparent conflict with earlier results using evoked potentials has been attributed to limitations inherent in evoked potential recordings, which may not accurately reflect events at a local neuronal level (Evarts, 1981).

Our experiment was designed to examine the effects of reversible suppression of neuronal function in area 2 on the relationships to forelimb movement and the responses to natural, passive manipulation of the contralateral forelimb of individual cells in area 4 of the conscious monkey's cerebral cortex. A cooling plate placed over the 'arm' representation on the convexity of the post-central gyrus of the cerebral cortex was used to depress synaptic transmission through area 2 and local surrounding tissue, while recordings were made from single neurones in area 4, both during movement and during natural activation of deep forelimb receptors.

METHODS

Training

Two monkeys (*Macaca fascicularis* spp.) were trained to allow passive manipulation of various joints of the right forelimb while remaining relaxed. Appropriate behaviour was rewarded with small pieces of apple or sunflower seeds. The animals were also trained to perform a simple lever-pulling task. When a horizontal lever was pulled into a target zone, a brief tone sounded and the animal received a small piece of food. Incorrect pulls were not rewarded. Training sessions took place for 45–60 min daily over 3 months. This approach is similar to that used in previous experiments from this laboratory (Lemon & Porter, 1976).

Recording

Once training was completed, a headpiece (modified from Porter, Lewis & Linklater, 1971) was attached to the skull under sterile conditions while the animal was deeply anaesthetized with ketamine (Ketalar, Parke Davis; 10 mg/kg) plus xylazine (Rompun, Bayer; 1 mg/kg) for induction, followed by intermittent maintenance doses as required. In addition the animals were given injections of atropine (0·2 mg/kg), dexamethazone (1·5 mg/kg) and penicillin (50 000 u.). The headpiece was positioned to allow access to the left forelimb motor representation in the precentral cortex. A hydraulic microdrive (Trent Wells) was mounted on the headpiece by means of a pair of eccentric disks. The discharges from single cortical neurones in area 4 were recorded with glass-coated tungsten micro-electrodes, sharpened to 2 to 3 μm, with an exposed tip approximately 16–20 μm in length. The neuronal discharges, the lever position and a signal indicating the approximate timing of the peripheral stimulus were recorded on magnetic tape as well as being analysed directly on-line using a PDP 11/40 computer (Lemon & Porter, 1976). E.m.g. responses were recorded from the brachio radialis, flexor carpi radialis and extensor digitorum communis muscles by means of pairs of multi-stranded, stainless-steel microwires inserted directly into the muscles, about 4 cm apart. The wires were led subcutaneously to the head-holder and soldered to a multi-pin connector.

The onset of the stimulation during passive movement about a joint was signalled by synchronizing the joint movement with a footswitch operated by the experimenter who also moved the joint. The footswitch produced a square-wave pulse. Single-unit discharges evoked by passive joint movement were recorded as post-stimulus time histograms (p.s.t.h.s) triggered by the footswitch. Single-unit discharges occurring relative to the lever pull were plotted as a peri-response time histogram (p.r.t.h.).

Cooling

Cooling of the arm representation of area 2 was accomplished by means of a hollow stainless-steel cooling plate ($10 \times 6 \times 2$ mm) placed directly on to the cortical surface, subdurally, and secured with dental acrylic cement to the head-holder. The plate was placed approximately parallel to the central sulcus, about 2 mm posterior to it and extended caudally to beyond the intraparietal sulcus (Fig. 1). A thermistor (Yellow Springs, YSI 44033) was attached to its upper surface to record plate temperature. The lower surface was smooth for application directly to the cortex with minimum deformation or opportunity for local damage. The wires from the thermistor were connected to the multipin connector on the head holder. During recordings from individual cortical neurones, the cooling plate could be perfused with iced water rapidly (at 175 ml/min) to lower the temperature of area 2 and surrounding local zones and thereby to depress synaptic transmission.

Experimental procedures

The conscious, co-operating animal performed the lever-pulling task while the micro-electrode was lowered through area 4 to record discharges of single cortical units in relation to the movement. A p.r.t.h. was constructed during twenty to forty repetitions of the task for each unit that was isolated. The forearm was then explored systematically by gentle stroking of the skin and by passive movements of the joints in order to localize any peripheral afferent input to the unit, after which a p.s.t.h. was obtained by twenty to forty repetitions of the appropriate passive joint movement. These two histograms served as controls of the unit discharge for active and imposed passive movements of the contralateral forearm. Once completed, the pump was turned on to perfuse the cooling plate with iced water. The animal continued to perform the lever-pulling task and another p.r.t.h. was obtained. This was followed by a p.s.t.h. of the responses to repetitions of the same passive joint manipulation. Both histograms were collected while the pump was on. In some trials a second pair of p.r.t.h. and p.s.t.h. was then collected or the pump was stopped after the first pair of histograms. The cooling plate was then rewarmed over a period of 3 min by perfusing it with warm water (37 °C). Subsequent series of p.r.t.h. and p.s.t.h. were collected until the unit's discharge recovered to approximately control levels.

Histology

The sites of electrode tracks were determined histologically at the end of the experiments in both animals. Stereotaxic placement of marker electrodes coated with Indian ink defined an anterior and posterior reference limit of the recording sites. The deeply anaesthetized animal was perfused through the dorsal aorta with saline, followed by 10% formalin. In one animal, serial

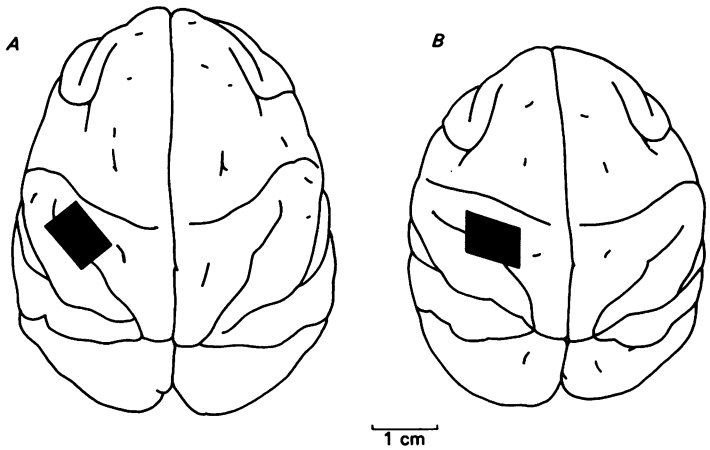

Fig. 1. View from above of both monkeys' brains indicating the location of the cooling plates. The rostral edge ran approximately parallel to the central sulcus while the caudal edge extended caudal to the intraparietal sulcus.

transverse sections (80 μm) and in the other animal, serial parasagittal sections (80 μm) were cut and stained with either thionin or Neutral Red and examined in order to plot all electrode tracks. All sections through the pericentral area lying immediately under and adjacent to the cooling plate were studied histologically. Examination of the cortex under the cooling plate in the first animal did not reveal any gross abnormality. All laminae were intact and followed the contour of a slight surface depression. There was no evidence of glial cell proliferation or other inflammatory response. A slight staining of haemosiderin was found at one corner of the depression, indicating that here the plate may have caused localized damage. In the second animal there was less depression of the surface and no evidence of cortical damage.

In both animals, the cooling plate was situated over the posterior half of the post-central gyrus. Histological examination, using the cytoarchitectural criteria of Powell & Mountcastle (1959*a*), confirmed that the plate covered virtually all of the superficial part of area 2 and extended for most of its length on to area 1 rostrally. Caudally the plate extended to beyond the intraparietal sulcus (Fig. 1) and could have influenced parts of areas 5 and 7.

Cooling

The temporal characteristics of the cooling plate's temperature responses were defined in order to correlate these with the changes in behaviour of the animals as the plate was being cooled. Fig. 2 shows the fall in temperature as the cooling plate was perfused with iced water and held in room air. It achieved an equilibrium of 6 °C in 80 s. In contrast, it was only possible to cool the plate to a temperature of approximately 8–10 °C when the plate was in contact with the post-central gyrus. In air, when the pump was turned off, there was spontaneous rewarming by 10 °C over 5 min, but the temperature increased by 20 °C over 3 min when the plate was in contact with the brain. Therefore observations of the effects of cooling were always made with the pump on. Pumping warm water (37 °C) through the cooling plate caused an initial fall in temperature, since cool water still remained in the tubing going to the plate. The rewarming of the plate to control temperature

was accomplished within 2 min. The time course of cooling is similar to that for direct application of iced saline to the cortex (Burchfiel & Duffy, 1974).

The first animal, over a period of 30 days, had twenty-three cooling trials in which the post-central gyrus was cooled for an average of 10 min/trial. The second animal had thirty-four cooling trials performed for an average of 6 min/trial and was studied over a 35 day period. The number of cooling trials per day of recording varied from one to four, but usually only a single cooling trial

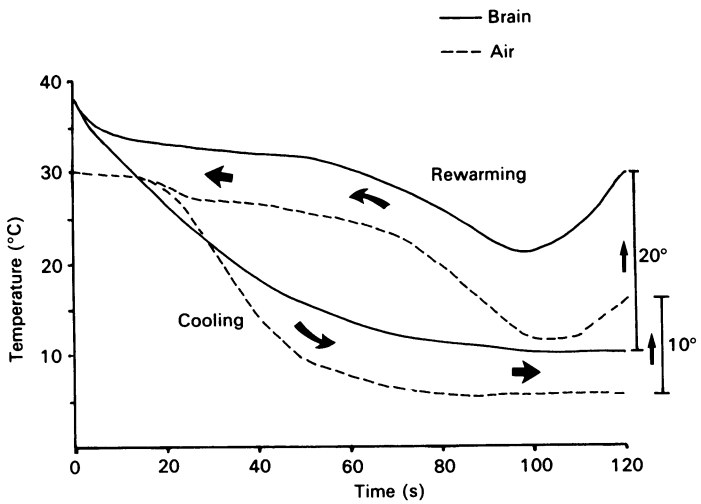

Fig. 2. Plot of temperature *vs.* time after perfusion of the cooling plate with iced water (175 ml/min) while held in room air (dashed line) or on the surface of the post-central gyrus (continuous line). Spontaneous rewarming occurred through 10 °C in air over 5 min, compared with 20 °C, when in contact with brain for 3 min. Upper curves show rewarming of plate following perfusion with warm water (37 °C) under both conditions.

was carried out on any one day. Two cooling trials were done on each of 10 days, three cooling trials on 4 days and four cooling trials on 1 day. In one animal, after completing the single-unit studies, an acute experiment was carried out in which evoked potentials and intra-cortical temperature were measured. During general anaesthesia with ketamine (10 mg/kg) and xylazine (1 mg/kg) a craniotomy was performed, exposing the right cerebral hemisphere, opposite to that used for the single-unit recordings. The pericentral area was exposed and a second cooling plate was placed over a corresponding site covering the post-central gyrus. A pool of paraffin oil held at 37 °C was formed over the exposed cortex. A platinum ball electrode (monopolar, referenced to scalp muscle) and a thermistor were placed over the arm area of the motor cortex on the surface of the precentral gyrus. The superficial radial nerve was dissected and a cuff electrode containing two platinum wires placed around it. Evoked potentials were unchanged or slightly increased in amplitude during cooling and there was no change in the latencies of the peaks recorded over precentral cortex (cf. Asanuma *et al.* 1980).

Recordings from the thermistor on the surface of the precentral cortex showed that the temperature fell 3 °C during prolonged cooling of the post-central cortex for several minutes. Direct intracortical temperature measurements were made within the post-central cortex using a thermistor attached to the tip of a 22 gauge needle. The thermistor was inserted through a perforation in the pia approximately 1 mm posterior to the cooling plate. At a depth of 3 mm the temperature fell to 24 °C after the cooling plate had been perfused with iced water for 5 min.

RESULTS

Behavioural effects of cooling

There was no obvious effect of cooling on the animal while it remained motionless, but after several minutes of cooling, abnormalities became apparent while the animal was pulling the lever. Within 3–5 min of the onset of cooling there was clumsiness and slowness of arm movement associated with over-reaching and poor co-ordination while attempting to grasp the lever. Later the animal stopped using the right limb and would use the other (ipsilateral) hand to grasp food. Sensory deficits could be demonstrated to occur in the contralateral hand. Food placed in the hand was dropped even when the animal could see it. There was no withdrawal response to a sharp pin prick to the hand, but when the forearm above the wrist was tested with pinprick the arm was rapidly withdrawn. There was no apparent effect of the cooling on the ipsilateral hand.

After rewarming for 3 min, the animal again began pulling the lever with only minimal abnormality. Typically by 5–10 min after the start of rewarming, the animal's performance was indistinguishable from that before cooling. Occasionally 'bursting' of neuronal firing was heard, usually after prolonged cooling, but no overt epileptiform twitches were ever seen.

After several weeks of daily recording it appeared that cooling caused fewer deficits in the performance of lever pulling. This suggests that the animal had learned to compensate for the sensory losses which occurred during the cooling or that the cooling trials were less effective in suppressing cortical function (see Discussion).

Single-unit recording in the arm area of the precentral gyrus in conscious monkeys

One hundred and fifty-two movement-related neurones were found and sixty-three were recorded in a stable condition for long enough to investigate their input from the contralateral arm. In fifty-seven of these (91 %), afferent input arising from receptors activated by natural joint movement could clearly be demonstrated. No input was found for the remainder. Cooling was begun during recording from forty-seven cells and, of these, thirty-seven were held without significant change in recording conditions for long enough to retest their afferent input during cooling. These thirty-seven cortical neurones form the basis of the observations reported here.

Most of the neurones studied were excited by passive manipulation of distal joints. Five were excited by passive thumb movements, thirteen by passive finger movements and thirteen were excited by passive wrist movements. Of the remaining six, three were excited by passive elbow movements and three (all post-central, see below) were excited by imposed shoulder movement. In none of these cells was the short-latency feed-back from imposed joint movements blocked by cooling area 2 and local surrounding regions. Rather, there was usually an increase in the total number of discharges included in the histograms of the same number of repetitions of passive joint movement during cooling. Typical of our results are those neurones illustrated in Figs. 3 and 4.

A neurone in area 4 discharging a brief burst preceding the lever displacement is shown in Fig. 3. Passive extension of the index finger at the metacarpo–phalangeal joint was shown consistently to excite this cell in the relaxed, conscious animal.

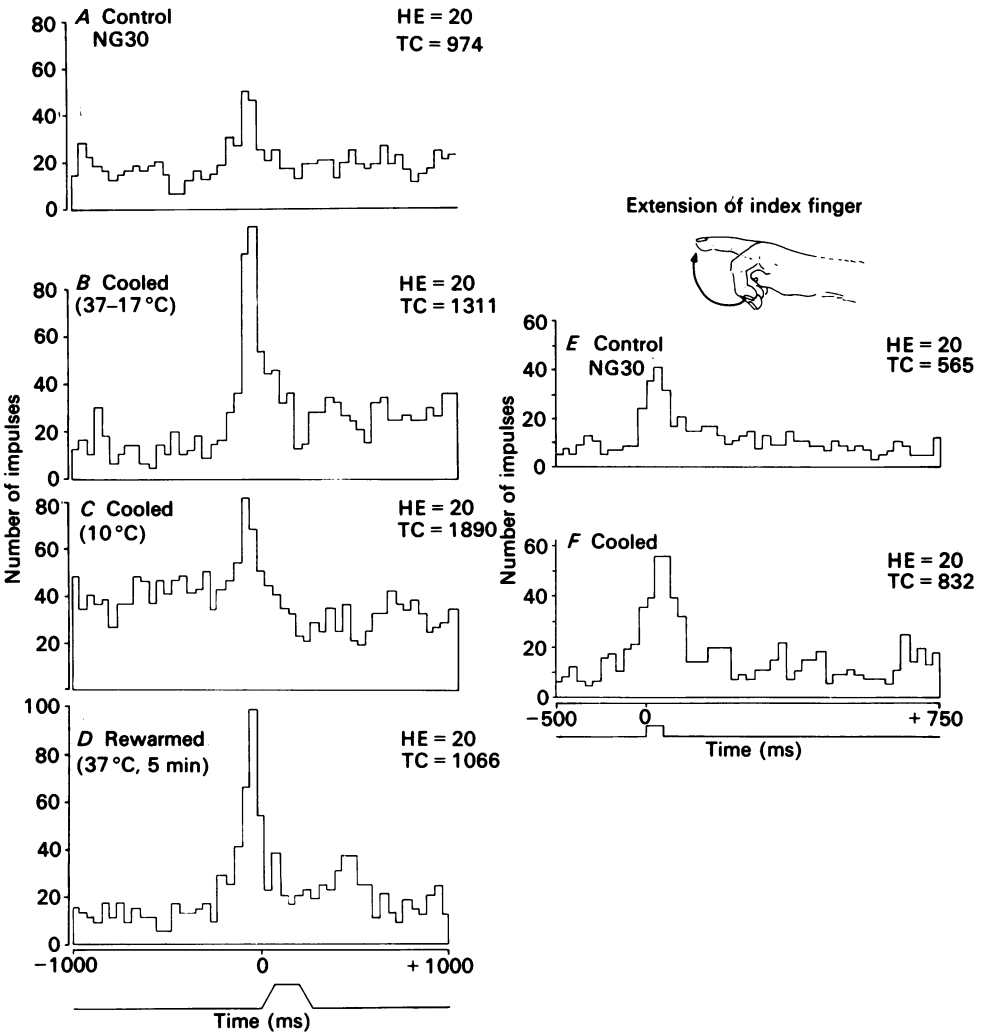

Fig. 3. Histograms of discharges of a movement-related neurone in area 4. *A*, this cell discharged maximally just prior to lever displacement (shown schematically below histogram *D*). B–D, histograms obtained with lever pulling during cooling and rewarming. Despite variation in total cellular discharge, the timing of maximal discharge is unaltered. *E–F*, this cell was excited by passive extension of the index finger before cooling and this response was still present with cooling (histogram *F* obtained after histogram *C*). Time zero is defined as the onset of lever movement for lever-pulling histograms (*A–D*), while, for natural stimulation of peripheral afferents (*E* and *F*) it is defined as the time that the footswitch was closed, signalling approximately the beginning of the imposed movement. HE, number of trials used to build up histogram; TC, total number of discharges accumulated in this number of repetitions of the designated analysis period (2 s for p.r.t.h. and 1·25 s for p.s.t.h., in this and subsequent figures) NG30 is the code number assigned to this unit.

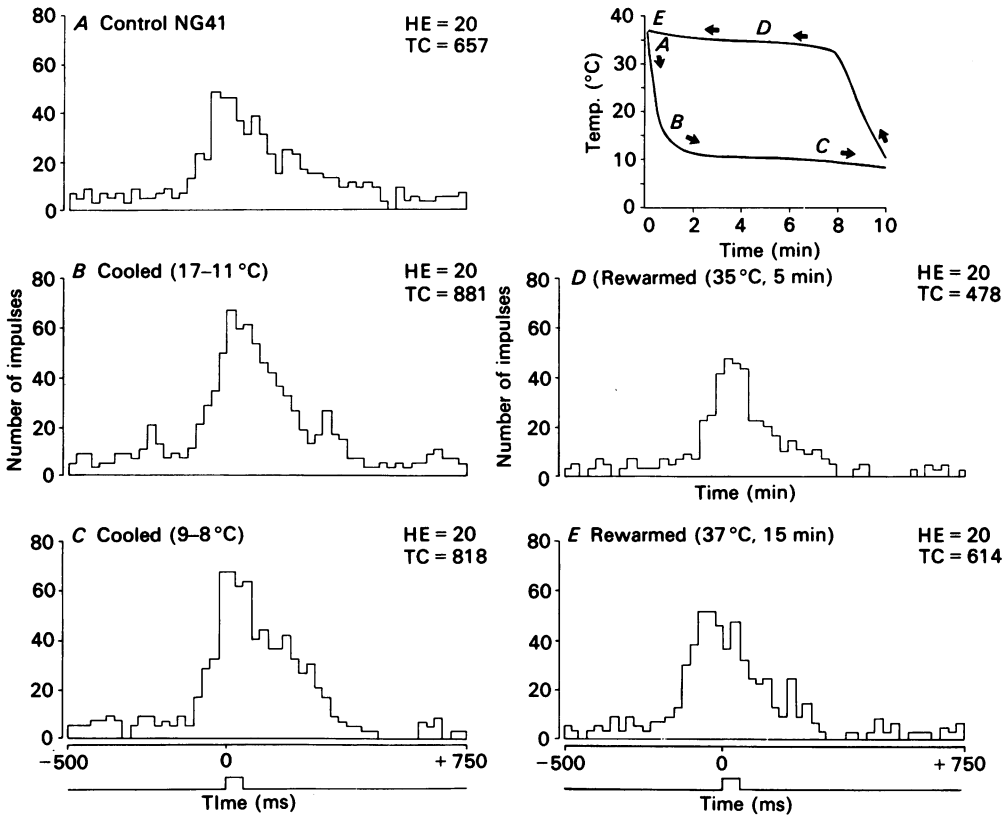

Fig. 4. Series of histograms showing discharges of a neurone in area 4 responding to passive abduction of the index finger. The histograms were obtained at the approximate times and temperatures indicated by the graph in the upper right corner. The response to passive abduction was preserved while total cellular discharge was moderately augmented by cooling. NG 41 codes the unit number in monkey NG.

During the initial period of cooling, the animal continued to pull the lever and there was an increase in the total number of spikes accumulated in histograms of the same number of repeated performances, from 974 in the control period to 1311 during the cooling period, and a marked augmentation in the burst of discharge of this cell just preceding lever displacement (Fig. 3*B*). After the plate had been cooled to 8 °C for 5 min, another 'active' p.r.t.h. revealed a further increase in the number of discharges both preceding and following the lever displacement (Fig. 3*C*): the level of over-all cellular activity accumulated over these 2 s periods including the movement had approximately doubled. Despite this, the timing of peak discharge was unaltered.

At this point, the animal's movements had become clumsy and poorly co-ordinated. The animal had difficulty making a grip around the lever and the arm frequently made groping passes in the general direction of the lever. Testing of the afferent input was undertaken 4 min after the beginning of cooling, with the pump still on. Extension of the index finger still resulted in consistent activation of this neurone (Fig. 3*F*). This response was also augmented during cooling.

After 6 min of cooling, the pump was switched to warm water (37 °C) and the plate was perfused over the next 5 min to return the plate temperature to 37 °C. The animal started to pull the lever after 1 min of rewarming, but was still clumsy for the next 4 min. After 5 min of rewarming, a p.r.t.h. trial was completed (Fig. 3*D*) which showed that the total number of impulses within the accumulated trial periods had returned to close to control levels (1066 *vs.* 974). The animal's use of the limb appeared to have recovered completely after the period of rewarming.

Fig. 4 shows the response of a neurone in area 4 to passive abduction of the index finger. Histograms were obtained at several stages of the cooling–rewarming cycle which correspond to the letters on the simultaneously registered temperature–time plot in the top right corner of the Fig. As the post-central gyrus was cooled, the general temporal characteristics of the afferent response to finger abduction were retained (Fig. 4*A* and *C*), although there was an increase in the number of impulses produced by each abduction movement. Upon rewarming, the response returned to close to control levels.

Three of the units studied were found to be in an electrode track which passed through the post-central gyrus. All three were recorded during a single electrode penetration and all were excited by abduction and internal rotation of the shoulder. An example of the deepest post-central unit, 7 mm from the cortical surface and probably within area 3a, is shown in Fig. 5; this unit differed from the area 4 neurones in that it did not show an increase of discharge preceding lever displacement (Fig. 5H) and it received widely convergent inputs from joint manipulation involving wrist flexion (*C*), wrist pronation–supination (*D*), wrist radial deviation (*B*) and finger abduction (*A*). Internal rotation and abduction at the shoulder was chosen as the stimulus to be evaluated during a cooling trial. As shown in Fig. 5*F*, the response to this afferent input was not blocked with cooling, but an increase in tonic firing was evident in the accumulated results of repetitions of the responses.

While there was usually an increase in the total number of discharges accumulated during many repetitions of the passive joint movement during cooling of area 2, this change could have been due to a general increase in tonic discharge or to an increase in the discharge specifically evoked by the passive joint movement. The discharges of thirty-two of the neurones studied were analysed in detail in an attempt to distinguish between these two possibilities and to quantify the effects of cooling. Tonic activity was assessed by counting the total discharge during a 125 ms period preceding afferent stimulation in a number of repetitions of the stimulus. This total was compared with the total discharges during a corresponding period during which area 2 was cooled. Cooling of area 2 caused an average increase in tonic discharge of 39% for the cells in area 4, which was statistically significant (paired Student's *t* test, $P < 0{\cdot}05$). The discharge considered to have been specifically evoked by natural peripheral stimulation was calculated by subtracting the value obtained for accumulated tonic discharge for the neurone from the total discharge which occurred during a 125 ms period centred around the peak excitation evoked by the peripheral stimulation. This technique was used to eliminate any contribution from increased tonic discharge to the apparent response evoked by peripheral stimulation. Moreover, the window was wide enough to make timing errors from the stimulus marker (which was of necessity approximate) less significant. Assessed in this way and for all the cells, cooling caused a small (average 11% over the total population of neurones)

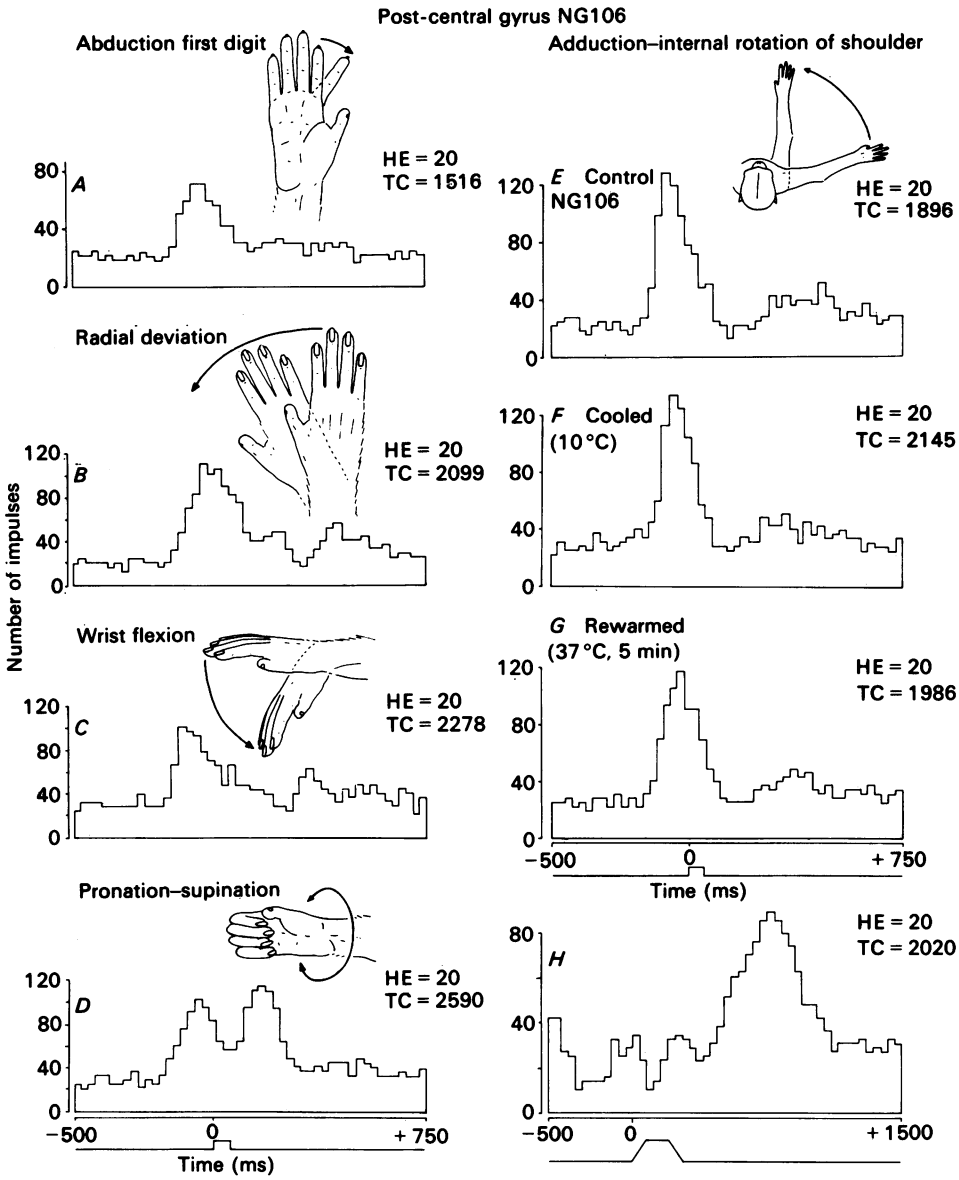

Fig. 5. Histograms of a unit in the postcentral gyrus showing a wide convergence of passive sensory activation by abduction of index finger (A), radial deviation of the wrist (B), flexion of the wrist (C), pronation-supination of the wrist (D) as well as adduction and internal rotation of the shoulder (E). Upon cooling the postcentral gyrus the discharges to passive adduction and internal rotation of the shoulder was not blocked (F), at a time when the animal was not capable of pulling the lever. Subsequent rewarming (G) caused a decrease in the number of impulses relative to that when cooled (F). A histogram of the unit's discharges during the lever pulling task is shown in H. NG 106 is the code for identification of this unit.

reduction in the effectiveness of peripheral excitation, but this was not statistically significant.

Neuronal discharge occurring with (lever) movement was also analysed to assess any change associated with cooling of area 2. Unlike the findings when the animal was relaxed, cooling did not cause any significant increase in firing during movement when assessed for the whole population sampled, even though a few neurones did show changes. There was no significant change in the duration of lever movement. Cooling also failed to cause any consistent shift in the timing of the bins containing either the peak of excitation or inhibition, and in most of the cells these did not change at all.

DISCUSSION

Local cooling has been widely used as a technique to investigate the nervous system (for review, see Brooks, 1983). Cooling has effects upon neurones both pre-and post-synaptically. Post-synaptically there is an initial increase in excitability produced by a fall in temperature of only a few degrees. More profound cooling causes reduced responsiveness. Presynaptic fibres are depolarized but are less sensitive to cooling than are post-synaptic elements. The net effect is one of increased responsiveness of cells cooled down to about 25 °C, then depression and block of synaptic transmission at about 20 °C. Fibre conduction persists to about 10 °C.

Although the cooling plate regularly reached temperatures lower than 10 °C, the cortical surface may not have been cooled to the same extent (Stein, 1978). Our own measurements of intracortical temperature indicate, however, that the function of the total thickness of all the grey matter directly beneath the plate would have been depressed by being cooled below 24 °C. Histological examination confirmed that the rostral edge of the cooling plate covered area 2. Posteriorly it extended to beyond the intraparietal sulcus. This would have ensured that all of area 2 except that lying in the depths of the intraparietal sulcus (Powell & Mountcastle, 1959*a*) would have been effectively cooled by the plate. In addition, parts of area 1 rostrally and areas 5 and 7 caudally would also have been affected. Importantly, areas 3b and 3a, which lie more rostrally and deeper, would not have been significantly cooled by the plate. The three post-central cells studied during cooling were in area 3.

The temperatures used should not have caused permanent damage to any of the areas cooled, and histological examination of the brains of both our monkeys confirmed that the sensory cortex had not been damaged. After rewarming, the neuronal discharge of the cells studied returned approximately to control levels. Other investigations have also found that the effects of repeated cooling with similar temperatures were always completely reversible (Pasztor & Kukorelli, 1967; O'Brien & Phillips, 1976; Brooks, 1983). The 5–10 min of rewarming required before the motor behaviour returned to normal is typical of previous reports (Pasztor & Kukorelli, 1967; Moseley, Ojemann & Ward, 1972; O'Brien & Phillips, 1976).

Behavioural effects of cooling area 2 in the post-central gyrus in conscious monkeys

The abnormalities in the use of the arm which became apparent during cooling resemble closely the changes which follow ablation of the post-central gyrus. Removal of areas 1, 2 and 5 causes ataxia and slowing of movement, failure to

appreciate food put within the hand, blunting of sensation and an apparent tendency to ignore the arm (Peele, 1944). We observed all these changes as prominent features following cooling. The sensory loss to pinprick is not seen with cooling or ablation of area 5 alone (Peele, 1944; Stein, 1978) and is strong evidence for a direct effect of the cooling probe upon sensory cortex, in our case principally on area 2. While the response to pinprick was blunted for stimuli only to the hand, pinprick sensation is relatively spared after parietal lesions (Holmes, 1927). More relevant to motor control, the loss of proprioceptive feed-back from the arms was probably more severely affected after area 2 suppression but we were unable to assess this directly.

Paralysis and an inability to move is not a feature of post-central lesions. Our animals would overcome their reluctance to use the affected arm if presented with a particularly desirable piece of food and they could and did move their affected limb in withdrawal from pinprick.

The ataxia and clumsiness which resulted from cooling sensory cortex are probably due in large part to loss of the normal proprioceptive feed-back from the arm because vision has been reported to correct most of the motor abnormalities (Peele, 1944; Stein, 1978). Our animals' heads were restrained but they were always able to see the lever and also their hand and forearm. Despite this, ataxia and clumsiness with each period of cooling could be demonstrated repeatedly during some weeks. Presumably the animals were unable to use visual feed-back to compensate completely for the brief periods of loss of proprioceptive information in the early stages.

Discharges of area 4 neurones after cooling the post-central cortex

Cooling of the post-central cortex caused an increase in tonic firing of area 4 cells while the animal was at rest. The simplest explanation for these findings would be abolition of cortico–cortical inhibition mediated by the projections from area 2 to area 4. However, some or all of the increase could have been due to facilitation resulting from mild cooling (by 3 °C) of area 4 such as did occur with our preparation during the acute experiment. While the sensory cortex appears to exert a tonic inhibitory effect upon the thalamus (Hosko & Helm, 1969; Burchfiel & Duffy, 1974), thalamo–cortical disinhibition of area 4 from cooling of area 2 seems less likely in view of recognized cortico-thalamic reciprocity, in which a given cortical area projects predominantly to the part of the thalamus which in turn projects back to it (Jones, 1984). Interestingly, during the periods of movement performance, this facilitation of area 4 neurones could not be demonstrated. This could indicate an active reduction in the effectiveness of an incoming inhibitory pathway, from whatever source, during movement. It could also be due to less spread of cooling to area 4 as a consequence of the increased blood flow which occurs in this region with movement (Roland, Meyer, Shibasakai, Yamamoto & Thompson, 1982). Cooling during lever pulling also did not alter either the timing or the general pattern of neuronal discharges in relation to movement.

Pathway mediating short-latency return signals

Cooling of area 2 so that synaptic transmission was blocked did not alter the return signals to area 4 generated by passive joint movement. This excludes cortico–cortical

efferents from area 2 to area 4 from mediating the response to joint movement unless they came from a localized zone of area 2 deep in the intraparietal sulcus. However, signals from sensory cortex could have a role in the responses of area 4 cells to cutaneous stimulation which were not examined in detail here. Different modalities may be transmitted by different pathways and subjected to differential control (Zarzecki & Asanuma, 1979; Asanuma *et al.* 1983). Moreover, area 5 projects cortico–cortical influences on to area 4 and some of these effects could have been preserved in these experiments.

Area 3a receives input from muscle receptors (Phillips, Powell & Wiesendanger, 1971; Lucier, Ruegg & Wiesendanger, 1975) and would not have been cooled to a level that would suppress function effectively in these experiments. Physiological evidence of a projection from area 3a to 4 is conflicting (Woolsey *et al.* 1947; Phillips *et al.* 1971; Zarzecki & Asanuma, 1979) while anatomical evidence shows that the major projection of area 3a is caudally to somatosensory cortex, not to area 4 (Jones & Porter, 1980).

The major input to area 4 from sensory cortex comes from area 2, the zone cooled in these experiments. The behavioural changes observed when area 2 was cooled provided ample evidence of suppression of function in this zone of cortex. Yet the short latency inputs to area 4 cells from peripheral stimuli were not depressed. Our results are consistent with a pathway via v.p.l.o. to area 4 for the short-latency responses to peripheral stimuli in the conscious monkey. They do not resolve the problem associated with the failure to demonstrate a dorsal column input to v.p.l.o. Local cooling, which allows observations to be made for a single cell before and after blocking its putative input, could be applied usefully to both the thalamus and dorsal columns to investigate this issue further.

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