J. Physiol. (1955) 128, 182–199

RESPONSES IN THE BRAINSTEM OF THE CAT TO STRETCH OF EXTRINSIC OCULAR MUSCLES

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(*Received* 4 *November* 1954)

Although cats' extraocular muscles lack muscle spindles they possess many sensory endings, some of which can be activated by passive stretch. Discharges from these proprioceptors were recently recorded in fibres of the third nerve in the orbit (Cooper & Fillenz, 1952, 1955). The present paper deals with the investigation of the further course of these afferent impulses. Recordings from the cell bodies of the afferent neurones are described, and an attempt is made to trace these responses to second-order neurones and to discover the change in pattern which occurs at the first synapse.

METHODS

Two kinds of preparations were used: cats under general anaesthesia, and decerebrate cats.

Operation. In twenty-two cats the general anaesthetic was 60–80 mg of chloralose given intravenously, after induction with ethyl chloride and ether. These were preliminary experiments of which only a few photographic records are available. In twenty-nine cats the general anaesthetic was intraperitoneal barbitone. The dose was 0·45 ml./kg body weight of Abbott's Veterinary Nembutal (60 mg pentobarbitone sodium per ml.). This initial dose had to be supplemented by further small doses given intravenously or subcutaneously throughout the day.

The ocular muscles were isolated, after opening the orbit and removing the eyeball, and separate ligatures were attached to the tendons of each of the six extraocular muscles. The ligatures were then passed to separate devices for applying passive stretch individually to the ocular muscles. Too clean a dissection of the muscles had to be avoided since the stretch receptors are dependent on a good blood supply for their continued functioning.

Since jaw muscles are in close relation anatomically with eye muscles, and may affect them mechanically, it was necessary to observe the effect of stretching those muscles which close the jaw. To do this a string was passed through the floor of the mouth and tied around the lower jaw at the symphysis. It was attached to a puller somewhat heavier, but generally similar to the pullers attached to the eye muscles.

The decerebrate preparations numbered 18. Ethyl chloride and ether by inhalation were used as preliminary anaesthetics while the above operation on the orbit was performed and during decerebration. The levels of decerebration ranged from the mid-thalamic to the intercollicular plane. Eleven of the cats needed no further anaesthetic, but in seven cats, two to three further doses of 0·3 ml. pentobarbitone intramuscularly were required on account of the forward level of decerebration and the consequent restlessness of the preparation. The bony tentorium was removed after decerebration.

Apparatus. The stereotaxic machine used was a modification of the Souttar-Beattie stereotaxic machine and was constructed in this laboratory.

Stretch applied to muscles was signalled through a system for converting changes in capacity into voltage fluctuations (Dickinson, 1950). The eye-muscle puller consisted of an L-shaped lever with its fulcrum at the right angle of the L. The string from the tendon of the eye muscle was attached to the short limb of the L. The long limb of the L was moved by hand until it struck a stop; the maximum stretch could thus be fixed. Another puller was used for the jaw muscles, working on the same principle, but having a larger, stouter lever.

The microelectrode was a steel needle insulated along the shaft and with a bare tip ground down to a diameter of 10–20 μ. The conventional R-C coupled amplifier and cathode-ray tube were used.

Histological methods. Needle electrode positions were always checked by serial sectioning of the fixed brain embedded in nitrocellulose (Chesterman & Leach, 1949). The sections were stained by Weil's modification of Weigert's iron haematoxylin with a final differentiation in 0·25% oxalic acid + 0·25% sodium hyposulphite. The sections were 100 μ thick. The sections showing needle tracks were enlarged and photographed, and the sites of responses were localized after allowing for shrinkage. For further details see Cooper, Daniel & Whitteridge (1953*a*).

RESULTS

Responses to passive stretch applied to the extrinsic ocular muscles of the cat were detected in the medulla oblongata, pons and midbrain. In some cases a certain pattern of response could always be associated with a certain anatomical structure; in other cases such a correlation was not possible and the responses had to be grouped according to their site or pattern.

The responses in anaesthetized and decerebrate preparations showed certain differences and they will therefore be described under separate headings.

Cats under Nembutal anaesthesia

Early sustained responses. Stretch applied to an eye muscle might cause the initiation of a discharge from a silent base-line or the acceleration of an already discharging unit. If the discharge resembled in pattern the responses obtained in a fibre of the third nerve in the orbit as a result of stretching an extraocular muscle (Cooper & Fillenz, 1955) and if the latency conformed to certain requirements, then the discharge was attributed to activity in part of a primary afferent neurone in the brainstem. Such discharges are shown in Fig. 1*a*, *b*.

Since the cat's extraocular muscles are somewhat small and fragile their resting tension was kept low. This would account for the frequent absence of a resting discharge and variations in the latent period. The latter was considered to be short when the discharge or increased rate of discharge began early in the rising phase of the stretch. Further, in these early sustained responses, the maximum rate of discharge was always reached during this rising phase. As the stretch was applied rather gently by hand, the rising phase might last from 20 to 120 msec. The latent period varied between 11 and 40 msec. The maximum rate of discharge recorded was between 100 and

280 impulses/sec. During the sustained pull, the unit either discharged at a steady rate rather below the maximum rate or there were slight irregularities giving a 'saw-tooth' type of frequency curve (Fig. 2). On releasing the stretch, there was a reduction of the frequency below the resting rate of discharge, which was gradually resumed if the unit had previously been discharging spontaneously. It was a feature of this type of response that it could be repeated many times and, if the unit was discharging spontaneously, it might continue to do so for an hour or more.

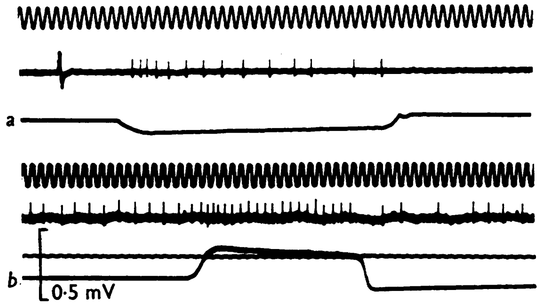

Fig. 1. Responses to stretching eye muscles recorded from the mesencephalic nucleus of the fifth nerve. *a*: stretch applied to inferior oblique muscle. The unit, which is a cell in the mesencephalic nucleus of the fifth nerve, has no resting discharge even when the muscle is under fairly high resting tension. Latency of onset of response varies with rate of application of the stretch; in this instance 33 msec. Time occupied by rising phase of pull, 60 msec. *b*: unit with a resting discharge. Stretch applied to medial rectus muscle accelerates resting discharge. At cessation of stretch, frequency of discharge falls below resting level. Stretching inferior rectus muscle caused inhibition of resting discharge (not shown). Latency 22 msec; duration of rising phase of pull, 65 msec. Above: time, 50 c/s. Below: stretch signal.

In the anaesthetized cats the exploration of the brainstem was confined to regions rostral to the bony tentorium. Responses to stretching the extraocular muscles could usually be picked up when the needle tip was in the lateral edges of the central grey matter or when it was at the base of the inferior colliculus near the fourth nerve. The sites were all found to lie on the midbrain course of the mesencephalic nucleus of the fifth nerve (Fig. 7, filled circles). The responses were from large single units suggesting that they represented soma spikes of the cells of this nucleus. Subsequent histological examination frequently showed that during an early sustained response the needle tip had lain in the vicinity of one or more of the large globoid cells which make up the nucleus. An example of this is shown in Pl. 1. The responses were found on the same side as the muscle to which the stretch was applied but the study was not sufficiently exhaustive to exclude contralateral responses.

At a large number of electrode positions within the distribution of the mesencephalic nucleus of the fifth nerve, early sustained responses could also be obtained by stretching the jaw muscles. In some cases the units activated in the two responses looked very similar; in other cases stretching the jaw muscles and stretching the extraocular muscles activated two clearly distinct units. The latencies of the jaw muscle responses to stretching were often very brief, a fact at least partly explained by the lower sensitivity of the jaw-muscle

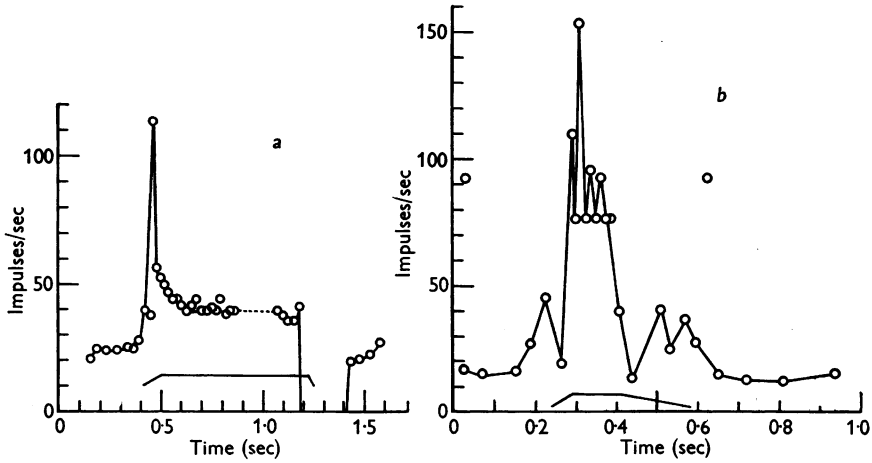

Fig. 2. Curves showing frequency of discharge during various phases of the applied stretch. Time course of stretch indicated by black line at the bottom of each graph. The frequency is measured by taking the reciprocal of the interval between two successive impulses. In graph *b*, the unit gives a double discharge at about 0·05 and 0·6 sec.

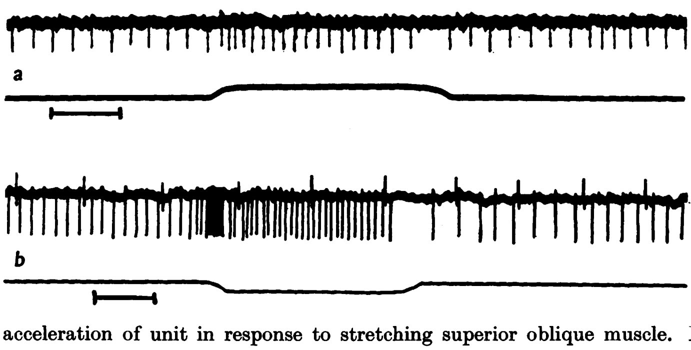

Fig. 3. *a*: acceleration of unit in response to stretching superior oblique muscle. Latency of response is 20 msec. *b*: acceleration of a different unit in response to opening jaw and so stretching jaw muscles. Acceleration of unit begins slightly earlier than signal indicating stretch, because stretch signalling system is not as sensitive as sensory discharge. Time, 0·1 sec. Signal for stretching eye muscles, upwards; for opening jaw, downwards.

puller and the vigorous treatment that could be applied to the jaw muscles in contrast with that applied to the eye muscles. Fig. 3 shows two different units, one responding to stretch of an eye muscle, the other to stretch of the jaw muscle.

It was thus necessary to try to distinguish between the two sets of responses and to be certain that the responses to stretching the eye muscles were not due to an indirect stimulation of the jaw muscles. In some positions of the needle tip it was possible to get a sustained response to pulling on a single eye muscle, the unit being quite unaffected by stretching the other eye muscles or the jaw muscles. Such a response, to pulling on the inferior oblique muscle, is shown in Pl. 1*c*. This muscle, in the absence of the eyeball, can have very little influence on the jaw muscles. During this response the needle tip lay near cells of the mesencephalic nucleus of the fifth nerve, shown in Pl. 1*b*, situated near the region of the fourth nerve.

Occasionally when the site of the receptor giving the discharge was doubtful, it could be identified by mechanical means. Pressing on a specific area in an eye muscle or in the pterygoids at the back of the orbit caused an alteration in the discharge of the same unit that had responded earlier to stretch.

Sometimes when an early sustained response to stretching an eye muscle was obtained, the resting discharge of the unit could be stopped by pulling on the antagonist of the muscle. An illustration of such a case is given in Fig. 4; the unit shows a resting discharge and stretching the lateral rectus muscle caused a short-latency, sustained acceleration of the discharge (Fig. 4*a*). On releasing the stretch, there is a very prolonged depression of the resting discharge. Stretching the medial rectus muscle (Fig. 4*b*), on the other hand, causes a complete suppression of the resting discharge throughout the application of the stretch. On release of the stretch, there is a return of the firing which starts at a high frequency and only very gradually returns to the low resting level. When the lateral rectus and the medial rectus are stretched simultaneously (Fig. 4*c*), the response resembles that of stretching the lateral rectus alone, i.e. the 'inhibitory' effect of the medial rectus does not become evident.

The 'brief-burst' response. In cats under Nembutal anaesthesia there was another group of responses of different character and possibly different provenance, which could be recorded from the midbrain in response to stretch of an eye muscle, and which showed a well-defined pattern. These are described as 'brief-burst' responses and examples are given in Fig. 5. Fig. 7 shows that these responses were also found at the edge of the central grey matter, although they were less frequent than the early sustained responses. Some 'brief-burst' responses were found in the deeper layers of the superior colliculus near the posterior commissure.

The response was characterized by a brief burst consisting of two to six discharges with a latency of 20–120 msec. The latency was usually longer than the rising phase of the pull; the frequency of discharge reached up to 200–300 impulses/sec. Both frequency and number of discharges seemed to be independent of the applied stretch. In successive stretches, with the electrodes in the same position, the response sometimes failed to occur, but when it was present it always showed much the same pattern.

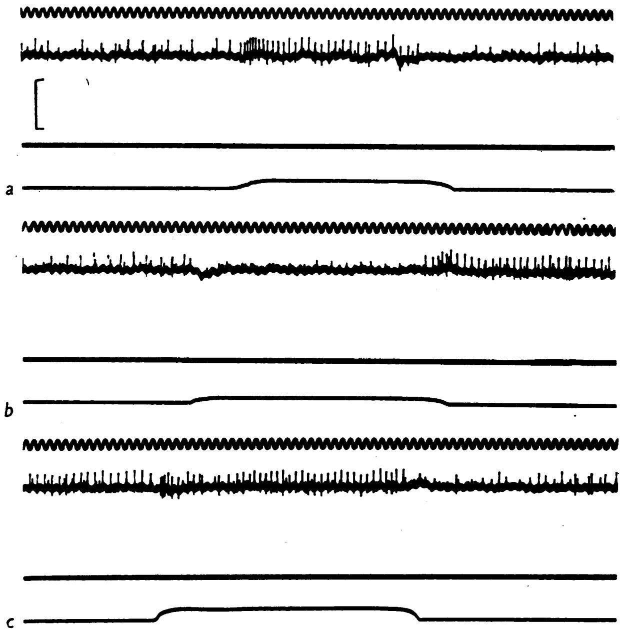

Fig. 4. Unit with a resting discharge which is accelerated in response to stretching one eye muscle and stopped by its mechanical antagonist. Mean frequency of resting discharge is 0·27 impulse/sec. *a*: stretching lateral rectus muscle produces an increase in the frequency of the discharge which during the maintained stretch is 59 impulses/sec. *b*: stretching medial rectus completely suppresses the resting discharge. On release of the stretch the frequency does not return to the previous low level but remains at about 50 impulses/sec. *c*: the signal for stretch indicates the simultaneous stretching of lateral rectus and medial rectus muscles. The acceleration is much the same as in *a*. On release of the stretch there is a pause and then a return to the initial low frequency resting discharge. Records *a*, *b*, *c*, run on continuously. Time: 50 c/s. Calibration: 0·1 mV.

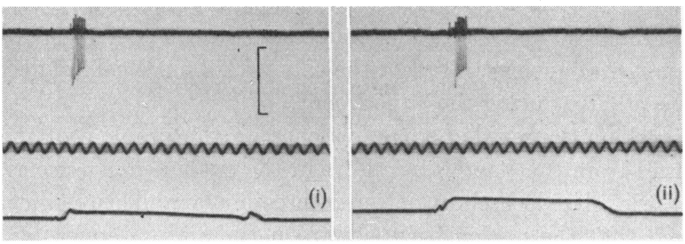

Fig. 5. 'Brief-burst' responses in cats under Nembutal anaesthesia. (i) Response to stretching medial rectus muscle. Latency of response 27 msec. (ii) Same unit as in (i) giving brief-burst response to stretching superior oblique muscle. Latency 25 msec. Time, 50 c/s. Bottom line: signal for muscle stretch. Voltage calibration, 0·5 mV.

The effective stimulus was a sharp tap applied to the lever carrying the string from the tendon of the muscle. Sometimes a number of extraocular muscles, if tapped, would produce a response in the unit under observation. The responses illustrated in Fig. 5 were recorded from the cephalic end of the deep layer of the superior colliculus. They were most readily obtained when a sharp pull was applied to the medial rectus or to the superior oblique muscle. The frequency of discharge is 350 impulses/sec, and the spike shows rapid diminution in size with successive impulses. This unit was quite unaffected by stretching or tapping the jaw muscles.

Other responses. A study of Fig. 7*a–c* shows that a number of responses (sites indicated by open circles) to stretching an eye muscle were heard but could not be classified. Many of these sites lay near the early sustained response sites; the unclassified responses may have been caused by first-order neurones firing at a distance, or they may have come from second and higher order neurones that were stimulated occasionally if the anaesthesia was light. Quite a number of the sites are seen to lie in the brachium conjunctivum and are thus interesting as suggesting a fairly direct link between the eye muscle proprioceptors and the cerebellum.

Numerous spontaneous units were heard as the needle tip explored the brainstem; some of these could be related to different anatomical structures such as the motor nuclei or the red nucleus, but they were quite unaffected by stretch of the eye muscles.

Decerebrate cats

The main region explored in these cats was rather different from that in the anaesthetized preparations. The level of decerebration varied between mid-thalamic and intercollicular. In a considerable number of cats the rostral end of the midbrain inevitably suffered from the neighbouring transection and decerebrate cats therefore gave less extensive results on exploring the mid-brain than anaesthetized preparations. On the other hand, the bony tentorium was always removed and the exploration extended caudally to the rostral level of the hypoglossal nucleus. Most of the cats with a more caudal decerebration had no anaesthetic during the experiment.

Two experiments provided some evidence on the problem of the pathway of the nerves from the stretch receptors in the extraocular muscles. In these two cats, the level of decerebration was intercollicular and histological examination showed that the nucleus of the third nerve and its emerging fibres had been removed. Both these preparations, however, gave responses to stretching the muscles supplied by the third nerve as well as the superior oblique and the lateral rectus. Some of the afferent discharges from the first group of muscles must, it is assumed, enter the brainstem through a pathway other than the third nerve.

The decerebrate preparations were characterized by the much greater level of background activity and the very much greater number and variety of responses to stretching eye muscles than were found in cats under barbiturate anaesthesia.

Early sustained responses. Since the region of the midbrain which contains the rostral part of the mesencephalic nucleus of the fifth nerve was often damaged in the decerebrate cats, this part of the nucleus could not be so thoroughly explored. But in those brainstems which had not suffered in this way a number of early sustained responses were recorded. The more caudal parts of the nucleus and tract were, however, easily accessible and early sustained responses to stretching the eye muscles and the jaw muscles were picked up frequently. Fig. 8*c*–*f* shows the sites of these responses from the rostral end of the central grey matter to fibres of the tract as it passes dorso-caudal to the motor nucleus of the fifth nerve. The more caudal responses were always multi-unit and the units were much smaller than those in the midbrain responses, suggesting that they probably represented the activity of fibre bundles.

The early sustained responses obtained from stretching the eye muscles and the jaw muscles were found in adjacent sites in the greater part of the mesencephalic nucleus of the fifth nerve. This does not seem to be the case in the caudal fibres of the tract, where early sustained jaw- and eye-muscle responses were recorded from consecutive layers of fibre bundles. This may point to the proprioceptive fibres of the eye and jaw muscles entering the brainstem in separate bundles.

Late sustained responses. A common type of response to stretch of the extraocular muscles recorded in the decerebrate cats was a sustained discharge starting from a low frequency resting discharge or from a silent base-line. In the former case (Fig. 6*a*, *b*) the frequency during the response was usually fairly regular; in the latter case (Fig. 6*c*–*e*) there was often a high-frequency burst at the beginning of the response, followed by a pause and then by an irregular low-frequency discharge. Rates of 200 impulses/sec or more were often seen in the first burst. The sustained discharge often resembled the early sustained responses in the primary afferent neurone, but there were two features which served to distinguish them: one was the fact that the latency was always longer than the duration of the rising phase of the pull; the other was the absence of the pause at the end of the stretch. The frequency of discharge was always highest at the onset of the response. The relation between the end of the stretch and the end of the response varied: sometimes the two were coincident but sometimes the response continued beyond the cessation of the stretch as seen in Fig. 6*a*. The response could usually be obtained by stretching each eye muscle in turn; occasionally, with repeated stretches of any one muscle, the frequency and duration of the response fell off rapidly.

Rather similar responses could be obtained in various parts of the brainstem to a stretch of the jaw muscles but only rarely were they found at identical sites with the late responses from stretching the eye muscles.

The sites of these late sustained responses are indicated by the symbol ◐ in Fig. 8. A rather striking group of them lies in the deeper layers of the superior colliculus near the posterior commissure; if these sites in Fig. 8*b* are compared with the corresponding region in Fig. 7*a*, it is seen that they must lie very close to the sites of early sustained responses. It is also known from other unpublished work on this region that many pathways concerned with visual responses lie near here.

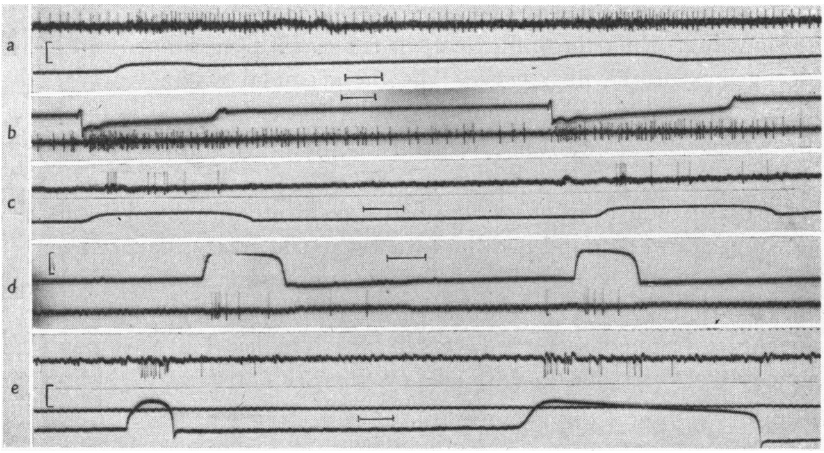

Fig. 6. Responses from reticular formation of brainstem in decerebrate cats. *a*: unit with resting discharge in reticular formation of pons. Stretching inferior oblique muscle produces acceleration of resting discharge which outlasts duration of stretch. Response also produced by stretching superior oblique muscle. *b*: unit with resting discharge in reticular formation of the midbrain. Stretching inferior rectus muscle accelerates resting discharge and also brings in a second unit. *c*: silent base-line. Stretching medial rectus muscle causes the discharge of a unit in the reticular formation of the pons. Response consists of a brief burst of discharges followed by a slow irregular discharge. *d*: response similar to above. Note diminution of second response. *e*: response from unit in the reticular formation of the pons near sixth nucleus to stretching inferior oblique muscle. Time mark in each record, 0·1 sec. Voltage calibration, 50 μV.

Another group of sites is indicated in Fig. 8*b* near the lateral edge of the nucleus of the third nerve, and near or among fibres of the medial longitudinal fasciculus, the tegmental and the tecto-tegmental tracts coming down by the lateral edge of the central grey matter. These are all significant pathways in relation to the nuclei of the eye muscle nerves.

The next group of sites lies between the nucleus of the sixth nerve and the mesencephalic root of the fifth nerve as it passes the motor nucleus of this nerve. This group is shown in Fig. 8*c*–*e*; again it lies close to sites of early sustained responses to stretching the eye muscles and near pathways connected with the nucleus of the sixth nerve.

The most caudal group of sites investigated are indicated in Fig. 8*a*–*d*; the sites lie just rostral to the nucleus of the twelfth nerve and dorsal to the inferior olive. The more dorsal sites lie near the medial longitudinal fasciculus and other longitudinal tracts which are probably on their way to and from the spinal cord. The more ventral sites are in the reticular formation rostral to the respiratory centres.

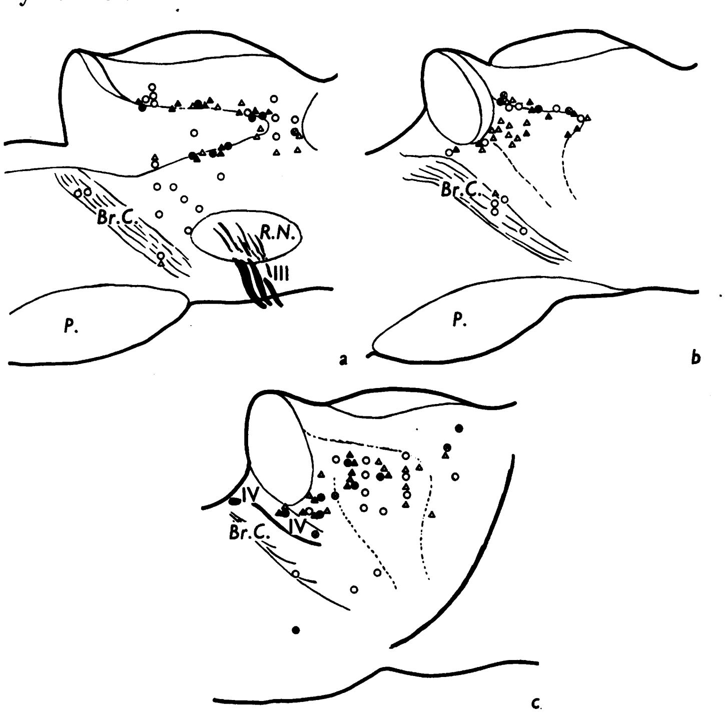

Fig. 7. Diagrams of sagittal sections through the cat's midbrain showing the distribution of responses in cats under Nembutal anaesthesia. The diagrams represent sections at 1·5, 2·0 and 2·5 mm from the midline. *Br.C.*, brachium conjunctivum; *P.*, pons; *R.N.*, red nucleus; III, IV, third and fourth cranial nerves respectively. ●, early sustained eye-muscle responses; ⊗, 'brief-burst' eye-muscle responses; ○, unclassified eye-muscle responses; ▲, early sustained jaw-muscle responses; △, unclassified jaw-muscle responses.

It is not always possible, with a fine needle tip, to be certain whether the response comes from a cell or a fibre; but with some of the responses from the reticular formation subsequent histological examination showed that, at the site of the responses, the needle tip lay close to large multipolar cells. An example of this is given in Pl. 2. The track in the medial part of the medulla is shown in *a*, and the end of the track, seen at greater magnification, in *b* and *c*.

In Pl. 2*d* is seen a response from a similar cell (the photomicrograph of the second cell and the record from the first cell were less suitable for reproduction). These large multipolar cells are very numerous among the fibres of the reticular formation, especially in the hindbrain. Large cells are also found in the layers of the superior colliculus in the cat, but it is not certain whether the responses in this region came from such cells.

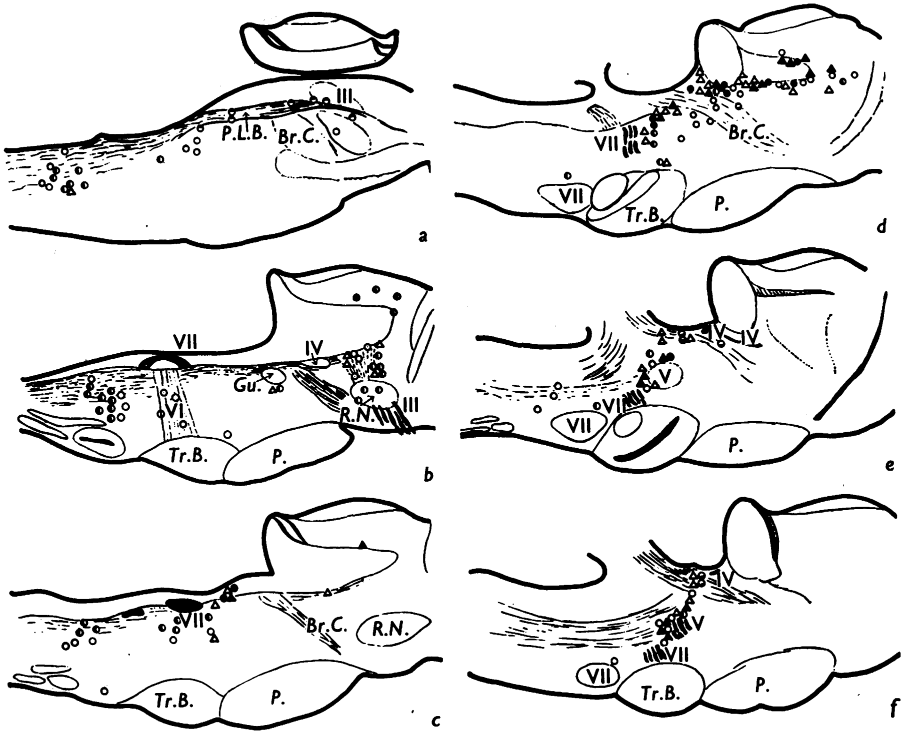

Fig. 8. Diagrams of sagittal sections through the brainstem showing the distribution of responses in decerebrate cats. *a* is a section through the midline: the other sections proceed laterally in steps of 0·5 mm. *Br.C.*, brachium conjunctivum; *Gu.*, nucleus of Gudden; *P.*, pons; *P.L.B.*, posterior longitudinal bundle; *R.N.*, red nucleus; *Tr.B.*, trapezoid body; III, IV, V, VI, VII, nucleus and fibres of third, fourth, fifth, sixth and seventh cranial nerves respectively. In the case of the fifth nerve the motor nucleus is referred to. ●, primary afferent neurone eye-muscle responses; ◐, second-order neurone eye-muscle responses; ◓, eye-muscle responses in medial longitudinal bundle; ◒, eye-muscle responses in brachium conjunctivum; ○, unclassified eye-muscle responses; ▲, primary afferent neurone jaw-muscle responses; △, unclassified jaw-muscle responses.

Inhibitory responses from the reticular formation of the brainstem. A few inhibitory responses were recorded in the reticular formation of the brainstem. They consisted in the inhibition of a unit which was showing a slow resting discharge. The time relation between the inhibition and the applied stretch was variable. Stretching the mechanical antagonist of the muscle producing inhibition did not cause acceleration of the unit.

Other responses to stretching eye muscles in the decerebrate cat. A number of needle tracks were placed close to the midline in an attempt to get responses from the eye-muscle nuclei. The nuclei were easily identified by the large diphasic spikes and the loud background activity; the position of the electrodes was confirmed by passing shocks through the needle tip: these caused contractions of individual eye muscles at a very low intensity. But no modification of the spontaneous activity in the nuclei in response to pulling on eye muscles could ever be observed.

A number of single unit responses were, however, obtained near the midline, but they varied in pattern. They all had long latencies and were unlike the sustained responses. On later examination of the brainstem the needle tip in each case was found to have been in the medial longitudinal fasciculus at sites extending from the rostral end of the nucleus of the third nerve to near the rostral part of the nucleus of the sixth nerve (Fig. 8*a*). A further small collection of responses were recorded in the region of the brachium conjunctivum (Fig. 8*e*, *f*).

The open circles in Fig. 8 indicate the occurrence of responses to stretching the eye muscles which either did not fit into any of the above categories of responses, or of which photographic records are not available.

Cats under chloralose anaesthesia

A number of cats under chloralose anaesthesia were also investigated. Few photographic records are available from these experiments, and therefore no detailed comparison can be made with the other two types of preparation. The most striking feature, however, was the very much greater number of responses to stretching eye muscles than in cats under Nembutal anaesthesia and the resemblance in this respect to decerebrate preparations.

DISCUSSION

The present work is largely concerned with two types of response that were recorded in the brainstem of the cat as a result of stretching the extraocular muscles. The first type, called the early sustained response, resembles in pattern the responses from the low threshold stretch receptors of the limb muscles which are associated with the main afferent endings of muscle spindles (Matthews, 1933). Similar responses were recorded by Cooper *et al.* (1953*a*) in the brainstem of the goat, on stretching the extraocular muscles. They concluded that if these responses could be obtained by pulling on one muscle only and were of short latency, then they were being recorded from the first sensory neurone of a spindle ending in that eye muscle. Such responses were not found easily in the goat, but there were several clear-cut cases, and the sites of the responses were always associated with some part of the mesencephalic tract of the fifth nerve.

The cat's eye muscles contain no muscle spindles, but by leading from peripheral branches of the third nerve in the orbit, Cooper & Fillenz (1952, 1955) showed that there were low threshold stretch receptors in these muscles, whose pattern of response to stretch was very like that from a muscle spindle. Similar discharges have now been picked up in the brainstem and the sites of the responses lie, very strikingly, along the course of the mesencephalic tract of the fifth nerve. There were more responses than were reported in the goat, and they were often mixed up with the sites of responses to stretching the jaw muscles, but the two sets of responses could usually be separated. It would be an interesting difference if the distribution of the afferent neurone cells of the eye muscle receptors in the two animals were not the same. A greater proportion of the cells in the goat may lie outside the brainstem.

In the present work the central responses to stretch of the eye muscles often had a longer latency and a lower rate of discharge than the responses in the third nerve of either the cat (Cooper & Fillenz, 1955) or the goat (Cooper, Daniel & Whitteridge, 1951). The cat's eye muscles are small, delicate and easily cooled or injured. They deteriorate sufficiently in the course of an experiment to account for changes in the latency and rate of discharge. The successful experiments on the peripheral nerve were always those in which the sensory fibres were isolated quickly. The goat has large tough muscles that will stand considerable stretching over long periods.

In some cases in the cat the central responses were obtained by stretching more than one muscle; this may be due to a mechanical transmission of the pull from one muscle to another through the closely packed and richly innervated tendons at the back of the orbit. In a few cases an 'inhibitory' response was caused in a discharging unit in the mesencephalic nucleus of the fifth nerve by stretch applied to an eye muscle. The same unit responded to stretch of the antagonistic muscle with a typical primary afferent neurone discharge. This again must be caused by mechanical interaction at the back of the orbit for there can be no question of true reflex inhibition.

The possibility of interaction between the jaw muscles and the eye muscles where they are in close proximity at the incomplete part of the bony orbit has to be kept in mind, as pointed out by Corbin & Harrison (1940). That some of the responses, where stretching eye muscles or jaw muscles appeared to activate identical units in the region of the mesencephalic nucleus of the fifth nerve, can be explained by such mechanical interaction, is probable. The possibility that all the eye muscle responses to stretch are merely due to pressure on jaw muscles is ruled out by the fact that afferent discharges from the eye muscles are known to make their way centrally starting in the eye-muscle nerves (Cardin & Rigotti, 1947, dog; Cooper *et al.* 1951, goat; Cooper & Fillenz, 1955, cat).

Extensive search in the brainstem in the goat and cat points strongly to the conclusion that these impulses in the primary neurones can only be detected in the mesencephalic tract of the fifth nerve. This now must be considered as a mixed afferent pathway for discharges from the jaw muscles and eye muscles, for we have very little reliable information about any topographical distribution of the two sets of sensory cells. In the experiments on the cat, the eyeball was removed, the line of pull of each muscle and the possibility of transmitted pressures were carefully studied, attempts were made to prevent interaction between the two sets of muscles and finally mechanical stimulation of the muscles sometimes gave a clue to the site of the receptor. It was concluded that many of the early sustained responses were undoubtedly initiated in the extraocular muscles.

The presence of early sustained responses to stretching the eye muscles in the pontine fibres of the fifth nerve strongly suggests that the path of the primary sensory neurone lies in the fifth nerve as it enters the brainstem. This is further borne out by the occurrence of responses to stretching the eye muscles supplied by the third nerve when this nerve and its nucleus have been destroyed by decerebration. It is not known whether the discharges actually enter the brainstem by the motor root of the fifth nerve, as is the case with the discharges from the jaw muscles (McIntyre, 1951). There is some indication that the two sets of responses are found in separate sites in the pontine fibres of the fifth nerve.

Outside the brainstem an accumulation of anatomical evidence proves connexions between the eye-muscle nerves and the fifth nerve (Wilkinson, 1930, between the fourth and fifth nerves in the cat's orbit; Stibbe, 1930, in the cavernous sinus in man and the cat; Winckler, 1937, in the ungulate orbit; Kiss, 1935, in numerous animals; and Coppini, 1952, in the cavernous sinus of man). Recently, Whitteridge (personal communication) has added physiological proof that the connecting strands between the eye-muscle nerves and the branches of the fifth nerve in the goat's orbit contain numerous fibres carrying low threshold discharges set up by stretching the eye muscles.

All this evidence has to be fitted in with that given by Sherrington (1898) and Tozer & Sherrington (1910) that the eye-muscle nerves are sensori-motor throughout their course and also with other evidence such as that produced by Tarkhan (1934) that some of the axons of the mesencephalic nucleus of the fifth nerve come into the brainstem by the third and fourth nerves. It is possible that the large nerve fibres associated with the low threshold stretch receptors enter the brainstem by the fifth nerve and fibres from other proprioceptors enter by the eye-muscle nerves. In the cat and monkey there are perhaps not a great number of these large nerve fibres.

A big difference between the present series of cats under Nembutal anaesthesia and decerebrate cats was that while both gave early sustained responses to stretching the extraocular muscles, the cats under Nembutal gave practically none of the later responses in various parts of the brainstem that were so numerous in decerebrate cats. In these latter preparations the absence of an anaesthetic would have a beneficial effect on synaptic transmission and responses in second or higher order neurones might be expected. A study of the late sustained responses, with their long latencies in relation to the rising phase of the stretch, their irregularities, the presence of after-discharge and the variability of the response with repeated stimulation all suggest a higher order neurone response; the picture is sufficiently like the early sustained response for it to be occurring in a second order neurone.

The sites of these late sustained responses are interesting. They were found in the superior colliculus close to the sites of first neurone responses and of visual responses (Fillenz, unpublished). This is very suggestive that information from the retina and from the proprioceptors of the eye muscles are associated in some of the lower visual reflexes. Other responses were found ventral and lateral to the nucleus of the third nerve and near the nucleus of the sixth nerve. The connexions between the afferent and efferent neurones of the eye muscles are still obscure, but impulses from the afferent cells in the mesencephalic nucleus of the fifth nerve must be carried in tecto-tegmental pathways to the ventro-lateral aspects of these motor nuclei. The tecto-spinal tract may be the one involved; in some of its course it lies close to the sites of late sustained responses in the midbrain, pons and medulla.

A number of the responses appear to come from the large cells of the reticular formation. The function of these cells is unknown; some of them may belong to the internuncial neurones of the cranial nerves, others may play a special part in the excitatory and inhibitory effects which these areas are now said to have on the body musculature. The sites of responses to stretch of the eye muscles in the medulla suggest that the electrode was near pathways leading to and from the spinal cord; a close connexion between the neurones of the eye muscles and the neck muscles is certainly to be expected. It must not be forgotten when dealing with the orbit and the reticular formation of the medulla oblongata that there are said to be many diffuse pathways in this formation which constitute secondary connexions of some of the orbital nerves belonging to the fifth nerve (McKinley & Magoun, 1942). Future work on the peripheral pathways of the fibres from the eye muscle proprioceptors may make it possible to exclude decisively any influence of the peripheral orbital endings (other than those in the eye muscles themselves) on results such as have been obtained in the present work.

The responses in the medial longitudinal fasciculus are interesting, not on account of their pattern which is rather ill-defined, though they are always late, but because responses to stretch of the eye muscles are found in a fasciculus so closely associated with eye-muscle connexions and with oculomotor-vestibular pathways.

Responses in the brachium conjunctivum are again ill-defined in pattern, but numerous enough to suggest that the cerebellum is concerned with the proprioceptors of the eye muscles as it is with the other muscle proprioceptors in the body.

The fact that late responses to stretching the jaw muscles were not often found at identical sites with the responses to stretching the eye muscles lends further support to the conclusion that two separate systems are being dealt with, and that the pathways for the two sets of responses become separate after the closely parallel pathways of parts of the first neurone responses.

The brief-burst type of response recorded in the cats under Nembutal is quite unlike anything recorded from fibres of the third nerve in the orbit; this makes it improbable that it is a first neurone response. It is much more suggestive of a cell that is injured, but if it is from a first neurone cell it is surprising that similar responses are not recorded in decerebrate cats. It might be from a second-order neurone cell that was being insufficiently stimulated through a partially blocked synapse. If this latter assumption were true, the brief-burst might be related to the first burst seen in some of the responses described in the results under late sustained responses in the decerebrate cats.

No responses were ever heard or recorded when the needle tip was in nuclei of the eye-muscle nerves; this is contrary to the experience of Cooper *et al.* (1953*b*) with the goat. There may have been a difference in the anaesthetic levels in the two kinds of animal, or there may be a difference in synaptic connexions between the eye muscle nuclei and the muscle spindle afferent fibres in the goat's eye muscle on the one hand, and the afferent fibres of the receptors in the cat's eye muscles on the other. But too much weight must not be attached to negative results in this type of work.

SUMMARY

1. Responses to passive stretch applied to the extrinsic ocular muscles were recorded with a microelectrode from the brainstem of the cat. The preparations were animals under pentobarbitone anaesthesia, under chloralose anaesthesia or decerebrated.

2. The features of the early sustained responses, found along the course of the mesencephalic nucleus of the fifth nerve and attributed to primary afferent neurones, are described. Their relation to responses from stretching the jaw muscles is discussed.

3. Brief-burst responses, recorded only in the midbrain of cats under pentobarbitone anaesthesia, are described and their possible significance discussed.

4. The characteristics and distribution of late sustained responses believed to be in second-order neurones found only in the decerebrate preparations are described.

5. The possible peripheral pathways of afferent nerves from stretch receptors in eye muscles are considered.

6. A few observations are made on the characteristics of the cat's brainstem during chloralose and pentobarbitone anaesthesia.

I wish to thank Prof. E. G. T. Liddell for the facilities of his laboratory. I am grateful to Dr Sybil Cooper for her help and advice. Mr E. H. Leach very kindly took the photomicrographs and Mr A. Austin did the large amount of photography involved in this work.

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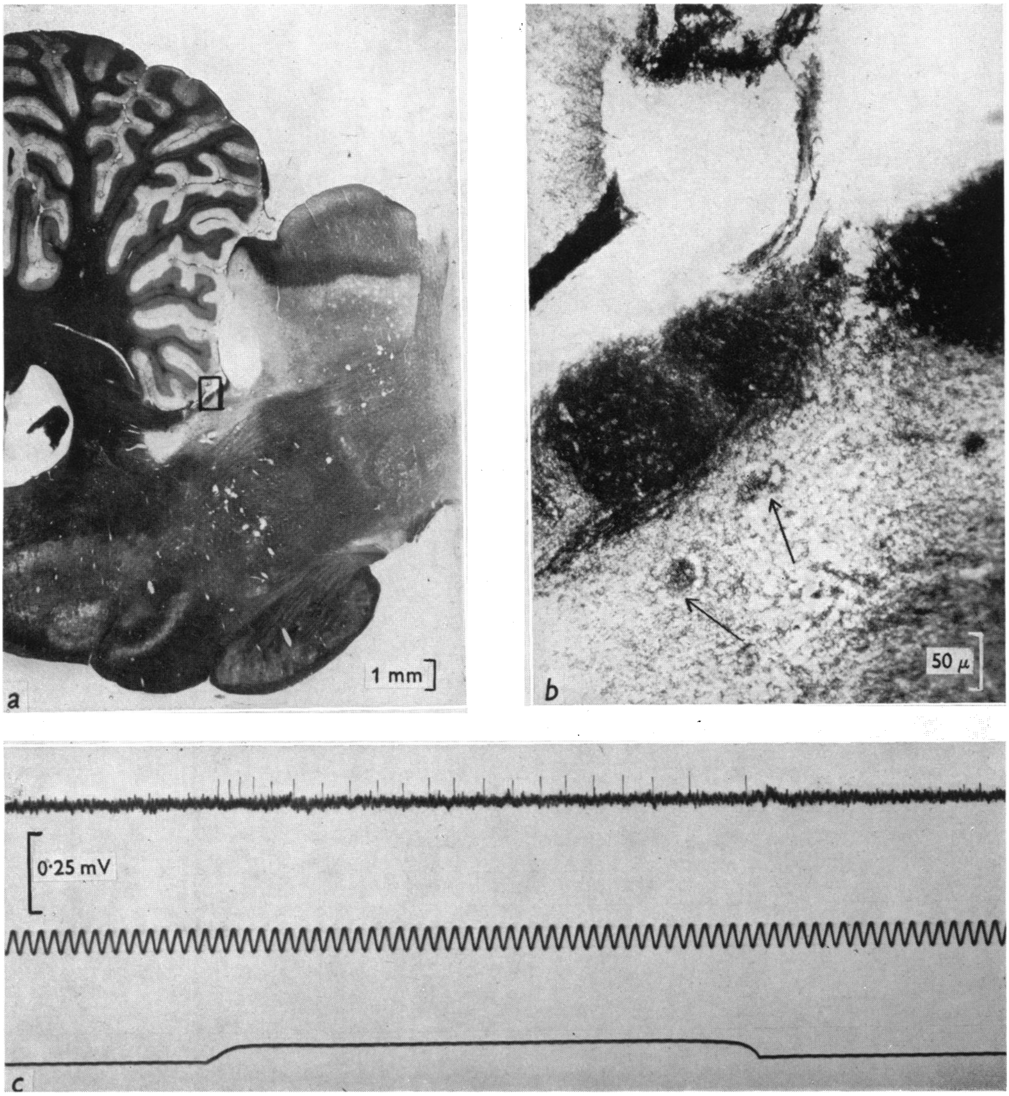

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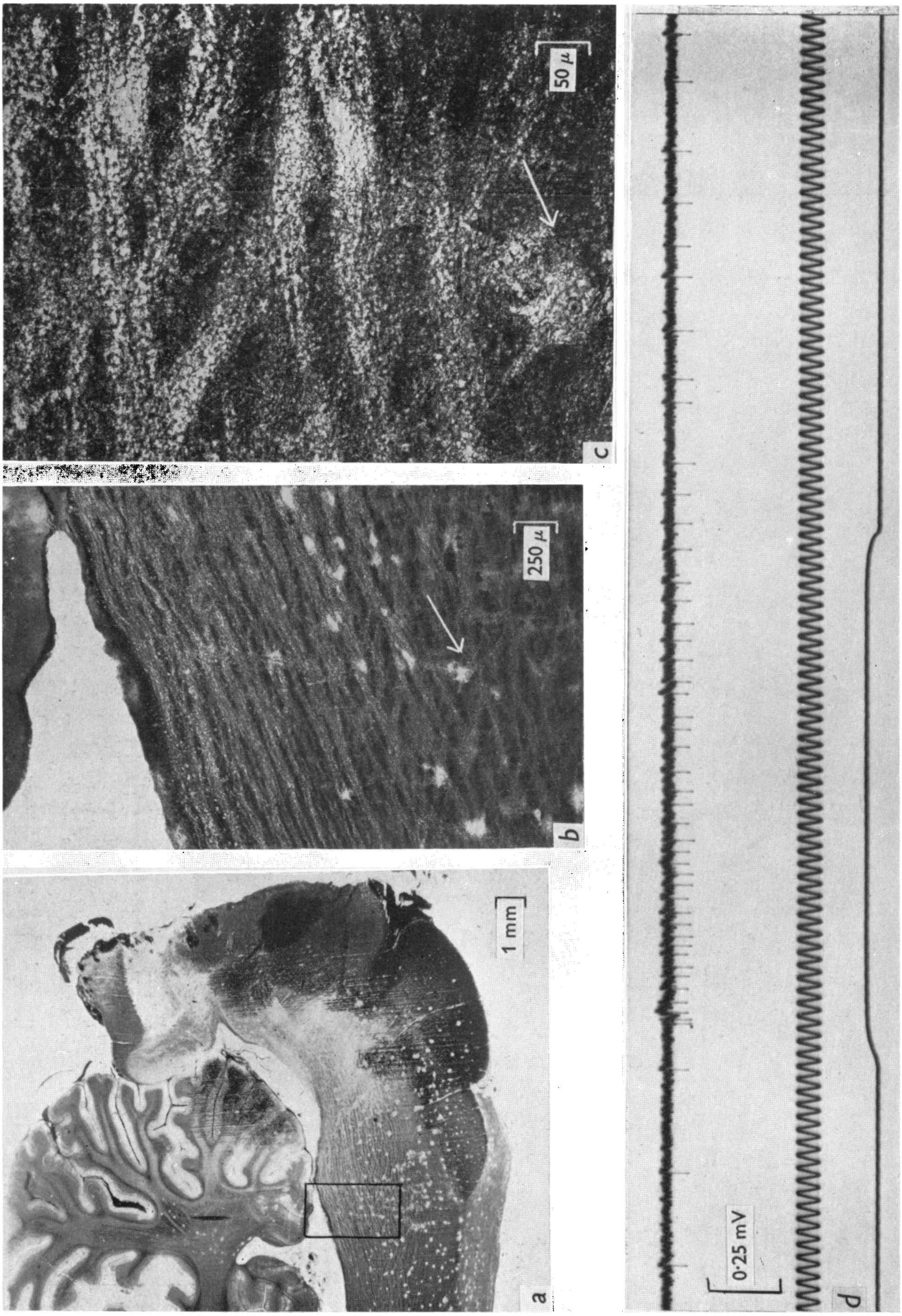
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EXPLANATION OF PLATES

PLATE 1

a: sagittal section through cat's brain showing needle track enclosed by black lines near tip of which stretching inferior oblique muscle gave an early, sustained discharge of a single unit.

b: needle track, at a magnification $\times 33 \cdot 3$ greater than in *a*: two globoid cells (indicated by arrows) of the mesencephalic nucleus of the fifth nerve. It is probably the upper of the two cells which gave rise to the record in *c*.

c: response to stretching inferior oblique muscle. This unit was unaffected by stretch applied to any other of the eye muscles or by moving the jaw.

PLATE 2

a: sagittal section through brainstem of decerebrate cat (cephalic end shows the level of decerebration) showing needle track in hindbrain (enclosed by black lines).

b: magnification $\times 6$ greater than in *a*. Needle track is seen to end opposite a large, multipolar cell (indicated by arrow) in the reticular formation.

c: further enlargement to show cell.

d: record from a cell similar to the one shown in *c*. Record from cell shown in *c* was not suitable for reproduction.