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DESCENDING INFLUENCES ON THE EXTEROCEPTIVE ORGANIZATIONS OF THE CAT'S GRACILE NUCLEUS

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The preceding paper (Gordon & Jukes, 1964) gave an account of the different exteroceptive components of the cat's gracile nucleus, and of their projections, determined by antidromic stimulation, into the contralateral mid-brain. The present paper describes synaptic effects on these different groups of cells, produced by electrical stimulation of the surface of the contralateral cerebral cortex, or in the mid-brain.

An influence of descending fibres on the dorsal column nuclei was first observed by Scherrer & Hernández-Peón (1955) in curarized unanaesthetized cats, and was interpreted by them as an action mediated by the mid-brain reticular formation. Functional evidence of a direct corticofugal influence was then provided by Dawson (1958), who showed that the focal potential evoked in the cuneate nucleus of the anaesthetized rat by stimulation of the forepaw could be reduced by 50% by a single shock given 5 msec previously to the contralateral sensorimotor cortex (see also Dawson, Podachin & Schatz, 1963). Corticofugal fibres were shown to end directly in these nuclei (Walberg, 1957; Chambers & Liu, 1957; Kuypers, 1958); and functional evidence of involvement of the pyramidal tract in descending effects upon them was provided by Magni, Melzack, Moruzzi & Smith (1959), Levitt, Carreras, Chambers & Liu (1960) and by Jabbur & Towe (1961). It became clear that the effects of the corticofugal system are not uniform: some cells are excited and others inhibited (Levitt *et al.* 1960; Towe & Jabbur, 1961). Excitatory and inhibitory influences are exerted differentially on cell-organizations which are also distinguishable on other grounds (Gordon & Jukes, 1962); and more detailed evidence on this question will be presented in this paper.

Synaptic actions on these nuclei can also be produced by stimulating in the lemniscal region of the mid-brain: these can be excitatory (Amassian & de Vito, 1957; Gordon & Seed, 1961) or inhibitory (Gordon & Paine, 1960; Gordon & Jukes, 1962). Such phenomena are difficult to interpret because of the anatomical complexity of the mid-brain. The evidence to be presented in this paper suggests that some of these effects can reasonably

be ascribed to activation, by an antidromic volley, of mechanisms of recurrent inhibition or excitation in the nucleus, and therefore have some relevance to a study of its organization.

METHODS

The experiments depended on making records from single cells in the gracile nucleus of the anaesthetized cat: they are included among those described in the preceding paper (Gordon & Jukes, 1964), which gives the general experimental method and most of the detailed techniques that were used. We describe below the additional points of technique that are now relevant.

Electrical stimulation of cerebral cortex. The cortical surface was stimulated in 14 experiments which gave useful results. The area of cortex exposed varied with the needs of the experiment. In this paper the term 'postcruciate' is used to mean an area bounded anteriorly by the cruciate sulcus and posteriorly by the ansate sulcus: it includes the primary somaesthetic cortex (S 1). This area, to as near the mid line as possible, was always included in the region exposed. Posterior and inferior to this, the exposure often included the anterior ectosylvian gyrus (corresponding to S 2). In some experiments the exposure extended anteriorly in front of the cruciate sulcus. In one experiment a bilateral exposure was made.

Early experiments were done with only elementary precautions to keep the cortex warm and moist. In later experiments a trough of dental cement was built round the area to be exposed, with its lower edge cemented to bone, and this was filled with warm liquid paraffin. The temperature of this pool of paraffin was kept at 37–38° C by immersing a torch-bulb operated from a battery.

Bifocal stimulation was used in early experiments, through a pair of silver-wire electrodes with their tips 2 mm apart and formed, by heating, into balls of about 0·5 mm *d*. Stimuli were rectangular pulses of 0·25 msec duration, delivered either singly or in brief trains (of e.g. 5 shocks at 500 shocks/sec), intensity being measured in volts. For later experiments we used unifocal stimulation, which has been shown by Phillips & Porter (1962) to give more regular and comprehensible results in cortical-surface stimulation. The focal electrode was a silver ball of 0·5 mm *d*, mounted on a piece of light watch-spring and operated by a micromanipulator. A silver indifferent electrode was placed in muscle. For threshold estimations with a unifocal electrode we measured current, not voltage: for this purpose an oscilloscope was used to monitor the voltage drop across a series resistance in the output of the stimulator during the delivery of the stimulating pulse, which was of 1 msec duration. When estimating threshold for inhibition by making successive approximations, it was specially helpful to use a test background made up of the cell's resting discharges represented in a number of sweeps superimposed on a storage oscilloscope (Gordon & Jukes, 1963*c*).

Excision of cortical tissue. In four experiments a large part of the frontal cerebral cortex of one side was removed before any electrical recording was started. This was done by suction: the tissue, including buried cortex, was removed to the depth of the white matter. Bleeding was stopped with gelatin sponge. The area removed included in each case the whole postcruciate area and anterior ectosylvian gyrus: in one case all the cortex in front of the cruciate sulcus was removed as well.

Notation. Position of a cell in the long axis of the gracile nucleus is given, as in the preceding paper, in a scale of mm, with zero as the rostral border. The region between zero and 4 mm is referred to as the 'rostral' part, and that between 4 and 7 mm as the 'middle' part of the nucleus. Beyond 7 mm, positions are described as 'caudal'. Cells are classified, according to their receptive characteristics, in the way described in the preceding paper.

RESULTS

Effects of cortical stimulation on cells in the gracile nucleus

In our experience almost all cells in the gracile nucleus with cutaneous or subcutaneous receptive fields can be either excited or inhibited by stimulating the contralateral sensorimotor cortex: this agrees with the results of

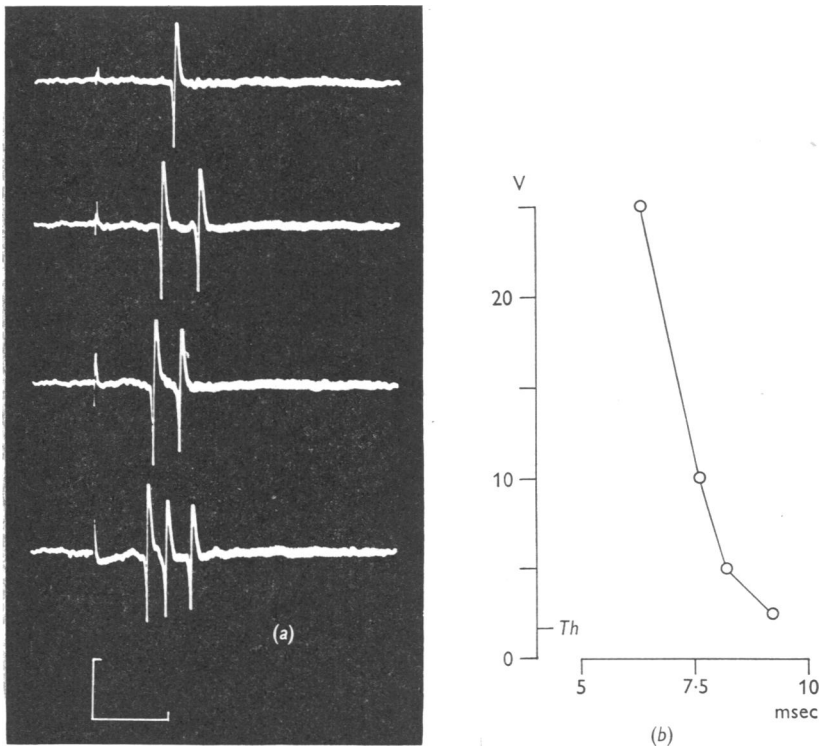
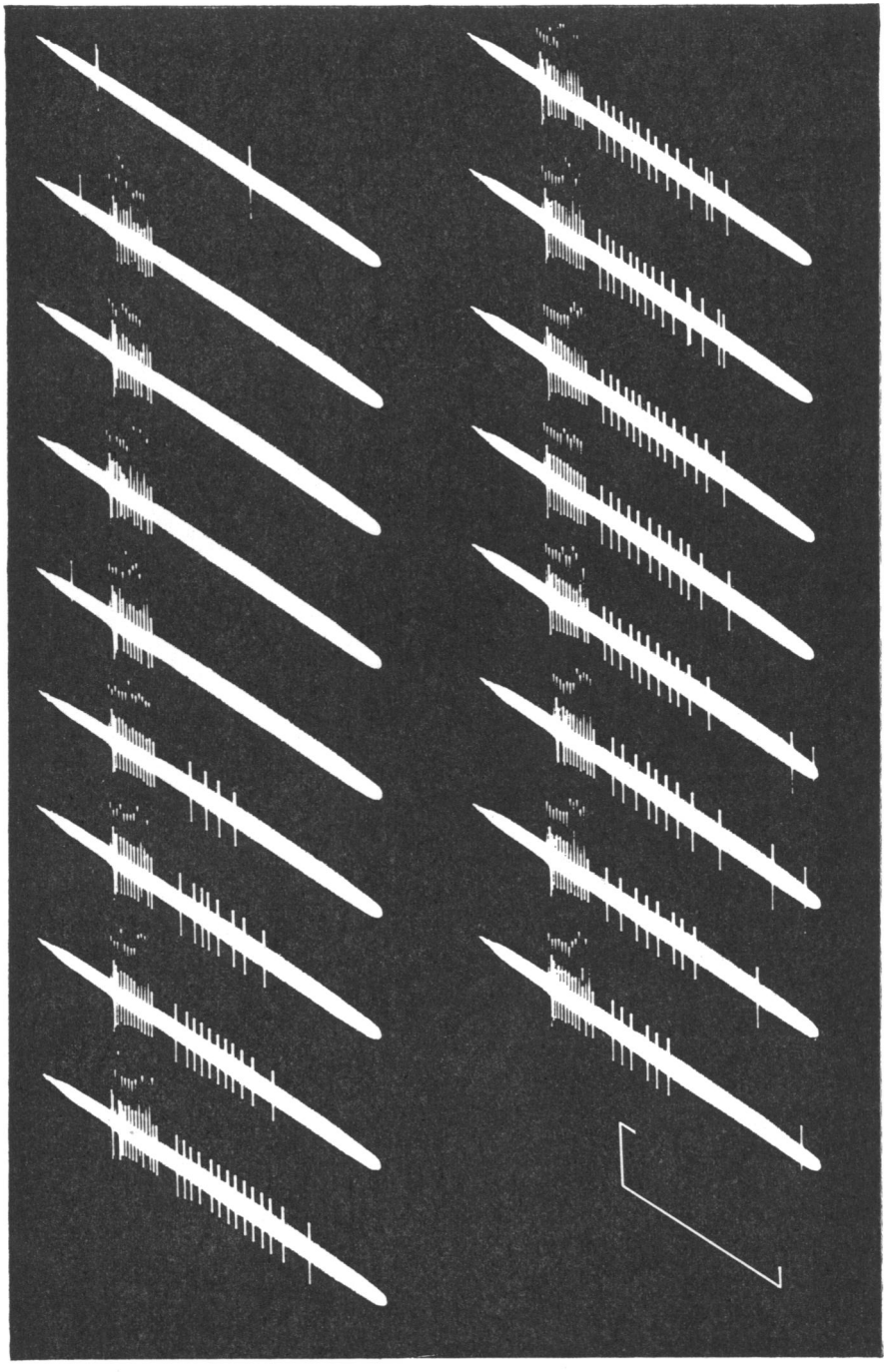


Fig. 1. Responses of a single cell in the middle part of the gracile nucleus (5·3 mm from rostral border) to single shocks (rectangular pulses of 0·25 msec duration) delivered through bifocal electrodes to the medial part of the contralateral postcruciate cortex. The figure shows the effects of increasing size of shock. This was a touch-pressure cell with a receptive field of *ca.* 25 cm² on the thigh. It was facilitated by stimuli outside this field (e.g. on the foot). It was excited transsynaptically from the lemniscal region of the contralateral brain stem (min. latency 9 msec for twice-threshold shocks). No inhibitory effects detected from cortical stimulation. (*a*) Representative records showing shortening of latency and increase in number of spikes as shock strength was increased (from above downwards). The four strengths of shock correspond to the ordinate positions of the points plotted in (*b*). Calibrations: 1 mV (negativity upwards), and 10 msec. (*b*) Graph showing variation of latency of initial spike with strength of cortical shock. Each point represents the mean latency for five observations at the same strength of shock. *Th*, threshold for excitation by cortical shock.



(*a*) (*b*)

Fig. 2. For legend see opposite page.

Towe & Jabbur (1961). We have observed cortical excitation of 27 cells, and inhibition of a further 28, for all of which the receptive characteristics and fields were satisfactorily investigated also. Cortical effects were observed on many more cells which were 'lost' before this additional and essential information could be obtained: among these was one cell on which both excitatory and inhibitory influences could be detected—the only occasion on which this phenomenon was clearly seen.

Excitatory effects. Cells excited by cortical stimulation discharged from one to three impulses in response to a single cortical shock. At threshold one impulse only was usually discharged, the number and frequency increasing with strength of shock (see Fig. 1*a*). The latency of the first impulse became shorter, and usually less variable, as shock strength was increased (see Fig. 1*b*). 'Minimal' latencies (the shortest latencies obtainable by increasing shock strength) for 22 cells ranged between 4·9 and 9·5 msec, with a mean at 6·7 msec. 'Threshold' latencies were longer than 'minimal' latencies by 1·9–19·4 msec (mean 7·6 msec) in the 11 cells in which this was studied, each figure for latency used here being the mean of at least three observations. This degree of shortening of latency with increasing stimuli indicates some neuronal complexity in the system responding to the stimulus; and this view is supported by the observation in two experiments of a cumulative facilitatory effect on a cell during the repeated delivery of a stimulus. This effect is shown in Fig. 2. A brief train of shocks, to which the cell responded, was delivered to the cortex in each sweep (i.e. every 2 sec). After four such sweeps an after-discharge appeared which increased during the next five sweeps, thereafter reaching

Legend to Fig. 2

Fig. 2. Responses of a single cell in the middle part of the gracile nucleus (5·3 mm) to brief trains of repetitive stimuli delivered through bifocal electrodes to the medial part of the contralateral postcruciate cortex. This was a touch-pressure cell with a receptive field of *ca.* 12 cm² on the dorsum of the foot: it was facilitated by electrical stimuli outside this field. One train of 12 shocks was delivered in each oscilloscope sweep, the sweep repeating every 2 sec. The sweeps run in a consecutive series starting at the top of column (*a*): column (*b*) runs on from the foot of column (*a*). The first sweep is a control without stimulation, to show occasional resting discharges. In sweeps 2–5 the cell responded with a brief burst to the first shock in each train and then with a single spike to some or all of the remaining shocks. Sweeps 6–17 show the growth, saturation and decline of a prolonged after-discharge following the early direct response to each train of shocks. When such a series of sweeps was interrupted at the height of the development of the after-discharge, the cell continued to discharge for many seconds at a higher frequency than that of its resting discharge. Calibrations: 2 mV (negativity upwards), and 50 msec. In each sweep in which stimuli were given, the peaks of the shock-escapes are seen, above the row of spikes forming the direct response. Rectal temp. 37–39° C throughout.

a peak and finally decreasing. Interruption of such a series of sweeps at the height of development of the after-discharge left the cell more excitable than in its resting state, its resting discharge continuing at an elevated level for many seconds. We can throw no light on the detailed neuronal basis for this effect.

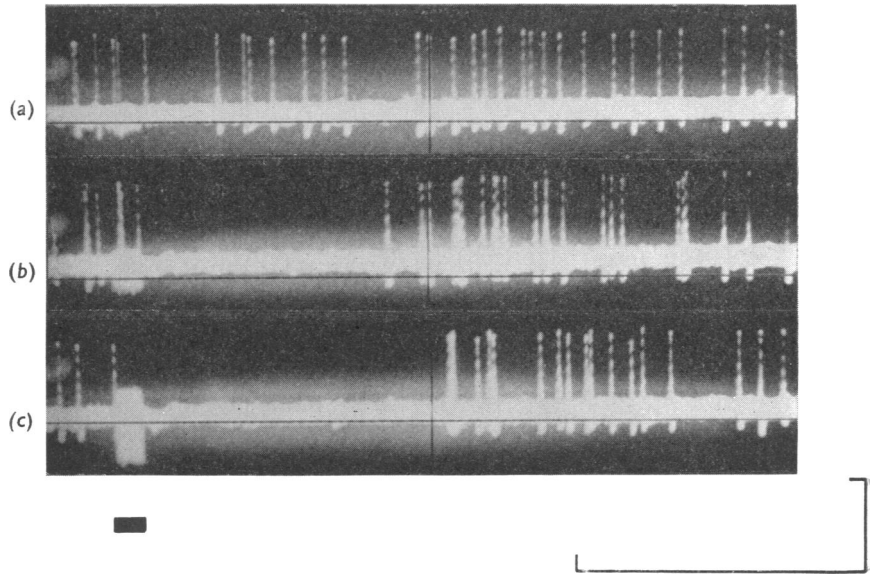


Fig. 3. Inhibition of resting activity of a single cell in the middle part of the gracile nucleus (5·3 mm) by a brief train of shocks to the medial part of the contralateral post-cruciate cortex. This was a hair-sensitive cell with a receptive field of *ca.* 2 cm² on the medial side of the foot: it was inhibited by peripheral stimuli outside this field. It responded to antidromic stimulation in the main body of the contralateral lemniscus. No cortical excitatory effects found. Each trace contains 25 sweeps superimposed on a storage oscilloscope. Timing of stimuli indicated for all traces by black rectangle under trace (*c*). Cortical stimulus at: (*a*) threshold strength for inhibition; (*b*) twice threshold; (*c*) four times threshold. Calibrations: 1 mV (positivity upwards), and 100 msec.

For five cells excited by cortical stimulation, we determined with a movable unifocal electrode the positions on the cortical surface from which excitation was elicited at lowest threshold ('best points'). These best points were well-localized, the threshold rising fairly steeply on all sides (see e.g. Fig. 4*a*). The points were distributed within an area corresponding roughly to that of the primary somaesthetic area, S1 (see Gordon & Jukes, 1963*a*, Fig. 1). Thresholds for these five cells at the best point were 0·40, 0·51, 0·55, 0·60 and 1·45 mA for a 1 msec pulse, cathodal sensitivity being in each case higher than anodal (by 30–120 %). There was no second focus

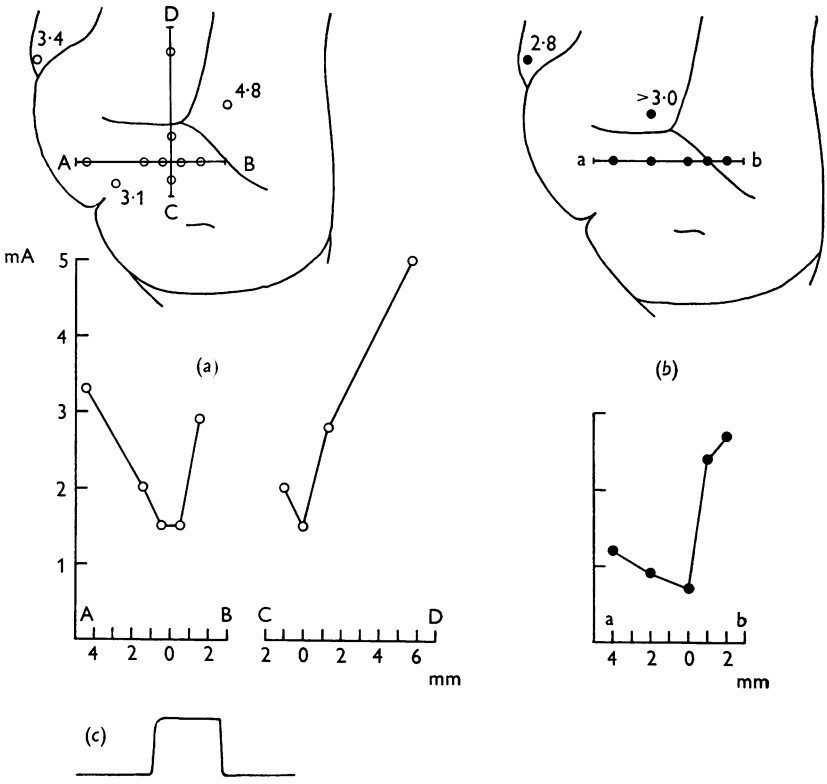


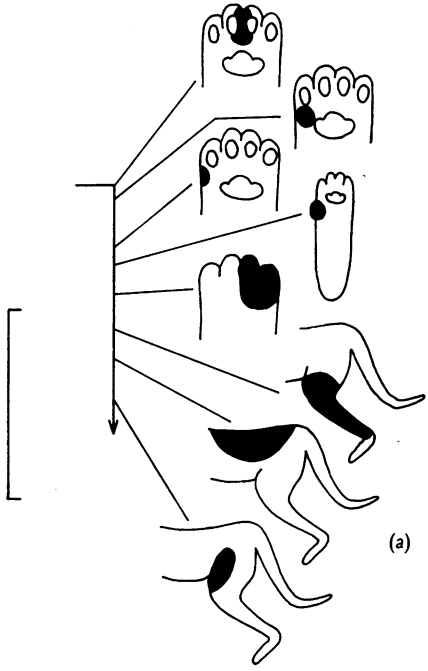
Fig. 4. Figure showing the current thresholds, at different points on the surface of the contralateral cortex, for excitation of one cell in the gracile nucleus (*a*) and for inhibition of another (*b*). Unifocal stimulation with single rectangular cathodal pulses of 1 msec duration: inset below (*c*) is a tracing of the shape of this current pulse with the focal electrode in contact with the cortex.

(*a*) The graphs below show the change in threshold for *excitation* of a cell in the gracile nucleus, produced by moving the stimulating electrode away from the point of lowest threshold. Abscissa AB refers to movements along a mediolateral line, abscissa CD to movements along an antero-posterior line. The diagrammatic drawing above shows, on the same scale, the positions of AB and CD on the surface of the cortex (superior view), the lowest-threshold point lying at their intersection. The open circles plotted on the diagram show the points at which threshold measurements were made: three points are included (marked with appropriate threshold in mA) which are additional to those plotted on the graphs.

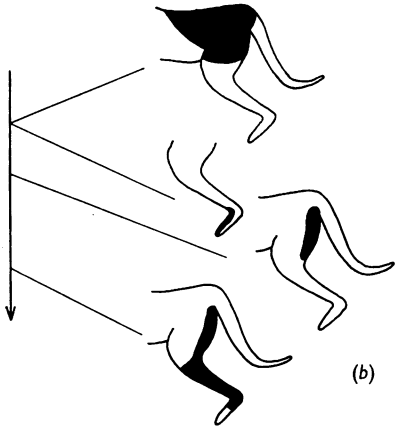
(*b*) The graph (below) and diagrammatic drawing (above) are constructed on the same principles as those in (*a*). They describe cortical thresholds for *inhibition* of a cell in the gracile nucleus, the points shown by filled circles. This cell was lost before accurate threshold measurements could be made along the line at right-angles to ab which passes through 0 on the abscissa; but rough estimates had indicated that ab passed through, or very near, the lowest-threshold point for this cell.

of low threshold in S2, where thresholds were all much higher than at the best point (by 2·4–4·7 times): the uppermost left-hand point in Fig. 4*a* is in S2. The stimuli used were not strong enough to cause muscular movements.

Inhibitory effects. Inhibition of a cell by a cortical stimulus was observed as an interruption of the cell's resting discharge (Fig. 3). Single shocks



Area (cm^2)	Type	Surround	Cortex	AD
2	*Hs*	*Inhib.*	*Inhib.*	+
1	*Hs*	*Inhib.*	*Inhib.*	+
0·5	*Hs*	*?*	*Exc.*	+
2	*Hs*	*Inhib.*	*Inhib.*	+
8	*Hs*	*Inhib.*	*Inhib.*	+
35	*TP*	*Facil.*	*Exc.*	–
40	*TP*	*Facil.*	*Exc.*	–
25	*TP*	*Facil.*	*Exc.*	–



Area (cm^2)	Type	Surround	Cortex	AD
70	*TP*	*n.t.*	*Exc.*	–
15	*H*	*n.t.*	*Exc.*	–
20	*TP*	*n.t.*	*Exc.*	–
40	*Hs*	*Facil.*	*No effect*†	+

Fig. 5. For legend see opposite page.

produced detectable inhibition; and brief trains of shocks were even more effective, as judged by the longer period of suppression of resting discharge. Increase in strength of stimulation also increased the period of inhibition (Fig. 3), which might become as long as 90 msec for a single shock and 220 msec for a train of 5 shocks at 500 shocks/sec. We did not systematically determine the minimum latencies of the inhibitory effects. The shortest latencies we found were of the order of 6 msec: a number were much longer than this (20–50 msec), and it seems likely that, as with cortical excitatory effects, they would have shortened considerably with stronger stimuli. In some cells we noticed an increased probability of firing impulses in the few milliseconds following the period in which the resting discharge was totally suppressed, an effect just detectable in Fig. 3*c*. This sort of 'rebound' might possibly represent a weak concurrent facilitatory influence of the stimulus.

Cortical best points were determined for four cells inhibited by cortical stimulation, using a unifocal stimulating electrode. These, like the best points for excitatory effects, were well localized and fell within the same cortical region (see Fig. 4*b*). The thresholds for these cells at the best point, for single 1 msec pulses, were 0·42, 0·57, 0·70 and 2·0 mA: these values are all for cathodal stimuli, threshold for anodal stimuli being higher.

Distribution of excitatory and inhibitory effects in different parts of the gracile nucleus and among cells of different types. Excitatory and inhibitory

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Legend to Fig. 5

Fig. 5. Scheme to show the sequence of cells encountered, with their receptive and other characteristics, in two representative electrode penetrations in the gracile nucleus in the same animal. The dorso-ventral movement of the electrode in each penetration is shown by the vertical arrow, and the receptive fields of the cells are shown in black on the inset diagrams. Lines connect these diagrams to the arrow giving the positions along the penetration at which the cells were encountered: the scale to the left of (*a*) = 1 mm. (*a*) Shows a penetration into the middle part of the nucleus, 5·3 mm from the rostral border. (*b*) Shows a penetration into the rostral part, 2·5 mm from rostral border. For each cell, the adjoining table on the right gives additional information under the following headings: Area (cm^2), approx. area of receptive field; Type, category of cell in terms of receptive characteristics (*Hs*, hair-sensitive; *H*, hairs only, not very sensitive; *TP*, touch-pressure); Surround, nature of any conditioning effect from the area surrounding the receptive field (*facil.*, facilitatory; *inhib.*, inhibitory; *n.t.*, not tested; *?*, not sufficiently tested); Cortex, nature of any effect observed on stimulating the contralateral postcruciate cortex (*exc.*, excitatory; *inhib.*, inhibitory); AD, antidromic excitation by electrodes in contralateral brain stem (+, antidromic response conforming to criteria in preceding paper, Gordon & Jukes, 1964; −, no response to stimulation in main body of lemniscus).

† The absence of effect on any cell is unusual enough to cause comment. In this case the cortical stimulating electrodes were not moved in an attempt to find some other, possibly effective, site.

effects resulting from stimulation of the opposite cerebral cortex were not randomly distributed among the cells of the gracile nucleus. This first became clear to us in comparing the effects when recording in rostral penetrations of the nucleus with those in penetrations through the middle region. In the rostral part, large numbers of cells throughout the depth of the penetration were excited from the cortex. In the middle region cortical excitation was unusual except in the deepest part of the nucleus: more superficially it could be seen that the resting activity of the cell groups was inhibited by cortical stimulation. Such a distribution of excitatory and inhibitory effects (see e.g. Fig 5) strongly suggested that inhibition was exerted only upon one of the two cell organizations already recognized in the nucleus (Gordon & Jukes, 1964)—that characterized by the presence of afferent inhibition—and that cortical excitation was exerted upon the other. All our subsequent experience supports this conclusion.

We investigated the receptive and other characteristics of twenty-eight cells in the gracile nucleus which were strongly *inhibited* from the contralateral postcruciate cortex. No excitatory effects from the contralateral cortex were found on any of these cells: the occasional appearance of 'rebound' following inhibition, mentioned above, represented the only possible facilitatory influence. The effect of stimulation in the surround of the receptive field was studied in twenty-six of these twenty-eight cells, and was invariably found also to be inhibitory. Conversely, all the cells with afferent-surround inhibition which were tested were also inhibited by cortical stimuli. In two cells the effects of cortical and afferent-surround stimuli were caused to sum by timing them so that each took effect on the cell at the same moment: the period of total inhibition was then longer than with either stimulus given alone. Twenty of these cells were hair-sensitive, with receptive fields mainly on the foot, but some on lower leg, thigh, or tail: fifteen lay in the middle part of the nucleus and five in the rostral part. The group also included one pad-sensitive cell, one pad-and-hair-sensitive, three claw-sensitive and three with subcutaneous receptive fields. For only one of the eighteen cells tested in this group did we fail to get evidence of antidromic excitation from the main body of the contralateral lemniscus. It was thus a representative sample of the dominant cell-organization in this nucleus, shown in the preceding paper (Gordon & Jukes, 1964) to be characterized by afferent inhibition and dense lemniscal projection; to which, therefore, we can now add the further characteristic of inhibition from the contralateral cortex.

One of these cells was also inhibited by stimulating the corresponding part of the other (ipsilateral) hemisphere. Our experience of ipsilateral cortical effects is fragmentary; but such an observation is compatible with the fuller results of Towe & Jabbur (1961).

We examined the receptive and other characteristics of 27 cells *excited* by stimulating the contralateral post-cruciate cortex. Fourteen of these were touch-pressure cells, some in the rostral part of the nucleus and some in the deep part of the middle region: every touch-pressure cell we tested was excited from the cortex, except one which was unaffected in either sense by cortical stimulation. Eight were hair-sensitive cells, five in the rostral, two in the middle and one in the caudal part of the nucleus; two were pad-and-hair-sensitive, one in the middle and one in the rostral part; and three were 'refractory' cutaneous cells in the rostral part. Twelve of these twenty-seven cells were shown to be facilitated by peripheral stimuli outside their receptive fields; and altogether fourteen of them were sufficiently investigated to exclude the presence of peripheral inhibition. We have never observed peripheral inhibition in a cell excited from the contralateral cortex.

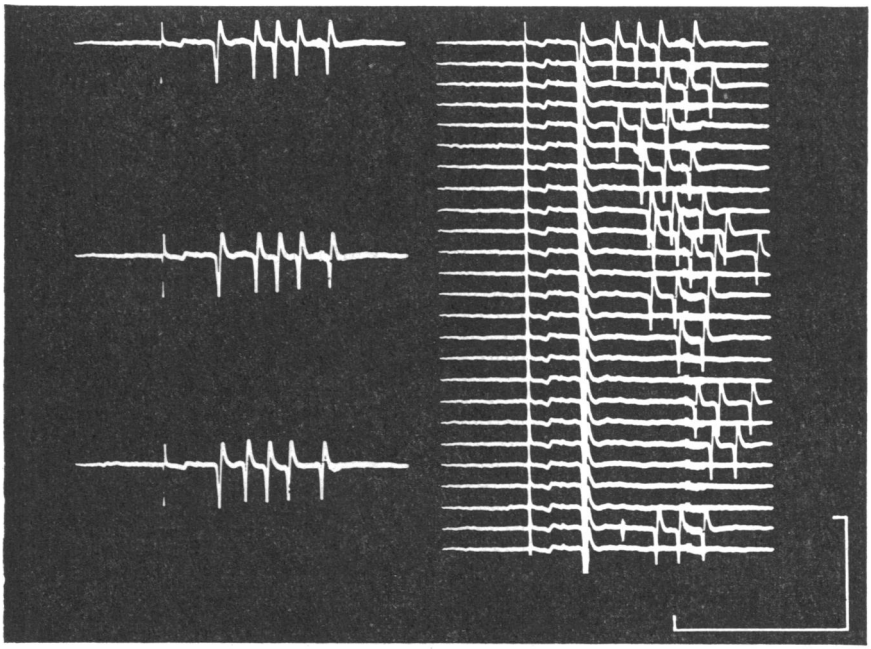
It will be seen that the types of cell excited from the cortex correspond with those belonging to the second type of cell-organization described in the preceding paper (Gordon & Jukes, 1964), being made up chiefly of rostral-lying cells of a variety of types, together with the deep-lying touch-pressure cells of the middle region. This organization is characterized by lack of peripheral inhibition, which is replaced by wide excitatory convergence from the periphery. It is also characterized by the more diffuse nature of its efferent projection from the nucleus: it is significant that of the twenty-one cortically excited cells which were tested, only one was antidromically excited from the main body of the medial lemniscus. Two others were excited antidromically from very medial positions in the contralateral mid-brain; but these medial regions were not explored systematically with stimulating electrodes (see Gordon & Jukes, 1964), so that although we can say categorically that some cortically excited cells project into the mid-brain, we cannot estimate the proportion which do so.

We have encountered only three cells with cutaneous receptive fields which we could neither excite nor inhibit by stimulating the contralateral postcruciate cortex (two hair-sensitive, and one touch-pressure); and it seems likely that few cutaneous cells escape one or other influence, at any rate in the rostral and middle parts of the nucleus. On the other hand we have on several occasions tried unsuccessfully to influence groups of vibration-sensitive cells in the gracile nucleus by cortical stimulation, and we regard this absence of effect as significant.

Trans-synaptic effects on the gracile nucleus resulting from mid-brain stimulation

Antidromic excitation of cells in the gracile nucleus by stimulation at suitable sites in the contralateral mid-brain has been described in previous

papers (Gordon & Seed, 1961; Gordon & Jukes, 1964): the effect is marked by constant threshold and latency, and by a short recovery cycle. Stimulation at the same sites in the mid-brain also produces effects, at thresholds similar to antidromic effects, which are clearly trans-synaptic in character. These may be either excitatory (Amassian & de Vito, 1957, cuneate nucleus; Gordon & Seed, 1961) or inhibitory (see Gordon & Paine, 1960, Fig. 7). It has to be remembered that even a weak electrical stimulus to the region of the medial lemniscus will give rise to an ascending



(*a*) (*b*)

Fig. 6. Repetitive discharge of a cell in the rostral part (0·82 mm) of the gracile nucleus to a single shock (0·06 msec duration) delivered to the contralateral medial lemniscus. This was a hair-sensitive cell with a receptive field of *ca.* 3 cm² on the side of the foot: it was inhibited both from the surround of this field and from the contralateral postcruciate cortex. In each sweep the initial response is an antidromic spike which occurred at constant threshold and latency (the cell could respond to a second twice-threshold shock at a minimal interval after the first of 0·6 msec). The succeeding spikes, although inconsistent in number and timing, appeared at precisely the same threshold as the antidromic spike: further increasing shock *intensity* above threshold had no apparent effect on their number or timing. Increasing *frequency* of stimulation differentiated sharply between the antidromic and later spikes, the latter being unable to follow even moderate frequencies. (*a*) Stimulation at 1 shock/sec. Three successive sweeps. (*b*) Stimulation at 10 shocks/sec. Twenty-five successive sweeps. Note increased inconsistency of the late discharge, which is entirely absent in about half the sweeps. Calibrations: 5 mV (negativity upwards), and 10 msec. Rectal temp. 37·8 °C.

orthodromic volley as well as to a descending antidromic volley, and that the ascending volley may affect the nucleus by a transcortical route. The stimulus will also excite any extraneous fibres which travel with, or cross through, the lemniscus near the tips of the stimulating electrodes: the possibility of this sort of complexity in the structure of the lemniscal region forces us to be tentative in classifying and interpreting some of these effects.

Trans-synaptic excitation

Trans-synaptic excitation linked with antidromic excitation. This is a very clear-cut phenomenon which we have observed with three cells in the gracile nucleus. These cells were excited antidromically by a stimulus in the contralateral lemniscus: the antidromic spike was followed after a short interval by a brief repetitive burst which varied, in number of impulses and in timing, from one observation to the next (Fig. 6*a*). The antidromic spike could follow a high stimulus frequency; but the later spikes, which must have been evoked trans-synaptically, failed at quite low frequencies of stimulation (Fig. 6*b*). A similar phenomenon was seen by Amassian & de Vito (1957) in the cuneate nucleus.

The feature which specially distinguished this type of trans-synaptic excitation was that the stimulation threshold for the later spikes was precisely the same as that for the initial antidromic spike, without which they never occurred. The precision of this linkage strongly suggests that the whole phenomenon depended on the antidromic excitation of a single axon projecting from the cell under observation, and that collaterals of this axon caused re-excitation of the cell through one or more interneurones. For one of these cells it was noticed that the resting discharge occurred in high-frequency bursts, each closely resembling the pattern of response to an antidromic shock: one would expect this under conditions of weak afferent drive if the above explanation is correct, because impulses fired orthodromically by the cell would themselves cause re-excitation. There was no record of the character of the orthodromic discharges of the other cells.

Two of these cells lay in the rostral part of the nucleus and responded to hair stimulation, of which one showed both afferent and cortical inhibition, and the other was not tested for inhibition. The third was a claw-sensitive cell in the middle part of the nucleus, and showed afferent inhibition.

Trans-synaptic excitation with long and variable latency. This type of excitation was seen fairly often, especially in the rostral part of the gracile nucleus (see also Gordon & Seed, 1961); and we have studied it with eleven cells whose receptive and other characteristics were also investigated. The discharge was often of one impulse only, sometimes two, with considerable variation in threshold and latency. Some of these cells did not respond to

a single lemniscal shock, but did so when two or more shocks were given at a separation of 1–2 msec (see e.g. Fig. 2*b* of Gordon & Jukes, 1962). The latency of the discharge was longer than that expected for antidromic excitation: minimum latency, among ten cells, ranged from 6 to 19 msec, and was 70 msec for the remaining cell. Latency shortened in some cells when the strength or number of shocks was increased. It is clear that spatial and temporal summation play a large part in determining these responses.

The effect was seen, for most cells, with stimulating electrodes in the main body of the medial lemniscus, but for one of them the most favourable position was its ventromedial extension. None of these cells was excited antidromically from the main body of the lemniscus: one was shown to project dorsomedially in the brain stem, and others may have had projections in areas we did not regularly explore with stimulating electrodes. Nine of them lay in the rostral part of the nucleus (four hair-sensitive, three touch-pressure, two 'refractory' cutaneous cells), and the other two in the deep part of the middle region (both touch-pressure cells). From their position in the nucleus, receptive character, and lack of projection in the main body of the lemniscus, they belong to the second type of cell organization described in the preceding paper (Gordon & Jukes, 1964). As such, one would expect from evidence given above that they would be excited by stimulating the contralateral cerebral cortex; and this proved to be true of all six we tested. The minimal latency for cortical excitation, for these cells, was shorter, by 1–11 msec, than the minimal latency for trans-synaptic excitation from the mid-brain: this evidence is compatible with the view that the effects of mid-brain stimulation depended on orthodromic excitation of lemniscal fibres and subsequent activation by thalamocortical fibres of the excitatory corticofugal path ending in the gracile nucleus. Such a route may have been concerned in the 'reflex' effects on the cuneate nucleus described by Towe & Zimmerman (1962): these effects were elicited by a peripherally evoked volley and depended on the intactness of the cerebral hemispheres. Such an explanation of the effects we have seen must, however, be extremely tentative.

A number of other cells in the rostral part of the gracile nucleus were excited by stimulation in the lemniscal or ventrobasal thalamic regions after latencies so long as to make it improbable that these responses were antidromic; but threshold and latency were sufficiently constant to leave this matter in doubt. It was shown in the preceding paper (Gordon & Jukes, 1964) that latency for antidromic responses in this part of the nucleus can be surprisingly long (5 msec or more). It was pointed out that the antidromic nature of a response can be precisely investigated; and the position will need to be clarified by further work.

Trans-synaptic inhibition

Gordon & Paine (1960) observed inhibition of the resting discharge of a cell in the gracile nucleus when stimulating the region of the contralateral medial lemniscus. We have now investigated this effect more extensively and find it to be common among the cells of this nucleus. Although a well-marked effect can sometimes be produced by a single shock, as in Gordon & Paine's experiment, a brief train of shocks (e.g. 5 shocks at 700–1000 shocks/sec) was always more effective. This fact, apart from showing that the effect depends on summation, was specially helpful when investigating cells which were also excited antidromically by a mid-brain stimulus. The unequivocal demonstration of inhibition required that the cell should not be excited, even antidromically, by the stimulus; but by setting the strength of shock below threshold for antidromic excitation, and the use of a train of shocks to achieve the necessary temporal summation, it was often possible to study the inhibitory effect in isolation. An example of inhibition by a short train of shocks is shown in Fig. 7*a*.

In studying the temporal relations of the inhibition, our usual procedure was to use an electrical test stimulus in the peripheral receptive field, above threshold for firing the cell, and delivered at various times relative to the application of the conditioning stimulus in the mid-brain.

The response to the test stimulus was characteristically composed of several spikes, the number varying from one observation to the next. The threshold for eliciting a response with a test shock was also somewhat variable. This variability in test threshold made it difficult to follow excitability changes by the conventional method in which one determines test threshold for each test-conditioning interval and expresses excitability as $\propto 1/\text{threshold}$. We used a different technique, in which the size of both test and conditioning shocks was fixed, and relative excitability estimated in terms of the average number of impulses in the test response over ten successive sweeps at 1 sec intervals. Ten control sweeps (test shock only) were interposed between successive ten-sweep conditioning periods. 'Excitability', with this method, is proportional to average number of impulses during conditioning expressed as percentage of average number of impulses during the relevant control period (complete abolition of test response, as in Fig. 7*a*, is represented as zero percentage excitability).

Although depending on this crude technique which yielded incomplete information, our data on the time course of this form of inhibition give it an order of magnitude; and in the absence of any other published description they seem worth reporting here. In four of five cells, investigation by this method showed the inhibitory process to have a rather slow time course (see e.g. Fig. 7*b*), with the inhibitory effect still detectable some tens of msec after its onset: in one cell, recovery proceeded much faster (Fig. 7*c*). Latency of onset of inhibition was studied, in different cells, either with a peripheral test stimulus, or by using the cell's resting discharge to provide a test background and superimposing 20–30 sweeps with a conditioning stimulus delivered in each. In nine cells, latency ranged from 5 to over

30 msec; but, as with our observations on latency of cortical inhibition, we cannot regard these as minimal latencies. Determination of minimal latency presents special problems here because the necessary increase in intensity of the lemniscal stimulus is likely to cause antidromic excitation.

The threshold for inhibiting cells in the gracile nucleus by stimulating in the lemniscal region was always comparable with that for antidromic excitation of cells in the same nucleus. This is shown for one cell in Fig. 8.

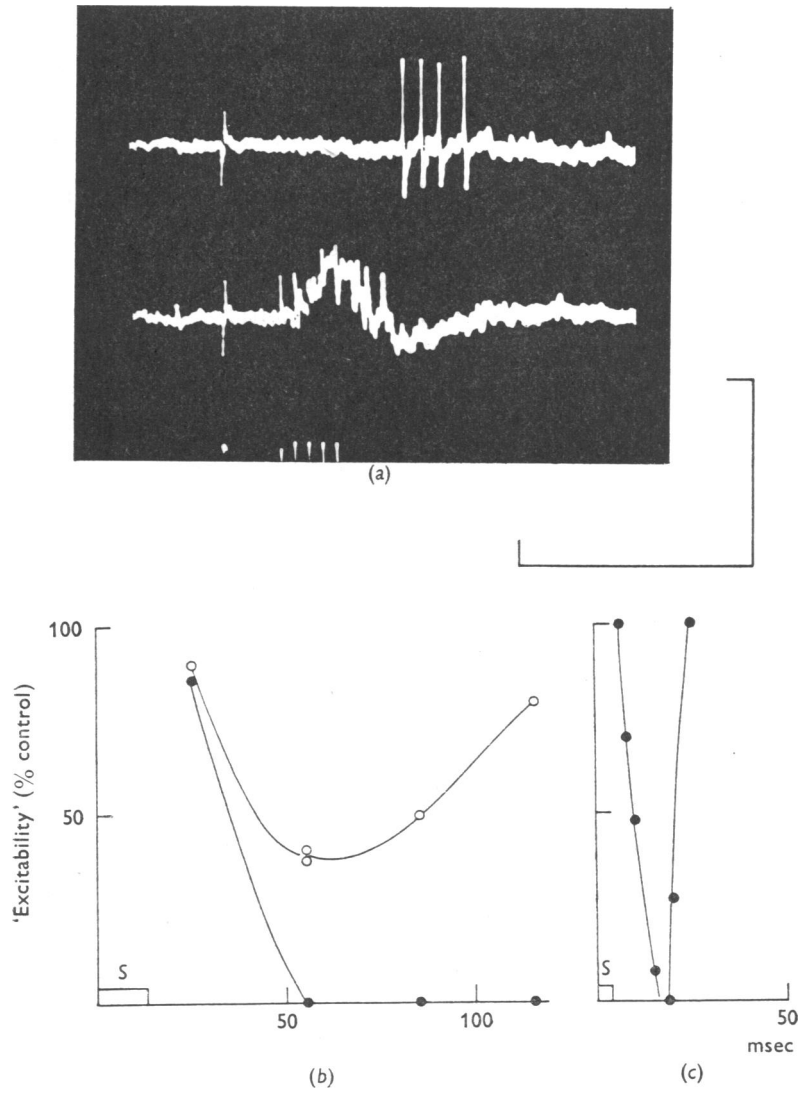


Fig. 7. For legend see opposite page.

This cell was fired antidromically; and it will be seen that the curve relating antidromic threshold to transverse position of stimulating cathode passes through a well-defined minimum where the threshold value is low enough to suggest that the relevant electrode lay very near the projecting fibre (see the preceding paper, Gordon & Jukes, 1964). Thresholds for inhibition of this cell by brief trains of shocks delivered through the same stimulating electrodes are also shown: they lie in the same range as the antidromic thresholds. The lowest thresholds for inhibition of two other cells in this experiment are also shown to lie in this range (Fig. 8). This comparability of antidromic and inhibitory thresholds led us to consider seriously the hypothesis that the inhibition was initiated by the stimulation of lemniscal fibres (though not necessarily the axon of projection of the particular cell inhibited), rather than by spread of stimulus to extralemniscal structures. We carried out a number of experiments in which thresholds for inhibition of a cell were determined for a number of different sites of stimulation in the mid-brain. One such attempt has been described (Fig. 8): in this case threshold rose sharply at the lateral border of the lemniscus, but the

Legend to Fig. 7

Fig. 7. Trans-synaptic inhibition.

(*a*) Representative extracts from a series of records showing inhibition of a touch-pressure cell by lemniscal stimulation. Further details about this cell are given in the legend to Fig. 10. Upper trace: repetitive response of the cell to a single test shock applied in the cutaneous receptive field. Lower trace: test response inhibited by a suitably timed train of conditioning shocks to the contralateral lemniscal region. Note that the conditioning shocks cause antidromic excitation of other cells. Onset of inhibition shown from other records to occur 5 msec after the onset of conditioning shocks. Timing of test shocks shown by shock-escapes on records and by left-hand mark below lower trace. Timing of conditioning stimuli shown by group of 5 marks below lower trace, following test shock. Calibrations: 1 mV (negativity upwards), and 20 msec.

(*b*) Graph illustrating the time course of change in excitability in a cell in the gracile nucleus, inhibited by a train of 10 shocks, below threshold for antidromic excitation, delivered to the contralateral lemniscal region. Method described in text. Ordinate, excitability expressed as percentage of control. Abscissa, time interval between onset of conditioning stimulus (period of stimulation marked by rectangle *S*) and expected response to test stimulus. Upper curve (open circles), conditioning stimuli just above threshold. Lower curve (filled circles), conditioning stimuli twice threshold. This cell responded to pressure on a pad, and showed surround inhibition. It could be excited antidromically from the lemniscus. It lay 3·2 mm from the rostral border of the nucleus.

(*c*) Graph constructed on the same principles as (*b*) above, showing the time-course of inhibition of another cell by a train of 5 shocks, below threshold for antidromic excitation, delivered to the contralateral lemniscal region. The contralateral post-cruciate and anterior ectosylvian cortex had been removed in this cat.

This was a hair-and-pad-sensitive cell, 0·3 mm from the rostral border of the nucleus. It could be excited antidromically from the lemniscus. Afferent inhibition not tested.

medial boundary of the effective area was not found. Several experiments of this kind gave the same result: in each case threshold remained low across the lemniscal region. Figure 9 shows the results of two other experiments, on different cells, in which threshold was measured as the electrode was moved either more deep (Fig. 9*a*) or more superficial (Fig. 9*b*). It can be seen from Fig. 9*a* that threshold remained steady with

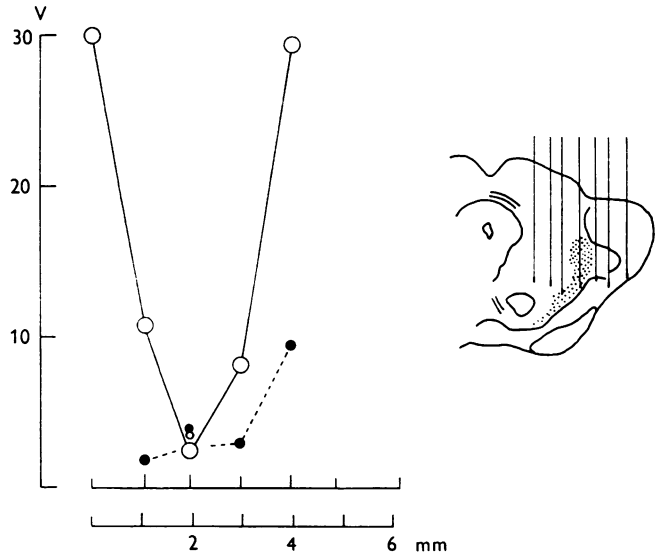


Fig. 8. Graph relating the threshold (ordinate), for antidromic excitation and for inhibition of a cell in the gracile nucleus, to the transverse position of the stimulating cathode in the contralateral brain stem (abscissa). The upper abscissal scale shows the transverse positions of the tips of the electrodes: the lower scale is in mm, referring to the brain before fixation. The inset tracing of a transverse section of the brain stem shows the positions of the stimulating electrodes in this experiment, their non-insulated tips represented by thickening of the lines: the dotted area shows the approximate position of the medial lemniscus at this level.

○—○, thresholds for antidromic excitation; ●···●, thresholds for inhibition of the same cell. The inhibitory effects were observed as interruptions of the cell's resting discharge: no reading for inhibition was made at the abscissal position 1·9 mm, because antidromic threshold was lower here than inhibitory threshold. This cell lay in the middle region of the nucleus (4·8 mm), and responded to hair stimulation in an area of *ca.* 1 cm^2 on a toe. It showed surround inhibition. The two points plotted in abscissal position 1·9 mm (○, ●) which are not connected with either line show lowest thresholds for inhibition of two other cells in this experiment.

the electrode in the lemniscus but rose sharply as it penetrated into the underlying substantia nigra. In Fig. 9*b* threshold is seen rising sharply at a point about 1·5 mm superficial to the supposed dorsal boundary of the

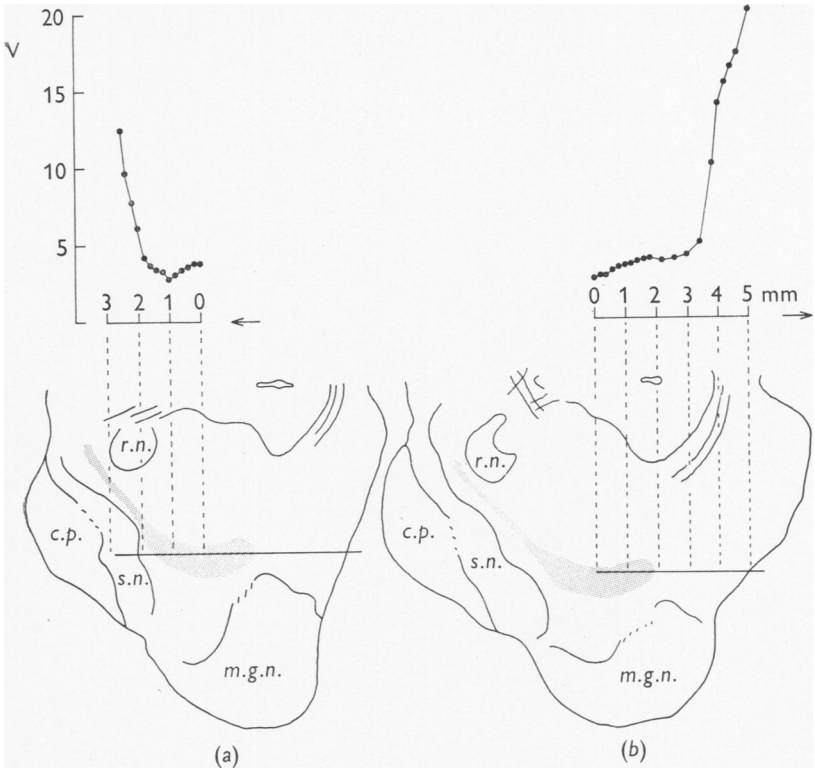


Fig. 9. Graphs showing the effect on the voltage thresholds (ordinates) for inhibition of two cells in the gracile nucleus caused by moving the cathodal stimulating electrode more superficial or deep in the contralateral brain stem. The conditioning stimulus was a brief train of pulses, each of 0·06 msec duration, always below threshold for antidromic excitation of the cell. Inhibitory effects were observed as depressions of the response to a weak electrical test stimulus in the cutaneous receptive field. The stimulating electrode was insulated to within 0·25 mm of its tip. (*a*) Threshold change for inhibition of a touch-pressure cell in the middle part of the nucleus (6·6 mm), as the stimulating electrode was driven progressively deeper into the brain stem. (*b*) Threshold change for inhibition of a cutaneous cell (receptive characteristics not further determined) in the rostral part of the nucleus (2·3 mm), as the stimulating electrode was progressively withdrawn from the brain stem. In each graph the abscissal scale refers to readings of depth within the brain stem made during the experiment, zero representing the original depth of the stimulating electrode: the arrow shows the direction of movement. The abscissal scale has been projected on to a tracing of the relevant histological section, corrected for shrinkage, showing the position of the electrode in relation to anatomical landmarks within the brain stem (*c.p.*, cerebral peduncle; *m.g.n.*, medial geniculate nucleus; *r.n.*, red nucleus; *s.n.*, substantia nigra; the shaded area shows the approximate position of the medial lemniscus).

lemniscus. Such experiments were usually terminated by the cell being 'lost' before the observations were complete; but with one cell we were more fortunate, and were able to investigate the dorsal, lateral and medial

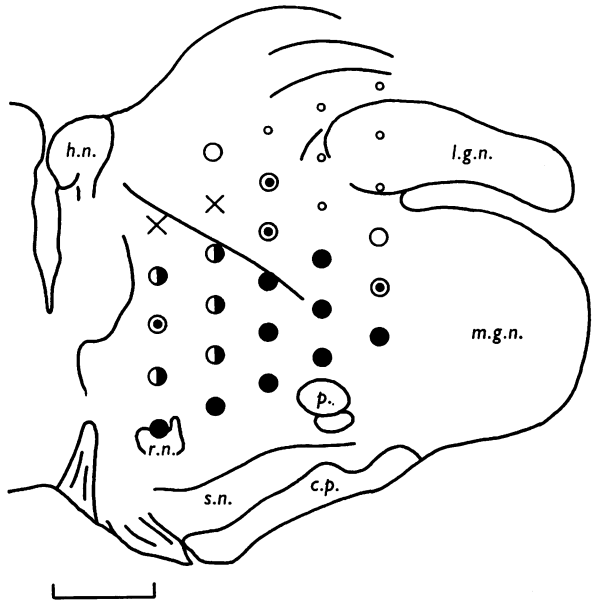


Fig. 10. The points plotted on this tracing of a transverse section of the brain stem represent the positions where stimulation either inhibited (large circles) or excited antidromically (crosses) a single cell in the gracile nucleus of the opposite side. The *inhibitory* effects were produced by brief trains of cathodal pulses, and the different circular symbols indicate the voltage ranges within which the thresholds lay: ●, threshold less than 6 V; ◑, between 6 and 12 V; ⊙, between 12 and 24 V; ○, between 24 and 48 V; ○ (small circles), no effect seen (threshold over 48 V). The *antidromic excitatory* effects (×) are plotted only where their threshold lay below that for inhibition: threshold for the left-hand point was 1 V, and for the right-hand point 1·5 V, so that the projecting fibre lay very near these points. Proof that these responses were antidromic is given by the records from the same cell in the preceding paper (Gordon & Jukes, 1964, Fig. 10). The positions of the five electrodes used as cathodes are indicated by the five vertical rows of symbols: their non-insulated tips lay initially in the most ventral positions shown. The assembly of electrodes was withdrawn in 1 mm steps and threshold measurements made for each step. Figure corrected for histological shrinkage. Figure 7*a* also refers to this cell. It was a touch-pressure cell in the rostral part of the nucleus (0·82 mm), with a receptive field of *ca.* 100 cm² on thigh, lower leg and foot. It showed afferent facilitation. It was excited by stimulating the contralateral postcruciate cortex. Stronger stimulation of the lemniscus excited it transsynaptically after long variable latency (range 14–140 msec). Scale = 2 mm. Abbreviations as in Fig. 9, with the following additions: *h.n.*, habenular nucleus; *l.g.n.*, lateral geniculate nucleus; *p.*, aberrant pyramidal bundles separated from the cerebral peduncle.

boundaries of the effective area fairly thoroughly. The results of this experiment are shown in Fig. 10, where symbols are used to indicate different threshold ranges: here the points in the lowest-threshold range (filled circles) lie together in an area corresponding reasonably well with the cross-sectional outline of the lemniscus.

In fact the combined evidence of all these experiments leads us to identify the contralateral lemniscus as the structure which, on electrical stimulation, is effective in producing this inhibition. We were unable to produce it by stimulating the ipsilateral lemniscus. Our evidence clearly excludes involvement of descending fibres in the cerebral peduncle, but does not exclude the possibility that the effect is due to stimulating aberrant pyramidal fibres running within the medial lemniscus. Such aberrant fibres have been described at this level of the mid-brain (Kuypers, 1958); and bundles of this kind are sometimes conspicuous (e.g. those marked *p* in Fig. 10). We have produced this type of inhibition, however, by stimulating more rostrally, in the ventrobasal region of the thalamus, where such fibres are not known, and feel that this finding weighs against this particular possibility. The most likely remaining possibility is clearly that the inhibition is caused by excitation of true lemniscal fibres, ascending towards the thalamus: in this case one must decide whether it is the antidromic volley that is effective, or the orthodromic volley acting on the nucleus through thalamus and cortex. The latter explanation is made most unlikely by the results of four experiments in which large parts of frontal cortex had been removed on the side stimulated (see Methods): of nine cells adequately tested by lemniscal stimulation, four showed the characteristic inhibition—a frequency of occurrence which, as will be seen below, is of the order expected for this phenomenon with the cortex intact.

Inhibition by lemniscal stimulation was seen in 32 of 57 (56%) cells tested in the gracile nucleus (28 of 48 with the cortex intact). It would probably be seen even more commonly if it were not that stimulus intensity has to be kept below threshold for antidromic excitation. The cells inhibited were distributed fairly uniformly through the rostral and middle parts of the nucleus, the parts chiefly investigated, and these cells were of a variety of types. Ten were hair-sensitive, one pad-sensitive, one claw-sensitive, three touch-pressure, two touch-pressure and hair-sensitive, seven 'refractory' cutaneous cells, and there were also six responding to hair and two to pad stimulation for which receptive data were inadequate. Inhibition by lemniscal stimulation occurred both among cells with peripheral and cortical inhibition, and among those with facilitatory influence from the peripheral surround which are characteristically excited by cortical stimulation. The touch-pressure cell whose properties are illustrated in Figs. 7*a* and 10 was of the latter kind. It may be added here that the

finding of this inhibitory action on cells which appear to receive a purely excitatory projection from the cortex adds further weight against corticofugal fibres being concerned in producing it—whether by transcortical means or by direct stimulation of corticofugal fibres in the mid-brain.

DISCUSSION

The investigation of exteroceptive influences on the cells of the gracile nucleus, described in the preceding paper (Gordon & Jukes, 1964), provided an essential physiological and anatomical background for the present study of descending influences upon this nucleus. In our study of peripheral influences we had the advantage of being able to use stimuli which were natural, or as nearly so as was compatible with achieving a degree of analysis of the functional components of the nucleus. The methods used in the present experiments were relatively very crude, since they always included the use of electrical stimuli, in mid-brain or cortex, capable of synchronous activation of a population of neurones which were contiguous but not necessarily closely related in function. Such conditions are very abnormal, involving among other things the obliteration of spatial pattern; and one must be content with demonstrating certain excitatory and inhibitory influences without being able to assess accurately their part in normal function. In spite of the anatomical complexity of the upper brain stem, the various anatomical controls in our experiments suggest that the effects which we produced by stimulating in this region can probably be attributed to either orthodromic or antidromic stimulation of a single tract, the medial lemniscus. The effects of stimulating the surface of the cortex certainly depended on the orthodromic excitation of corticofugal fibres directed to the gracile nucleus: at the same time our experiments do not indicate the position of the cells of origin of these fibres.

We have shown that the best points on the cortex for excitation or inhibition of cells in the gracile nucleus were well localized, and that threshold at the best point was of the order required for excitation of motor pyramidal cells (cf. Hern, Phillips & Porter, 1962); but there are reasons for suspecting that our stimuli acted, not directly on the corticofugal cells, but indirectly through intrinsic cellular networks of the cortex. This opinion rests in part on the considerable shortening of latency observed when a stimulus causing excitation of a cell in the gracile nucleus was increased from threshold to maximal (see also Jabbur & Towe, 1961), and also on the cumulative facilitation of gracile cells by repeated cortical stimuli (see Fig. 2), observations which suggest the interpolation of a polysynaptic path. It also rests in part on the fact that thresholds for excitation or inhibition were lower for surface-cathodal than for surface-anodal shocks. Surface-anodal shocks are consistently more effective than cathodal in exciting the deep-lying corticofugal cell bodies when the electrode lies directly over the cortex containing them (Phillips & Porter, 1962). Therefore the corticofugal cells responsible for the effects we observed in the gracile nucleus may well have lain in the extensive buried cortex in the frontal part of the cat's cerebral hemisphere (see Livingston & Phillips, 1957, Fig. 5). We do not attach special significance to the exact positions of the best points we determined on the cortex, compared with the regions of lowest

threshold found by Towe & Jabbur (1961) and Jabbur & Towe (1961), which were somewhat more rostral, in front of the cruciate sulcus. It is known that the spatial distribution of cells excited by stimulating the surface of the cortex varies according to the method of stimulation, and in particular that it can be markedly different with bifocal and with unifocal stimulation (Phillips & Porter, 1962). Our determinations of best points differ from those of the authors quoted in being made by unifocal stimulation. There is a broad agreement that the responsive area for these effects is limited to the more medial parts of the sensorimotor area.

In the preceding paper we presented evidence and arguments justifying division of the exteroceptive components of the gracile nucleus into two main functional groups, according to the presence or absence of afferent surround inhibition. The distinction between them has now been emphasized by showing that the two groups are acted upon in opposite senses when the sensorimotor area of the contralateral cortex is stimulated. The larger group of cells is that showing afferent inhibition: they are also consistently inhibited by cortical stimulation, and are, in our experience, the only cells so affected. Dawson *et al.* (1963) have also observed cortical inhibition of cells subject to afferent inhibition, in the rat's cuneate nucleus. The constant association of afferent and cortical inhibition indicates that, whatever role afferent inhibition plays in sensory analysis, the extent of its effect is potentially under cortical control. It is generally assumed that afferent inhibition is an analytical mechanism concerned in sharpening spatial contrast in the incoming impulse-pattern, and in suppressing at the same time fluctuations not depending on the afferent input (in the so-called 'spontaneous' activity). The system of afferent inhibition operates actively in the absence of descending control from the cortex, for instance in decerebrate animals (Gordon & Paine, 1960; Perl, Whitlock & Gentry, 1962). On the assumptions suggested above, the corticofugal system acting on these cells would have the capacity to increase further the contrast. Any flexibility gained in this way, allowing modification from the cortex of the amount of spatial contrast in the output of the nucleus, might well be lost if uncontrolled drift in excitatory and inhibitory levels allowed total suppression of this output to occur readily; and it is likely therefore that some element of feed-back occurs, relating the descending inhibitory force to the output of the nucleus, operating at some threshold determined in the cortex, and discounting any such drift. This is a speculation, however: no evidence yet exists as to the afferent supply of these corticofugal neurones, and this question needs precise investigation.

As afferent inhibition and cortical inhibition appear to affect the same cells, the simplest hypothesis would propose that their effects are produced through a common inhibitory mechanism, such as a population of inhibitory interneurones. It is relevant here that large numbers of corticofugal

fibres end in the rostral part of the nucleus and in the deep part of the middle region (Walberg, 1957; Kuypers, 1958; Kuypers & Tuerk, 1964), in which places we found many cells excited by cortical stimulation; but that very few fibres end in the region of the cell-clusters (Kuypers & Tuerk, 1964), where, as we have shown, the cells subject to afferent and cortical inhibition mainly lie. We have to consider, therefore, whether some or all of the cells on which corticofugal fibres terminate could be inhibitory interneurones, a possibility raised by Andersen, Eccles & Schmidt (1962) in connexion with mechanisms of presynaptic inhibition (depolarization) in the cuneate nucleus. Some preliminary experiments suggest that the cells in the rostral part of the gracile nucleus are not essential for inhibition, since after removal of the rostral 4 mm of the nucleus both cortical and afferent inhibitory effects of normal intensity were observed on cells in the middle region of the nucleus. Another possibility is that cells lying deep in the middle region, and excited by corticofugal fibres, act as inhibitory interneurones for the cells of the clusters lying superficial to them. This may be so; but the cells of this kind that we have observed were mainly touch-pressure cells with very low sensitivity to hair stimulation, whereas afferent inhibition of the superficial cells, although it may be produced by light pressure on the skin, can also usually be produced by very light hair stimulation. It seems necessary, therefore, to postulate the existence of some cells acting as afferent inhibitory neurones which have hair-sensitive properties. Such cells need not be shared by the corticofugal inhibitory system. Cells in the caudal part of the nucleus might play such a part, but their receptive properties have not yet been adequately studied.

We have given reasons for believing that the inhibition of cells in the gracile nucleus, produced by stimulating the lemniscal region of the upper brain stem, is the result of antidromic excitation of lemniscal fibres. If this interpretation is right, it would seem that these fibres must have collateral branches which act in a recurrent fashion on the nucleus, presumably through one or more interneurones. Although not proved, our interpretation is supported strongly by circumstantial evidence: rigid proof would require an unambiguous anatomical situation in which no descending fibres could have been stimulated. Similar interpretations of inhibitory effects produced by stimulating in the path of projection of the inhibited cells have been made for Betz cells (Phillips, 1959), for pyramidal cells of the hippocampus (Kandel, Spencer & Brinley, 1961) and for olfactory mitral cells (Phillips, Powell & Shepherd, 1963). Recurrent inhibition of this kind has been shown unambiguously in the 'Renshaw inhibition' of spinal motoneurones (Eccles, Fatt & Koketsu, 1954).

Brooks (1959) has drawn an analogy between mutual recurrent inhibition in a population of motoneurones and the surround inhibition of

afferent systems. Could such a recurrent mechanism explain afferent inhibition in the gracile nucleus? On the face of it this seems most unlikely, because this 'lemniscal' inhibition was observed equally in cells with inhibitory surrounds and in those with facilitatory surrounds. In particular, it was observed in touch-pressure cells, which characteristically have facilitatory surrounds and are excited from the contralateral cortex. It was also seen in cutaneous cells of the lateral cervical nucleus, none of which showed surround inhibition (Gordon & Jukes, 1963*b*). Further consideration of the neuronal basis for surround inhibition, however, shows that these very persuasive objections are not conclusive. In terms of algebraic sums of excitation and inhibition, the surround must by definition have a *net* inhibitory effect under the circumstances of the test, and the central field a *net* excitatory effect, on a given cell: this does not deny to the surround some excitatory connexions with the cell or to the centre some inhibitory connexions. It follows that an afferent inhibitory mechanism, recurrent or otherwise, may be equally present for all cells; and that the presence or absence of surround inhibition, as a characteristic pattern of response to natural stimuli, could be determined by the density and spatial extent of afferent *excitatory* connexions to the particular cell. There is at present no evidence bearing on this question, and consequently no overriding reason for ruling out the involvement of this 'lemniscal' inhibition in the mechanism for surround inhibition. It may be pointed out, however, that there might be operational disadvantages in a mechanism for surround inhibition in which, compared with afferent facilitation, afferent inhibitory processes were subject to the appreciable time-lag involved in a recurrent system: it might also be argued that if recurrent inhibition were involved, consistently longer latency should have been observed for afferent inhibition than was actually the case (see Gordon & Jukes, 1964). We are inclined to prefer the alternative interpretation that this is an independent mechanism exerting mutual restraint throughout the output of the nucleus. No exact assessment of its function can be made without having more accurate information about its spatial and threshold relations than can be obtained by electrical stimulation of the lemniscus.

There is also evidence of recurrent excitatory influences upon cells in the gracile nucleus ('trans-synaptic excitation linked with antidromic excitation'). It has already been suggested that, in view of the precision of the linkage between antidromic and trans-synaptic excitation in these cells, the mechanism of re-excitation may be spatially very restricted: it may even be confined to single cells. In this respect it contrasts strongly with the mechanism for recurrent inhibition which has been proposed above: here a considerable degree of spatial summation was involved, and

inhibition of a cell readily occurred as a result of lemniscal stimulation without the axon of that cell being excited by the stimulus. As the mechanism of re-excitation will only follow at low frequencies (see Fig. 6), it appears that such a mechanism will elevate the response of the cell preferentially when its afferent drive is weak, thereby flattening the stimulus/response curve and giving greater security to weak signals. We have only seen this phenomenon occasionally, and therefore cannot argue as to its functional importance. The severe depressant action of barbiturates on interneuronal systems may well account for its rare occurrence in our experiments; and further investigation is needed under more favourable conditions.

The system of cells characterized by afferent and cortical inhibition, with their virtually complete projection in the main body of the contralateral lemniscus, has a striking homogeneity in its organization; and its various subdivisions, each distinguished according to the type of receptor involved, must represent the main exteroceptive contribution of this nucleus to the ventrobasal region of the thalamus. This system must contain much spatial information. The cells of the gracile nucleus which lack surround inhibition and characteristically receive excitatory connexions from the cortex are probably less homogeneous in function. It has already been suggested that some of them may play the part of inhibitory interneurones. A number of them have long axons projecting into the contralateral mid-brain—a fact not necessarily inconsistent with inhibitory functions in the nucleus: some fibres project in the main body of the lemniscus and some in more medial areas (Gordon & Jukes, 1964). The former are likely to terminate in the ventrobasal region of the thalamus; but the terminations and significance of the latter are at present imponderable. The cells of this second system must carry less spatial information, but with their generally larger receptive fields and facilitatory surrounds they should carry more information as to average levels of stimulus intensity over the receptive surface. Cells of this kind which project in the main route of the lemniscus could provide the afferent basis of the cells with large receptive fields, lacking surround inhibition, which were studied by Andersson (1962) in the second somaesthetic area of cats in which the whole spinal cord was cut except for the dorsal columns. Cells with surround inhibition, usually with small receptive fields, were also found in such experiments. The approach used by Andersson seems appropriate to further investigation of the contributions of the different components we have recognized in the gracile nucleus to the inputs of different thalamic and cortical systems, whose properties have been studied in some detail (see, e.g. Poggio & Mountcastle, 1960); and our methods of identifying these components, by peripheral and cortical

stimulation, would prove useful here. Such information as to their more rostral connexions seems essential for enlarging our view of their functional significance.

SUMMARY

1. Excitatory and inhibitory effects, produced by electrical stimulation of the surface of the cerebral cortex, were studied on single cells in the rostral 8 mm of the gracile nucleus. Nearly all exteroceptive cells studied were affected in one or other sense.

2. Cortical 'best points' for these effects were well-localized, in the post-cruciate region. Unifocal cathodal stimuli were more effective than anodal: for this and other reasons it is considered that the stimuli probably affected the corticofugal cells indirectly.

3. Corticofugal inhibitory influences on the gracile nucleus were apparently confined to cells also affected by afferent surround inhibition, and were seen on all such cells observed. The majority of these were hair-sensitive, others pad-sensitive, pad-and-hair-sensitive, claw-sensitive, or responded to subcutaneous pressure. They lay mainly in the middle region of the nucleus.

4. Corticofugal excitatory effects were found mainly in the rostral region and deep part of the middle region of the nucleus. The cells affected were mostly touch-pressure cells; others were hair-sensitive or pad-and-hair-sensitive. None of these cells that was tested showed surround inhibition.

5. Three types of trans-synaptic influence on the nucleus were found to result from electrical stimuli to the lemniscal region of the contralateral mid-brain. Anatomical controls suggest that these probably depended on excitation of fibres of the medial lemniscus.

(*a*) Excitation in which the threshold for the late trans-synaptic discharge was identical with that for an early antidromic spike in the same cell: this probably depends on a mechanism for re-excitation through recurrent collaterals.

(*b*) Excitation with long variable latency: cells affected were of the kind excited from the cortex, and the effect may have had a transcortical path.

(*c*) Inhibition with slow time course, which was seen in many cells, both in those with, and in those without surround inhibition. It is considered to depend on a mechanism of recurrent mutual inhibition, similar to that for 'Renshaw inhibition' of motoneurones.

6. The relation of these various processes is discussed; and consideration given to the possible functional significance of the main divisions of the nucleus in the light of ascending and descending influences upon them.

We would like to thank Mrs Lilian Artis for help of many kinds, including the preparation of our histological sections; and Mr W. J. Bannister for constructing and maintaining electronic equipment. We would also like to acknowledge a grant for scientific assistance from the M.R.C.; and a grant to G.G. from the Royal Society for the purchase of a storage oscilloscope.

Note added in proof. Since this paper was submitted, fuller accounts have come to our notice of the work of Andersen *et al.* and of Levitt *et al.* referred to here. References follow for these new papers:

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