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SOMATIC AFFERENT INPUT TO POSTERIOR THALAMIC NEURONES AND THEIR AXON PROJECTION TO THE CEREBRAL CORTEX IN THE CAT

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SUMMARY

1. A technique of reversible block of synaptic transmission through the dorsal column nuclei and the trigeminal nucleus caudalis (n. caudalis) has been employed to assess the somatic afferent input to individual posterior thalamic neurones in the cat. The axon projection to the cerebral cortex of these neurones has been identified by antidromic activation following cortical stimulation.

2. Unitary responses in the nucleus ventralis posterolateralis (VPL) evoked by cutaneous stimulation were abolished or depressed following block of transmission in the dorsal column nuclei. Block in n. caudalis, however, depressed unitary responses in nucleus ventralis posteromedialis (VPM) evoked by facial skin stimulation in less than 10 % of cells.

3. A more complex source of the somatic input to the posterior nuclear region of the thalamus (PO) was found. It was most commonly noted that PO unitary activity evoked by cutaneous stimulation of the face was unaffected by block of synaptic transmission in n. caudalis. No uniform effect was observed on unitary responses in PO evoked by limb stimulation when transmission in the dorsal column nuclei was blocked.

4. Antidromic activation from the cerebral cortex was seen in 69 % of ventrobasal neurones. Most cells (66 %) had 'antidromic cortical fields' restricted to a region consisting of a third to a half of the specific somatic projection areas. In 10 % of cells evidence was obtained for discontinuous cortical 'antidromic fields' suggesting subcortical bifurcation of the projecting axon.

5. An axon projection to the cortex was found in 35 % of PO cells, about half of which projected only to specific somatic projection areas. Evidence for subcortical branching of the axon was obtained for seven PO cells.

INTRODUCTION

The present experiments have been designed to evaluate the relative contribution of different components of the ascending somatic afferent pathways to the cutaneously evoked activity of posterior thalamic neurones, and to investigate the axon projections of the latter to the cerebral cortex in the cat. Evaluation of the input to posterior thalamic neurones was made by studying the effect on unitary discharge evoked by skin stimulation of localized cooling of the dorsal quadrant of the medulla caudal to the obex. This cooling produced unilateral block of synaptic transmission simultaneously in the dorsal column nuclei and in nucleus caudalis of the trigeminal system; for spinal inputs this block was in the medial lemniscal pathway, while for trigeminal inputs it occurred in the anatomical analogue of the dorsal horn of the spinal cord. Synaptic block achieved by localized cooling had the considerable advantage of reversibility which allowed repetition of the blocking action during studies on a single neurone and also the blocking of cells successively isolated in the one animal.

General agreement exists on the projection of ventrobasal (VB) neurones to the somatic area I (SI) of the cerebral cortex, and Darian-Smith (1964) found that VB neurones can be activated antidromically from the somatic area II (SII) as well. In addition, the static functional characteristics of SII neurones were found by Darian-Smith, Isbister, Mok & Yokota (1966), and Carreras & Andersson (1963) in their area 'C' of SII, to be of a 'lemniscal' character and thus similar to those of SI. However, conflicting anatomical reports exist regarding SII. Macchi, Angeleri & Guazzi (1959) concluded that 'essential' projections to the SII area arise in VB, while Rose & Woolsey (1958) have favoured only 'sustaining' projections to SII. In the present study, the cortical projection of posterior thalamic neurones has been investigated by mapping the cortical fields from which individual neurones could be discharged antidromically by electrical stimulation.

In the posterior thalamic nuclear region (PO) Darian-Smith (1964), using the technique of cortical stimulation, failed to identify a projection of these neurones to the cortex, although strong anatomical evidence exists for a cortical dependency of PO neurones. Rose & Woolsey (1958) and Peacock & Combs (1965) found severe degeneration in the PO region as well as the VB nucleus as a result of extensive cortical removal. In the present experiments physiological evidence has been obtained for a cortical projection of PO neurones.

METHODS

Preparation of the animal. Cats weighing between 2·2 and 4·6 kg were anaesthetized with intravenous chloralose (55–65 mg/kg). Gallamine triethiodide (Flaxedil, May and Baker) was given intravenously to eliminate movement at approximately 20 min intervals during the recording period. However, the administration was suspended every 2 hr, permitting recovery of the animal from the effect of the muscle relaxant and assessment of the depth of anaesthesia. At such times the animal showed no spontaneous reflex movement. The respiratory ventilation was maintained artificially so that the end-tidal P_{CO_2}, monitored in the lower part of the trachea with a Beckman LB-1 medical gas analyser, could be held at 3–4 %. The arterial blood pressure was recorded continuously and in this study the mean pressure was 100 mm Hg or more during the recording period. Rectal temperature was maintained at 37–38° C. A cervical laminectomy and craniotomy were carried out as described previously (Darian-Smith, Phillips & Ryan, 1963; Darian-Smith, 1964).

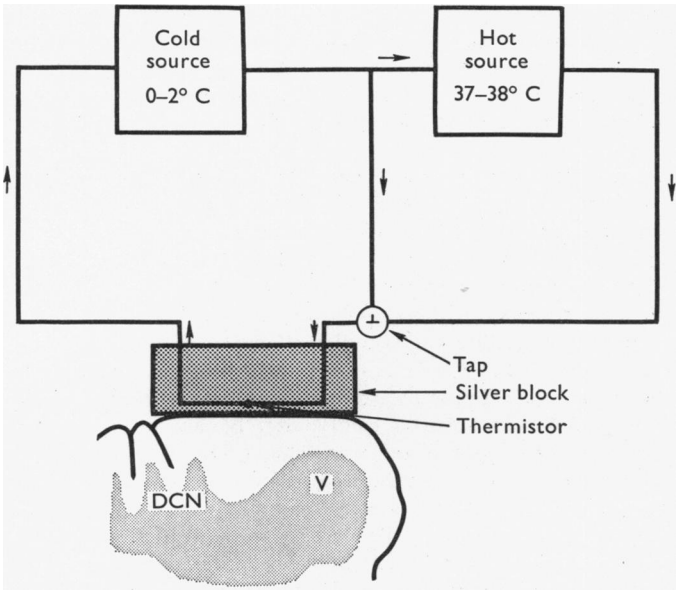
Recording and stimulation techniques. Extracellular single cell recordings were made in the posterior thalamus using tungsten micro-electrodes (Hubel, 1957). Identification of thalamic unitary activity was made by electrical stimulation of the skin of the face and forelimb, using methods similar to those applied to the face by Darian-Smith (1964). Subsequently the cells were characterized in terms of their responsiveness to mechanical stimulation and their peripheral receptive fields defined. Afferent inhibition of VB cells was tested by applying a conditioning stimulus, 40 msec before the test stimulus, to some fixed point outside the excitatory receptive field of the cell, usually on the ipsilateral upper lip and contralateral forepaw. In most cases the stimulus consisted of four electrical pulses with an interval of 2·5 msec between each pulse. Sometimes, however, a mechanical conditioning stimulus was employed and was achieved by a 4 msec duration rectangular pulse wave applied by a probe which produced a skin indentation of 500–700 μ.

Cortical axon projections of the thalamic neurones were investigated by antidromic stimulation techniques utilizing ten pairs of bipolar electrodes (interpolar distance 1·5–2·0 mm) situated on specific somatic and auditory projection areas and on motor and association regions of the cerebral cortex. Five or six pairs were distributed over the sensorimotor cortex, the remainder over the auditory and association areas. The somatic areas SI, II and III (Darian-Smith *et al.* 1966) and the auditory cortex were routinely determined by mapping on to a photograph of the exposed cortex the evoked potentials at the cortical surface following peripheral stimuli, as described by Darian-Smith & Yokota (1966*a*). For the somatic projection the contralateral upper lip and forepaw were stimulated electrically; for the auditory projection a 1 msec duration click was delivered from a small loudspeaker. As a consequence the cortical bipolar stimulating electrodes could be positioned precisely on the sensory regions of maximum evoked activity. A uniselector was employed for sequential stimulation by the ten pairs of electrodes for checking cortical projections from the thalamic neurones. Rectangular current pulses of 50 μsec duration and intensity not exceeding 7 mA were employed for cortical stimulation. The most reliable criterion of antidromic firing is provided by the 'collision' technique (Darian-Smith *et al.* 1963) which allows one to distinguish antidromic from transynaptic activation. In a previous study of posterior thalamic axon projections to cortex (Darian-Smith, 1964) it was found that those cells firing with a latency $\leqslant$ 2 msec were antidromic. The same criterion for identification of antidromic invasion was used in the present study; however, the 'collision' technique was employed when any doubt existed.

The nomenclature for the somatic projection areas, SI, II and III, as defined by Darian-Smith *et al.* (1966), is employed in this study of cortical 'antidromic fields'. These three areas correspond closely with those noted for the cat by Marshall, Woolsey & Bard (1941), and they seem identical with the triple projection of Oscarsson & Rosén (1963, 1966) whose

rostral and caudal division of SI would correspond with SI and SIII respectively. A triple projection has also been noted in the cat by Morse & Towe (1964). Although their SII and pericruciate areas agree with findings of Marshall *et al.* (1941), Oscarsson & Rosén (1963, 1966) and Darian-Smith *et al.* (1966), their third region, the pericoronal area, appears more laterally situated than the corresponding area in the above three studies.

Block of synaptic transmission in the brain stem. The dorsal column nuclei, the nucleus caudalis of the trigeminal complex and the lateral cervical nucleus are in juxtaposition in the lower medulla and upper cervical spinal cord, a situation which permits synaptic



Text-fig. 1. Experimental arrangement for cooling of caudal brain stem. A two-way tap controlled the circulation of either cold (0–2° C) or warm (37–38° C) alcohol through the silver block overlying the caudal brain stem. The temperature of the block was monitored by a thermistor. Cooling the block to 0–2° C caused reversible block of synaptic transmission simultaneously in the dorsal column nuclei (DCN) and the caudal trigeminal nucleus (V).

transmission in these nuclei to be blocked synchronously by localized cooling. The dorsal column nuclei extend from 2–3 mm in front of the obex to 7–8 mm caudal to the obex; the functional extent of n. caudalis is from 1–2 mm rostral to the obex to the caudal end of C2 and the lateral cervical nucleus from the caudal pole of the dorsal column nuclei to the caudal end of C2. Appropriate cooling of this region was achieved experimentally by positioning a silver thermode 15 × 3 mm on the dorsal surface of the brain stem and upper cervical cord; this overlaid the sensory relay nuclei on one side and extended from the caudal end of C2 to a level 2–3 mm rostral to the obex (Text-figs. 1 and 2). Cold alcohol (0–2° C) was pumped at a rate of 3–5 l./min from a Lauda Ultra-Kryomat through insulated tubing to the silver block and back again to the Kryomat. Alternatively, the alcohol could be pumped from the Kryomat to the block via a copper coil situated in a water-bath where the alcohol was heated to 37–38° C. A two-way tap controlled the flow of warm or cold fluid through the block. Warm alcohol circulated throughout the experiment except when cooling of the caudal brain stem was required, when cold alcohol circulated. A thermistor

was incorporated in the silver block to monitor the temperature of the surface of the block in contact with the brain stem. There was a steep, but undetermined, temperature gradient through the brain stem, and the temperature at the trigeminal n. caudalis was probably several degrees higher than that recorded by the thermistor. To obviate tissue damage, the thermistor temperature was never allowed to fall below 0° C; cooling to 0–2° C was always sufficient to cause block of synaptic transmission in n. caudalis, but not conduction in the adjacent, more superficial trigeminal spinal tract.

Monitoring of synaptic block. The effects of cooling on the trigeminal nucleus were continuously monitored by the micro-electrode recording of post-synaptic activity in n. caudalis. A similar recording in the trigeminal n. oralis allowed the detection of effects on transmission through this rostral region during the periods of brain stem cooling. With the temperature levels chosen, no such effects were detected in the rostral response recorded by the electrode placed within 3–4 mm of the rostral edge of the silver block. The effect of blocking synaptic transmission through the above relays on the responses of thalamic neurones to peripheral stimulation was assessed by initially recording approximately forty responses of the neurone to a fixed stimulus delivered to its excitatory receptive field at a repetition rate of 1/2 sec, and thereby estimating the mean number of impulses per stimulus. Then, on cooling the brain stem until synaptic block ensued, a further sequence of responses was recorded to the same peripheral stimulus and the mean discharge again determined. On rewarming to 37–38° C a third series of records was taken to check that the neurone had returned to its precooling responsiveness. If it failed to satisfy this requirement it was rejected from the sample. The continuous recording of blood pressure before and during the period of cooling revealed a fall in the mean systemic pressure of 5–20 mm Hg if cooling was prolonged beyond 3–4 min. This was taken to indicate disruption of synaptic activity within the medullary vasomotor areas ventral to n. caudalis. Data collection during cooling, however, never extended beyond a period of 2 min, and the cooling procedure could be repeated many times during the recording period without evidence of deterioration of the preparation.

Identification of thalamic recording site. This procedure was similar to the stereotaxic and histological techniques used by Darian-Smith (1964), excepting that the Nissl-stained serial paraffin sections were 15 μ thick.

RESULTS

Unitary activity was recorded in 255 tactile neurones of the thalamic ventrobasal nucleus (VB), 110 of which had receptive fields on the face and the remaining 145 had fields on the contralateral limb or trunk. Ninety neurones were located in the posterior nuclear region (PO) as defined by Poggio & Mountcastle (1960). Our observations in PO were restricted to the magnocellular division of the medial geniculate nucleus, the suprageniculate nucleus, and the posterior nucleus of the thalamus as described by Rioch (1929).

Histological criteria were employed in classifying neurones into the VB or PO group. There was, however, a clear-cut functional correlation with the location of each neurone in the posterior thalamus, agreeing with previous observations (Poggio & Mountcastle, 1960, 1963; Perl & Whitlock, 1961; Whitlock & Perl, 1959, 1961; Darian-Smith, 1964). Thus VB cells were discharged by mechanical stimulation of the skin but never by an auditory stimulus, had localized receptive fields, fired with a short

latency following peripheral stimulation, and were topographically organized. Cells with receptive fields on the forelimb were localized within the nucleus ventralis posterolateralis (VPL) of VB and those with receptive fields on the face were confined to the nucleus ventralis posteromedialis (VPM). The PO cells in contrast often responded to an auditory click stimulus, their cutaneous receptive fields were extensive, commonly bilateral and sometimes discontinuous; somatotopic organization was precluded by the nature of their receptive fields. Furthermore the latency for discharge following peripheral stimulation was considerably longer than for VB cells, as shown in Table 1. The PO cells included in the

TABLE 1. The latencies to electrical stimulation at the periphery and incidence of afferent inhibition in posterior thalamic neurones

Cell type	Cell no.	Mean latency ± S.D. (msec)	Afferent inhibition
VB, face	110	5·0 ± 2·4	22/68
VB, limb	145	7·8 ± 3·2	44/44
PO (from face)	68	13·9 ± 8·7	22/23

latency estimate were all activated from facial components of their receptive fields. Table 1 also shows the incidence of afferent inhibition in VB cells tested with a conditioning electrical stimulus of the ipsilateral upper lip or contralateral forepaw. A conditioning stimulus, applied to the skin adjacent to the test site, induced marked depression of the test response in twenty-two of twenty-three PO cells. However, the conditioning stimulus was generally applied within the extensive receptive field of the PO cell and usually evoked some discharge itself. Because of this, differentiation between true inhibitory action and post-excitatory depression was not possible for these cells. In the few neurones in which a conditioning mechanical stimulus was used, afferent inhibition was elicited in six out of nine VB cells and in six of seven PO cells.

The tactile receptive fields in 80% of the VB cells activated from the face were smaller than a third of the contralateral face. The remainder were either slightly larger or, in a few cases, had a small ipsilateral extension of the field. Over 70% of the VPL cells had receptive fields limited to the contralateral forepaw; for the other 30% there was some proximal extension on to the skin of the forelimb. All cells with facial receptive fields and 117 out of 124 cells with receptive fields on the contralateral forepaw adapted rapidly to sustained indentation of the skin. Of the facial cells tested, fifty-one were activated by hair movement, forty-five by light touch, and six by pressure. Among cells activated from the limb, seventy-eight responded to hair displacement, thirty-eight to light touch and seventeen to pressure.

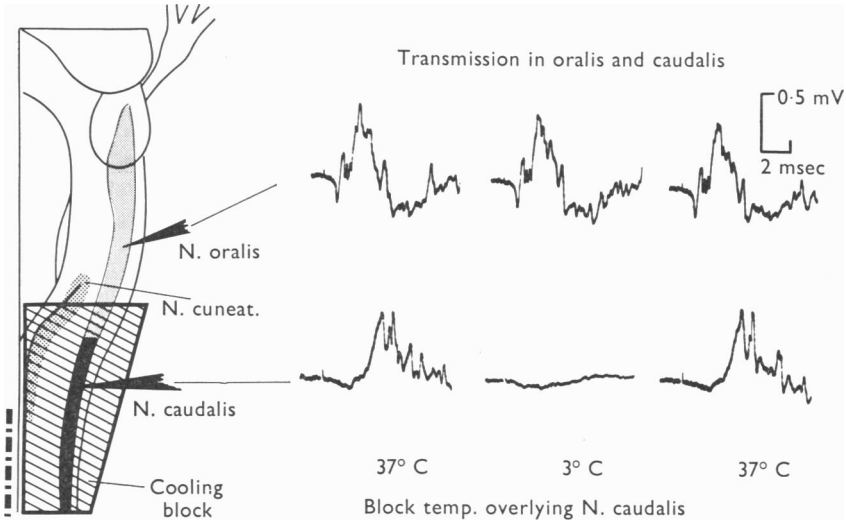
The typically extensive receptive fields of the PO cells usually included large areas of the contralateral face and forelimb and not infrequently involved neck, trunk and ipsilateral face and part or the whole of other limbs. The modality of these cells was generally less specific than those of VB cells as they were sometimes activated by light touch from one position in their peripheral field but required firm pressure at other points. It was found that nineteen of fifty-one (37 %) PO cells tested were responsive to an auditory stimulus in the form of a click from a small loudspeaker, confirming previous observations (Poggio & Mountcastle, 1960; Darian-Smith, 1964).

Brain stem input to thalamus

The effect of localized cooling of the brain stem on synaptic transmission within the trigeminal complex is illustrated in Text-fig. 2. When the overlying silver block was cooled to 3° C the post-synaptic response evoked in n. caudalis was abolished, while that in n. oralis was virtually unaltered. The reversibility of the block in transmission in the caudal nucleus is shown by the return to the original response on rewarming. Many repetitions of the cooling sequence produced no attenuation of the normal response in n. caudalis indicating that no deterioration of the underlying tissue had resulted. Provided the test response on rewarming the block was not significantly different from that before cooling, this technique of reversible cooling permitted an assessment of the relative contribution of the oralis and caudalis nuclei to the activation of posterior thalamic units. Micro-electrode monitoring of the response was employed in every experiment to confirm the synaptic block in n. caudalis. In a number of experiments the dorsal column nuclei response was also monitored and it was confirmed that the cooling procedure blocked transmission in both the caudalis and dorsal column nuclei. Thus it was possible to evaluate synchronously the effects of blocking the lemniscal input and the trigeminal n. caudalis input to the posterior thalamus.

Effect of cooling on VB units. The effect of cooling the caudal brain stem was studied in eighty-four neurones of the VB, thirty-seven of these having receptive fields in the contralateral facial region and the remainder on the contralateral forelimb. Among the VPL cells the response was abolished in thirty-seven of the forty-seven cells tested, confirming a predominantly lemniscal input to these cells. In ten VPL cells, however, the responses were not fully depressed; this may have been due to convergence of both lemniscal and non-lemniscal pathways upon such cells or to incomplete block of transmission within the dorsal column nuclei during cooling. On the other hand, in 80 % (twenty-nine out of thirty-seven) of cells with receptive fields in the trigeminal area the thalamic

response was unaltered by cooling, suggesting little convergence, excitatory or inhibitory, of axons from relay neurones in the n. caudalis. In only three out of the thirty-seven VPM cells tested was there a depression of the response, and then only slight. This indicated that input to the VPM cells was predominantly from sources other than the caudalis component of the trigeminal spinal complex and is thus in accord with earlier findings which indicated that the major input to these neurones arises from more rostral elements of the trigeminal complex, namely the main sensory nucleus and n. oralis (Walker, 1939; Carpenter & Hanna, 1961).



Text-fig. 2. Effects of cooling on synaptic transmission in the caudal and rostral trigeminal brain stem nuclei. The field potentials evoked in the trigeminal oralis (n. oralis) and caudalis (n. caudalis) nuclei were recorded following electrical stimulation of the ipsilateral upper lip. Cooling of the silver block overlying nucleus caudalis to 3° C abolished the caudalis response while that in the nucleus oralis was unaffected. On rewarming to 37° C the caudalis response returned indicating the reversibility of the procedure. With all records the time calibration equals 2 msec and the amplitude calibration equals 0·5 mV. Upward deflexion represents a negative voltage change; n. cuneat. = nucleus cuneatus. The interrupted vertical line on the left of the figure indicates the rostro-caudal extent of the lateral cervical nucleus which is situated ventrolaterally to the nuclei cuneatus and caudalis.

An interesting finding in five VPM cells was the occurrence of an enhanced thalamic response during cooling. This result suggests that the cooling procedure eliminated a tonic inhibitory influence on these cells from n. caudalis. This may be subserved by an intratrigeminal system or mediated at the thalamic level.

Effect of cooling on PO units. Previous work has shown that the predominant PO input arises from the anterolateral system (Mehler, Feferman & Nauta, 1960) and from the caudal component of the trigeminal nucleus (Stewart & King, 1963). In view of this there was some expectation that caudal brain stem cooling might suppress the responses to facial stimulation while those to limb stimulation would remain intact. In fact this was not seen. Table 2 summarizes the results for the twenty-six PO cells studied. The cells of the first group in Table 2, in which cooling had no effect, were presumably activated from the limb component of their receptive field via the spinothalamic system. Responses evoked from the face in this

TABLE 2. Effect of cooling on PO unitary responses

No. of PO cells	Face component	Limb component
8	0	0
10	0	−
3	−	0
2	−	−
1	+	+
2	0	+

same group of cells and in the other major group in Table 2 were unaffected by cooling, indicating involvement of pathways via more rostral components of the trigeminal nuclear complex. The depression of responses evoked from the limb suggests that excitation of these PO neurones from the periphery is mediated via one or more of the following relays, which were blocked by cooling: dorsal column nuclei, the lateral cervical nucleus, or medullary reticular relays.

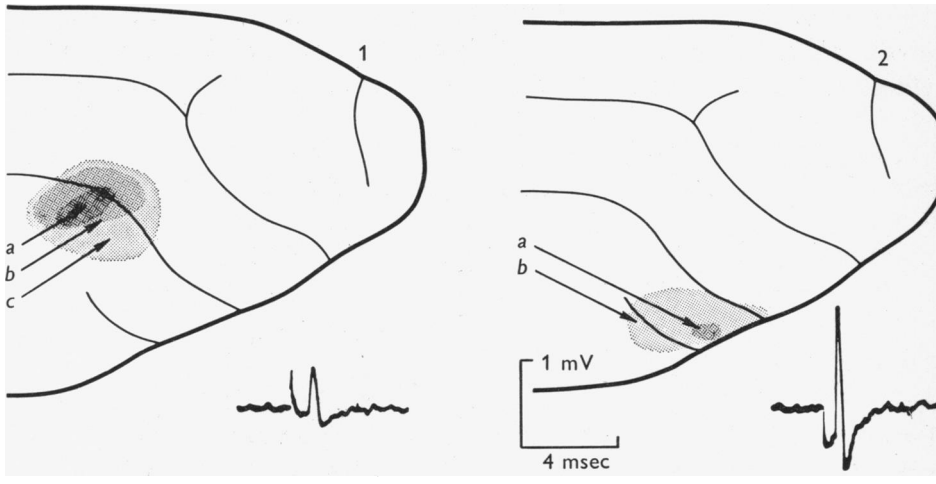
Cortical projection of VB and PO cells

Most cells, both VB and PO, responded antidromically with latencies $< 1{\cdot}0$ msec. The mean and standard deviation of the latency for cortical antidromic activation determined for ninety VB units was $0{\cdot}76$ msec $\pm$ $0{\cdot}33$; that for twenty-seven PO cells was $0{\cdot}77$ msec $\pm$ $0{\cdot}31$. Responses with a latency > 2 msec were not accepted as antidromic.

The size of the cortical area from which a unit could be discharged antidromically ('antidromic field') depended on the intensity of the stimulating current employed, larger currents tending to spread and activate units from more distant points. Currents employed for antidromic activation studies did not exceed 7 mA and were of 50 μsec duration. Usually the minimum current intensity necessary to activate cells antidromically was approximately 3 mA. Text-figure 3 illustrates the variation in size of the 'antidromic fields' at different current intensities for two VB cells with receptive fields on the contralateral upper lip.

Of 206 VB neurones tested, 142 (69 %) responded antidromically from

cortex; 66% of these were confined in their projection to about a third or a half of the specific somatic projection areas SI, II and III. Among VB cells projecting to restricted areas of somatic projection regions we found no segregation to a particular area. For example, of the fifty limb VB units activated from restricted projection areas, twenty were from SI, twenty-two from SII, and eight from SIII. For VPM cells such



Text-fig. 3. Effect of variation in intensity of cortical stimulating current on the size of the cortical 'antidromic' field of two VB units. In '1', antidromic activation of the unit from the central shaded area '*a*' could be achieved by current intensities less than 1·5 mA (duration = 50 μsec), whereas currents up to 5 mA were required for activation from an area represented by '*b*'. Currents up to 10 mA could not activate the cell beyond area '*c*'. Activation of the unit illustrated in '2' could not be achieved beyond area '*a*' until current intensities exceeded 7 mA. No antidromic discharge could be elicited beyond area '*b*' by currents up to 10 mA. The antidromic response for each unit is shown. The time and voltage calibrations are 4 msec and 1 mV respectively.

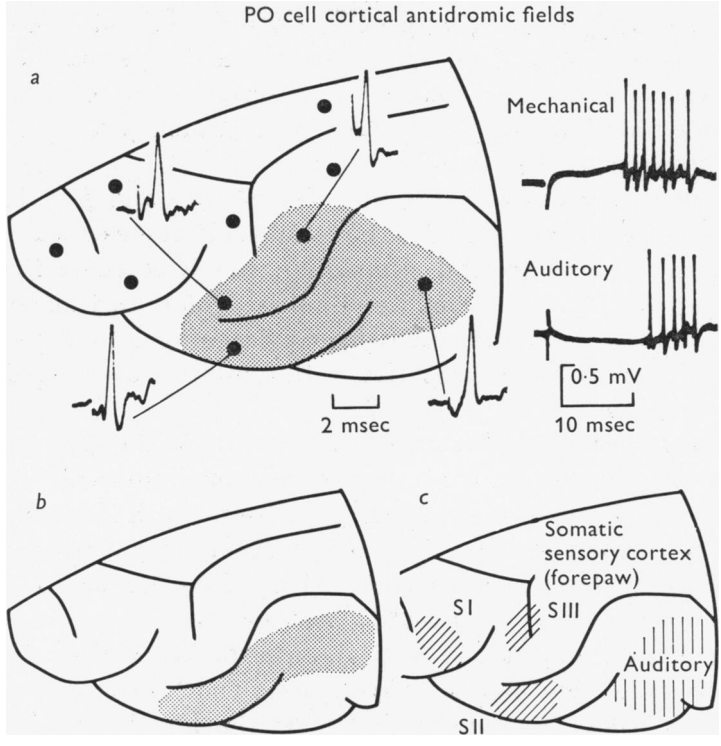
resolution was not as readily obtained since the SI and SII areas for face merge (Woolsey, 1960; Darian-Smith *et al.* 1966). However, of forty-four VPM cells antidromically activated from the SI–II region no obvious concentration was evident in either the SI or SII pole of the merged projection area. A further 24% of units had more extensive sensory cortex projections including in some cases all the somatic sensory projection areas. The shaded areas in Pl. 1*b*, *c* and *d* indicate the 'antidromic fields' for three different VB units. Part *b* illustrates an extensive 'antidromic field' which involved all three somatic projection areas. Part *a* shows the regions of maximum evoked activity in the SI, II and III areas. The 'antidromic field' of part *d* is a typical localized field, in this case lying in the anterior part of SI or the motor cortex.

It was found that fourteen (10%) of the 'antidromic fields' were of a discontinuous type involving generally the sensorimotor cortex. Such a situation is seen in *c* of Pl. 1. Bipolar stimulating electrodes situated between the two shaded areas failed to activate this cell. This result suggests a bifurcating axon projection, one branch passing to the SII area, the other to the motor cortex.

The peripheral and cortical evoked responses *e* and *f* in Pl. 1 were recorded from the unit with 'antidromic field' represented in *b*. The repetitive response to cortical stimulation was a common finding, the initial response being antidromic and subsequent ones transynaptically produced. Transynaptic firing following cortical stimulation also occurred in many of the thalamic cells not antidromically discharged by this particular stimulus.

Among PO cells studied, thirty-one (35%) out of eighty-eight could be fired antidromically, in contrast with previous observations made in this laboratory (Darian-Smith, 1964) in which no such identification was made. Seven of the thirty-one antidromic PO cells projected to localized regions of the somatic sensory cortex, i.e. SI or SII or SIII, and an additional twelve to areas including two or all three specific somatic projection areas. Four cells had cortical 'antidromic fields' located outside the somatic projection areas. Plate 2 shows the 'antidromic fields' for five PO cells whose position is shown on the histological illustration. The SI, II and III projection areas of maximum activity are indicated by the shading on the cortex photograph.

The remaining eight PO neurones had axon projections to additional areas beyond somatic sensory regions. In six, this involved auditory and somatic cortex, usually SII, and all six were responsive to both auditory and somatic peripheral stimulation. The other two units had projections to association areas. Text-figure 4*a* illustrates an extensive 'antidromic field' including auditory and somatic projection regions. The response of this neurone to peripheral mechanical and auditory stimulation is shown on the right. In Text-fig. 4*b* is shown the 'antidromic field' of another unit involving somatic area SII and auditory cortex. The separation of each pair of bipolar stimulating electrodes from which this neurone was activated was approximately 15 mm, a distance precluding the possibility of stimulus current spread from the two loci of stimulation to some common intermediate point at which the axon terminated. Thus the evidence from the neurones of this type is in favour of either a bifurcating axon projection, one branch to SII and the other to auditory cortex, of the type suggested by Rose & Woolsey (1958), or, alternatively, an extensive bushy termination to an area of cortex extending between these two stimulus sites.



Text-fig. 4. The cortical 'antidromic fields' for two PO cells indicated by the shaded areas in '*a*' and '*b*'. The field illustrated in '*a*' is extensive as the unit could be antidromically activated from the four different cortical sites indicated thus ●. The antidromic responses to stimulation at each of these points are shown on the figure. This PO cell responded to auditory stimulation and to mechanical stimulation of the skin. These responses are indicated on the right of the figure. The threshold current intensities required for antidromic activation at these four sites varied between 3·0 and 4·5 mA. The 'antidromic field' illustrated in '*b*' is for a PO unit which was antidromically activated from two cortical sites, SII and the auditory cortex, the distance between the stimulating electrodes being approximately 15 mm. The threshold current intensities required were 2·5–3·5 mA. The SI, II and III and auditory projection areas of maximum evoked activity in this cat are illustrated in '*c*'. The time and voltage calibrations are 10 msec and 0·5 mV respectively.

DISCUSSION

The general static functional characteristics of VB and PO neurones sampled in our study were similar to those previously observed (Poggio & Mountcastle, 1960, 1963; Perl & Whitlock, 1961; Whitlock & Perl, 1959, 1961; Darian-Smith, 1964), though the incidence of afferent inhibition in our results was considerably greater than that observed by Poggio & Mountcastle (1963). Their estimates of afferent inhibition were, however,

based on alteration in 'spontaneous' discharge, whereas we employed electrical conditioning and test stimuli. By using a test response evoked by cutaneous stimulation, both post-synaptic and presynaptic inhibitory action should be detected; use of 'spontaneous' discharge may fail to identify presynaptic action.

Input to posterior thalamus. The almost total suppression of the cutaneously evoked unitary activity in VPL produced by block of synaptic transmission in the dorsal column nuclei was to be expected, and supports Mehler's (1957) report that in the cat only 10 % of the projection to VLP is non-lemniscal. Complementing this result was the absence of any effect of block of n. caudalis on responses of 80 % of VPM cells. This confirms that the major source of input to these cells arises in the rostral trigeminal complex, and is in accord with the degeneration studies of Le Gros Clark (1936), Walker (1939), Russell (1954), and Carpenter & Hanna (1961).

An increase in the discharge evoked from the skin was observed in five VPM neurones during block of transmission in n. caudalis. This suggested that an inhibitory pathway arises from this nucleus and modulates activity of certain neurones in the more rostral regions. Anatomical evidence has been obtained for fibres arising in n. caudalis and projecting within the trigeminal complex (Stewart & King, 1963; Stewart, Stoops, Pillone & King, 1964; Kusama, Otani & Kawana, 1966).

The present experiments revealed a more complex source of the somatic input to the PO region. The response to facial stimulation was unaltered by synaptic block in n. caudalis in over three-quarters of the cells, suggesting a projection of rostral trigeminal divisions to these PO neurones. This does not necessarily imply a lemniscal projection to these PO cells, since Carpenter & Hanna (1961) have evidence of secondary fibres from rostral trigeminal divisions terminating in the reticular formation, from which impulses could traverse reticular pathways to the PO cell. Darian-Smith & Yokota (1966*b*) obtained physiological evidence for such reticular cells; they found that about a third of reticular cells sampled at the level of the trigeminal nuclear complex could be antidromically activated by contralateral thalamic stimulation.

In only five of twenty-six PO cells was the response to facial stimulation suppressed by synaptic block in n. caudalis. The suppression of activity in these five cells indicates an excitatory input from this nucleus. Gordon, Landgren & Seed (1961) and Darian-Smith & Yokota (1966*b*) have shown that up to 40 % of n. caudalis neurones could be antidromically discharged from the contralateral posterior thalamus. As the present results have shown little contribution from n. caudalis to the activity of VB or PO neurones, it is likely that a large component of the fibres projecting to

the contralateral thalamus from n. caudalis terminate in other regions, e.g. the mid line thalamic nuclei and the subthalamus.

The responses of PO cells to stimulation of the contralateral forepaw were unaltered in more than a third by block of synaptic transmission in the dorsal column nuclei. This suggests that other pathways mediated these responses. In another third of the PO cells the response to limb stimulation was depressed by this synaptic block. This may indicate a lemniscal projection to these PO cells or a non-lemniscal projection from the dorsal column nuclei via medullary reticular relays which are blocked by cooling. A third possibility is an anterolateral pathway involving medullary reticular relays in a region close to the dorsal column nuclei and thus susceptible to block by cooling. Anatomical evidence for a lemniscal input to PO cells has been obtained by Bowsher (1961, 1965), and in addition Perl & Whitlock (1961) have presented physiological results suggesting a dorsal column contribution to PO.

Axon projections to the cerebral cortex. In the identification of axon projections involving antidromic activation of the cell body, only positive findings can be considered relevant. Failure to demonstrate such an antidromic invasion may reflect inaccessibility of the axon terminals to the stimulus current, because of their location, calibre, the stimulus parameters, etc. Our finding that 69% of all VB neurones could be antidromically fired from the sensorimotor cortex is in accord with the observations of Andersen, Eccles & Sears (1964) and implies that a very large proportion of this neurone population projects to the cerebral cortex.

The results of our antidromic studies indicate a projection of VB cells not only to SI but also to the SII area of the cortex, agreeing with previous physiological findings of Darian-Smith (1964). In addition, Carreras & Andersson (1963) found predominantly cells with 'lemniscal' characteristics in their area 'C' of SII which appears to correspond with the core of our SII region. Their result implies an input to this SII region from the ventrobasal complex. The anatomical degeneration studies of Macchi *et al.* (1959) also gave evidence of a projection of VB cells to the SII cortical area. Our results and these other findings suggest that the focal degenerations found in VB by Rose & Woolsey (1958) following SII lesions may in fact reflect 'essential' projections of the VB to SII, rather than damage of subcortical fibres to SI as they suggest. The studies of axon projections from VB provided evidence of axon bifurcation, one branch passing to the SII region, the other to SI or motor cortex. Similar findings have been reported by Andersson, Landgren & Wolsk (1966) and Andersen, Andersson & Landgren (1966).

Results of the present investigation have indicated that at least 35%

of somatically activated PO units have cortical projections, whereas none was detected in a previous study by Darian-Smith (1964). This disparity is probably explained by certain differences in the conditions of cortical stimulation in the two studies, e.g. Darian-Smith (1964) employed tungsten electrodes insulated except at their cut ends which were inserted just below the pial surface. The present results agree with degeneration studies of Rose & Woolsey (1958), Peacock & Combs (1965) and Macchi *et al.* (1959). Knighton (1950) and Calma (1965) have also suggested a cortical projection from neurones within PO. Over 50% of the antidromically activated PO cells in the present study had an axon projection confined to the somatic sensory areas. These may account for the activity in the 10% of non-specific cortical cells detected in these projection areas by Darian-Smith *et al.* (1966). However, with the cortical stimulation utilized in our study it is not possible to specify accurately the location of terminals in the cortex. Thus the axon terminals of PO cells activated by stimulation of specific somatic areas may, in fact, be situated at the periphery of the specific projection area and activated by current spread.

Of particular interest in our antidromic studies of PO axon projections is the functional indication of bifid axon projections to auditory and SII cortical areas. The existence of such a 'sustaining' projection was suggested by Rose & Woolsey (1958) from their degeneration studies. This projection to both auditory and SII regions may account in part for the overlap of auditory and somatic projections described by Berman (1961).

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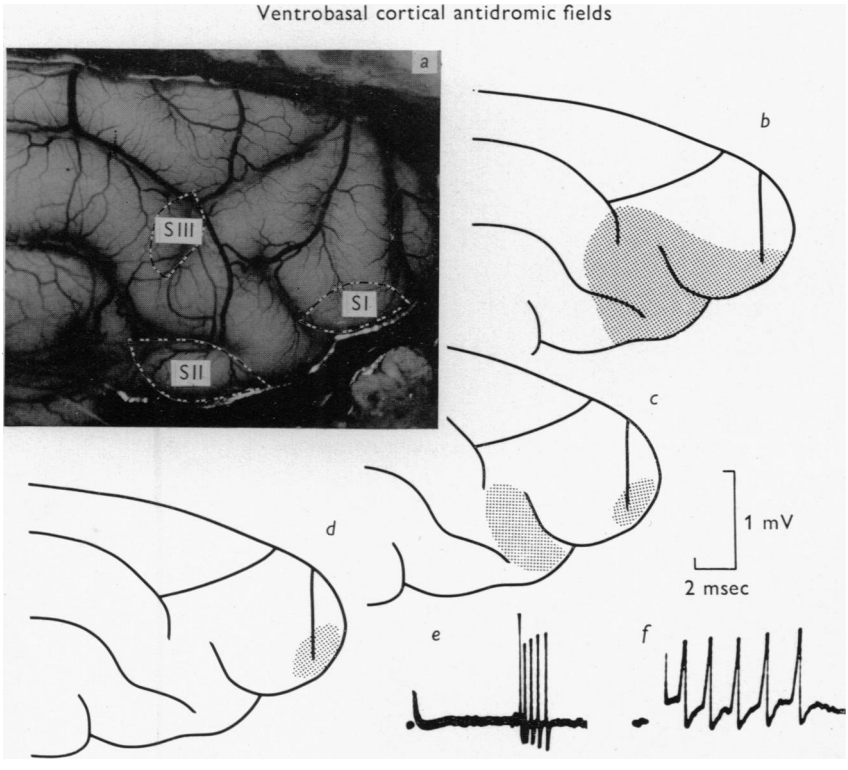
Ventrobasal cortical antidromic fields
a
SIII
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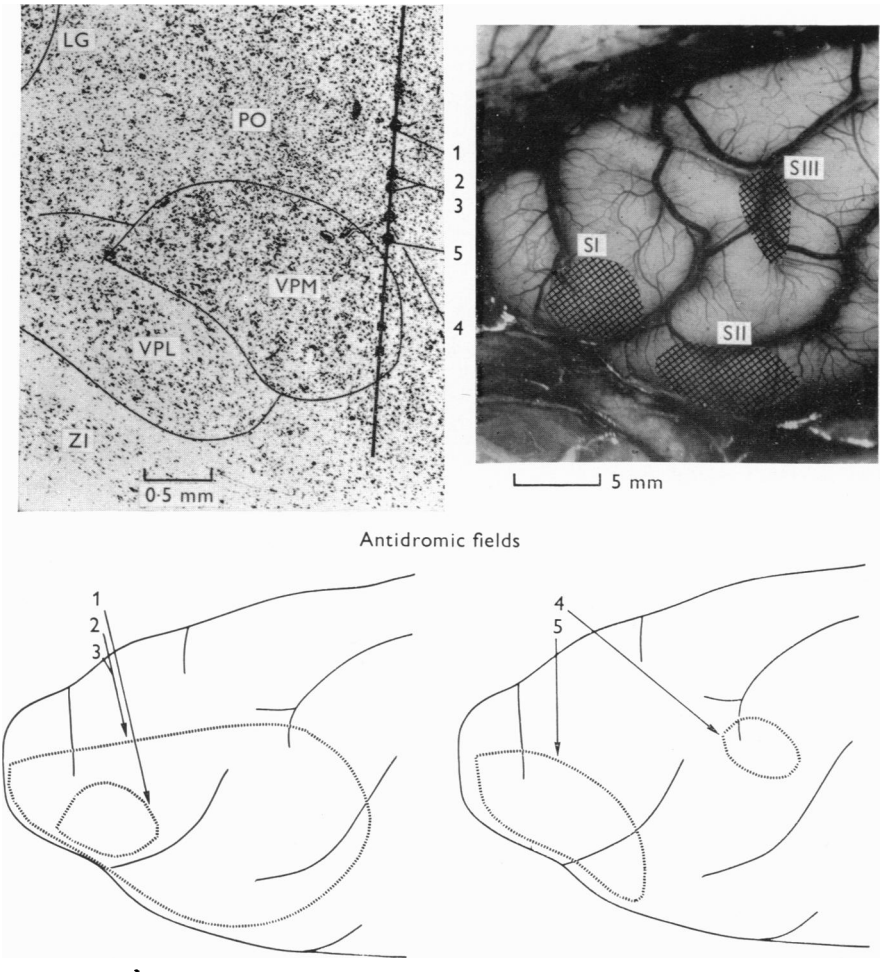
LG
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Antidromic fields
1
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EXPLANATION OF PLATES

PLATE 1

Cortical 'antidromic fields' represented by the shaded areas '*b*', '*c*' and '*d*' for three ventrobasal neurones. '*b*' indicates an extensive 'antidromic field', '*c*' a discontinuous one and '*d*' a localized field. The response of the unit with 'antidromic field' '*b*' to peripheral stimulation is indicated in '*e*' and to cortical stimulation in '*f*'. '*a*' illustrates the cortical regions of maximum evoked activity in the SI, II and III somatic projection areas. The time and voltage calibrations are 2 msec and 1 mV respectively. The current intensities required for threshold antidromic activation of the three neurones were 2·0–4·0 mA.

PLATE 2

The cortical 'antidromic fields' for five cells in the posterior nuclear region are indicated in the lower half of the figure. The position of these five cells is shown in the Nissl-stained transverse section through the posterior thalamus of the cat. VPM = nucleus ventralis posteromedialis; VPL = nucleus ventralis posterolateralis; LG = lateral geniculate nucleus; PO = posterior nuclear region; ZI = zona incerta. The vertical line in the section passing through PO and VPM indicates an electrode penetration and along it the position of VPM (■) and PO (●) cells studied. The cortical areas of maximum evoked activity in somatic projection areas SI, SII and SIII in this experimental animal are shown on the photograph of the cortical surface. The threshold current intensities required for antidromic activation of the five cells varied between 2·0 and 4·5 mA.