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ACTIVATION OF CELLS IN THE ANTERIOR PRETECTAL NUCLEUS BY DORSAL COLUMN STIMULATION IN THE RAT

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SUMMARY

1. The responses of neurones in the anterior pretectal nucleus (APTN) to electrical stimulation of the dorsal columns at twice the threshold for A fibres were studied in the rat anaesthetized with urethane.

2. APTN cells were excited by dorsal column stimulation. Forty-six discharged phasically in response to a single stimulus. Sixteen cells did not respond phasically but slowly increased the discharge rate with repeated stimulation.

3. Electrical stimulation of the contralateral gracile fasciculus caused neurones in the APTN to discharge with a variable latency of 2–22 ms. Stimulations of the ipsilateral gracile and contralateral cuneate fasciculi had weaker effects.

4. Microinjection of DL-homocysteic acid into the contralateral gracile nucleus increased the discharge rate of APTN neurones. Microinjection of γ-aminobutyric acid into the contralateral gracile nucleus blocked the gracile fasciculus evoked excitation of APTN neurones.

5. On thirteen occasions cells in the gracile nucleus were driven antidromically by electrical stimulation of the APTN.

6. It is concluded that electrical stimulation of the gracile fasciculus activates a monosynaptic excitatory input to the APTN.

INTRODUCTION

The anterior pretectal nucleus (APTN) is the only nucleus of the pretectal complex apparently not involved in visual function (Gregory, 1985). In the rat it is a bilateral structure positioned dorsomedially on the diencephalic–mesencephalic border. Neuroanatomical studies demonstrate a dense reciprocal innervation between the two APTNs, which receive afferents from somatosensory cortex and dorsal column nuclei (Berkley & Mash, 1978; Weber & Harting, 1980; Foster, Sizer, Rees & Roberts, 1989). Efferents from APTN terminate in the intralaminar complex of the thalamus, thalamic reticular nucleus, hypothalamus, zona incerta and mesencephalic reticular formation (Berman, 1977; Berkley & Mash, 1978; Weber & Harting, 1980; Foster *et al.* 1989). On the basis of these neuroanatomical data several authors have suggested a role for the APTN in somatosensory processing (Berkley & Mash, 1978; Itoh, Takada, Yasu, Kudo & Mizuno, 1983). Until recently, however, there were few behavioural or electrophysiological data to support this postulate.

Prado & Roberts (1985) demonstrated that the APTN was one of the few sites where electrical stimulation caused inhibition of behavioural responses to intense cutaneous stimuli (50 °C) without at the same time causing escape behaviour. Furthermore, when compared to the effects of electrical stimulation of the ventrolateral part of the central gray, the inhibition of the tail flick reflex to noxious heat was much longer lasting and the stimulation was less disrupting to motor performance (Roberts & Rees, 1986). It is likely that the electrical stimulation of APTN excites cell bodies in the region because discrete microinjections of excitatory amino acids into APTN also cause inhibition of the tail flick reflex (Rees, Roberts & Sherwood, 1987). Electrophysiological experiments with spinal neurones have shown that APTN stimulation specifically inhibits the responses to intense cutaneous stimuli of multireceptive neurones deep in the dorsal horn of the spinal cord (Rees & Roberts, 1987*a*). Stimulation of APTN did not inhibit the responses of these neurones to brush or touch stimuli nor were the responses of nociceptive lamina 1 cells affected. Section of the dorsolateral funiculus at cervical levels abolished the effects of APTN stimulation.

These studies have indicated that cells in the APTN activate a descending inhibitory influence on spinal neurones which is associated with an inhibition of behavioural responses to intense thermal stimuli. Very little is known of the circumstances which control the excitability of cells in the APTN and, in view of the known afferents from dorsal column nuclei, an attempt has been made in the present study to change the excitability of APTN cells by stimulating the dorsal columns.

It has been known for many years that dorsal column stimulation is an effective clinical treatment for some forms of chronic pain (Shealy, Mortimer & Reswick, 1967; Sweet & Wespic, 1968). The treatment was developed from the 'gate control' theory which offered a physiological explanation for the observation that activation of low-threshold primary afferent fibres reduced rating scale assessments of chronic pain and also reduced responsiveness to intense acute stimuli (Melzack & Wall, 1965). As many low-threshold primary afferent fibres send collaterals to dorsal columns, it appeared likely that dorsal column stimulation activated these collaterals antidromically to close the spinal gate and reduce responses to C fibre activation. However, the 'gate control theory' clearly included a supraspinal element which, potentially, could be activated by ascending dorsal column fibres. Some of these fibres could be the postsynaptic dorsal column fibres which have been shown to respond to intense cutaneous stimuli (Angaut-Petit, 1975; Noble & Riddell, 1988). It has become apparent that many (but not all) of the analgesic actions of low-threshold dorsal column stimulation are due to supraspinal effects (Lindblom, Tapper & Wiesenfeld, 1977; Saade, Tabet, Banna, Atweh & Jabbur, 1985). It is clear that the dorsal columns play some role in the processing of intense sensory information but the precise nature of this involvement remains unclear.

The present study has examined the projections from dorsal columns to APTN and reports that stimulation of the medial gracile fasciculus activates a facilitatory input to the APTN. Some of these data have been presented to the Physiological Society (Rees & Roberts, 1987*b*).

METHODS

All the experiments were conducted upon adult male Wistar rats (270–290 g) which were anaesthetized with urethane (1·2 mg kg^{-1} I.P.). Tracheal and carotid cannulae were inserted and the animals placed into a stereotaxic frame. The blood pressure, electrocardiogram and rectal temperature were recorded and maintained within normal limits. A hole was drilled in the skull above the APTN, at stereotaxic co-ordinates: AP −4·5 and L +1·8. The reference planes and incisor bar orientation of Paxinos & Watson (1982) were used. The cervical cord was exposed by laminectomy between C2 and C4 and the dura mater reflected and pinned back. The arachnoid was removed with a glass probe and the cord covered with warm mineral oil.

Microelectrodes were used to record extracellularly the activity of cells in the APTN or gracile nuclei. Single-barrelled glass microelectrodes were used with a tip diameter of less than 1 μm, filled with a 2% (w/v) solution of Pontamine Sky Blue dye in 0·5 M-sodium acetate. The electrical resistance of these electrodes was 4–8 MΩ. Extracellular recordings of a neurone were displayed on oscilloscopes and at regular intervals permanent records of the action potentials were made. The study was abandoned if there were any changes in the amplitude, signal-to-noise ratio or shape of the action potential. The rate of discharge of the cell was recorded on a curvilinear pen-writing chart recorder.

The dorsal columns were discretely transected unilaterally at the level of C3 in every experiment. This was done with radio frequency diathermy using a very fine needle. Subsequent histological examination of the cord confirmed the completeness of the lesion and that adjacent structures were undamaged. Bipolar silver-ball stimulating electrodes, with a ball dimaeter of less than 150 μm, were placed on the dorsal surface of the cord under microscopic control. Square-wave stimuli for 0·1 ms at 2 times A fibre threshold were applied intermittently and the response of APTN cells examined by means of a peristimulus time histogram (PSTH) constructed 'off-line' by a microcomputer. The effects of stimulating dorsal columns above and below the transection as well as at medial and lateral placements on the cord surface helped to determine whether effects were due to stimulation of ascending fibres in dorsal columns *per se* or due to current spread to adjacent ascending or descending tracts.

Dorsal column stimuli were applied at voltages known to be 2 times threshold for A fibre activation using electrodes and stimulation parameters of this type. In four animals the A fibre threshold was checked by performing a lumbar laminectomy at the level of L5 and using bipolar silver-ball electrodes to record the compound action potential which descended in the dorsal columns following stimulation at the cervical level below the transection.

It was likely that the responses of APTN cells to stimulation of the dorsal columns were secondary to activation of cells in the dorsal column nuclei. It was necessary, however, to demonstrate conclusively that this was the case and also that cells of the dorsal column nuclei projected directly to the APTN. This was attempted in fourteen animals by removal of the posterior cerebellum and exposing the floor of the fourth ventricle. A solution (0·5 μl) of the amino acid DL-homocysteic acid (DLH, 0·05 M) or γ-aminobutyric acid (GABA, 0·1 M) were microinjected into the gracile nucleus via a fine glass needle of 70–90 μm o.d. (Azami, Llewelyn & Roberts, 1980). The alteration in discharge frequency of APTN cells was recorded as previously and then Pontamine Sky Blue dye was microinjected to enable histological determination of the exact microinjection site. The direct nature of the gracile to APTN projection was studied in similarly prepared animals in which a concentric steel bipolar stimulating electrode (o.d. 150 μm) was lowered into the APTN and microelectrode recordings made from the gracile nucleus. 'Collision' and other tests for antidromic driving of gracile cells by APTN stimulation were carried out.

At the end of each experiment Pontamine Sky Blue dye was ejected ionophoretically from the recording electrode with 10 μA for 10 min. The animal was perfused with formal saline and the brain removed for histological determination of the location of the dye spots.

RESULTS

Dorsal column stimulation intensity

In four animals, bipolar silver-ball electrodes were placed on the dorsal columns at both cervical (C3) and lumbar (L5) levels. The compound action potential resulting

from cervical stimulation was recorded at the lumbar electrodes. The fastest fibres conducted at a velocity of $24{\cdot}30 \pm 2{\cdot}43$ m s^{-1}. Figure 1 illustrates one study where the electrodes were separated by 76 mm. At 1·5 times threshold (0·3 V) the latency was 3·5 ms and the conduction velocity was 21·7 m s^{-1}. A synapse was unlikely to be

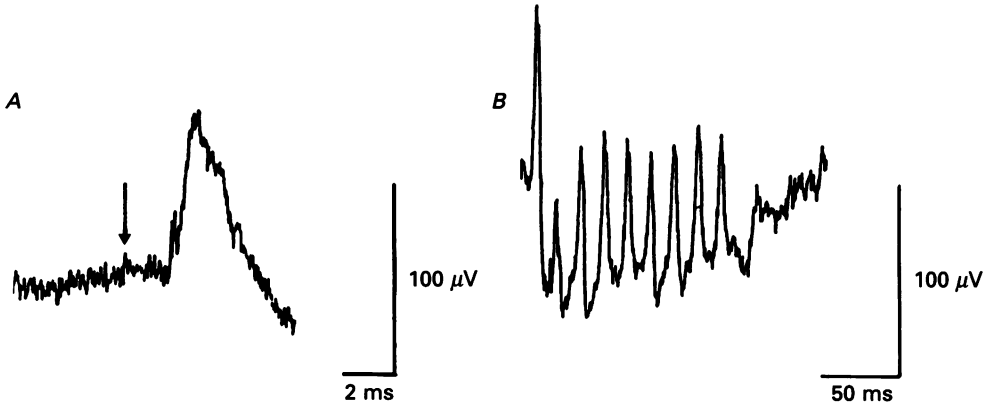

Fig. 1. Compound action potentials recorded from the lumbar dorsal column in response to stimulation of the cervical dorsal columns. In *A* the arrow above the record indicates the time of stimulation; 1·6 ms later the compound action potential was recorded at the lumbar enlargement. *B* shows the effects of stimulating the cervical dorsal columns at a frequency of 70 Hz.

present between stimulating and recording electrodes because the action potentials followed stimulation frequencies in excess of 70 spikes s^{-1}. In subsequent studies of neuronal activity recorded with microelectrodes, the dorsal columns were stimulated above the transaction at 2 times A fibre threshold (0·4 V) except that for each cell the threshold stimulation intensity was established. In almost every case the neuronal responses reported here could be evoked by stimulation at slightly above 0·2 V, which suggests that in all cases the responses were due to A fibre activation.

The discharge of neurones in APTN

Eighty-nine neurones in the posterior diencephalon were studied and subsequently seventy-four were shown to be located in the APTN. Forty-six of the APTN cells were spontaneously active at $13{\cdot}63 \pm 1{\cdot}24$ (mean ± S.E.M.) spikes s^{-1} but twenty-eight were silent, being made to discharge only by dorsal column stimulation. Low-threshold cutaneous stimuli, including hair movements, light pressure or limb flexion, did not reliably increase the firing rate of these cells in animals with intact dorsal columns. Many of the cells increased their discharge rate with dorsal column stimulation but there were two distinct types of response. Forty-six cells discharged phasically in response to a single stimulus (Fig. 2*A*). Sixteen cells did not respond phasically but slowly increased the firing frequency with repeated test stimulation of dorsal columns. To some extent, the nature of the response depended upon the precise location of the recorded neurone and the part of the dorsal columns stimulated.

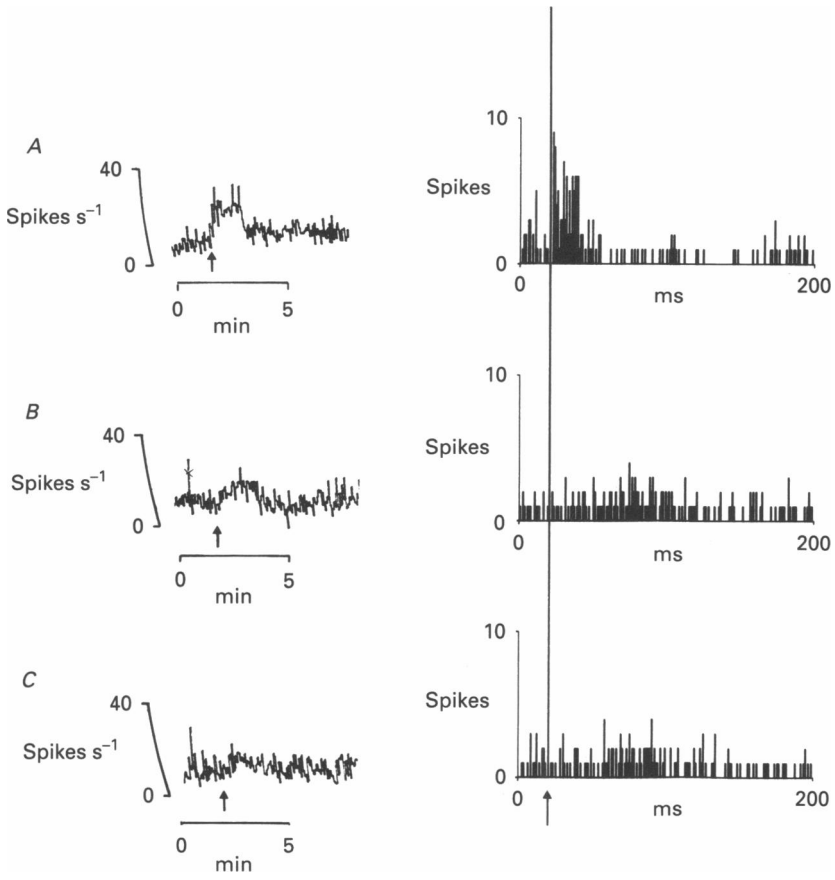

Fig. 2. The response of an APTN neurone to electrical stimulation of the dorsal fasciculi of the spinal cord. *A*, the discharge rate of the neurone was increased sharply by electrical stimulation of the contralateral gracile fasciculus. At the point indicated by the arrow the gracile fasciculus was stimulated for 20 s. The 100 stimuli were subjected to peristimulus time (PSTH) analysis and this is shown to the right of the rate-meter record. At 20 ms a single dorsal column stimulus occurred each trial. The majority of recorded action potentials occurred between 22 and 32 ms. *B* shows the effects of stimulating the ipsilateral gracile fasciculus. A much smaller increase in firing rate was seen and PSTH analysis fails to show any convincing relationship between stimuli and spikes. *C* shows a similar result following stimulation of the contralateral cuneate fasciculus. The absence of a large number of action potentials immediately following stimulation in the PSTHs shown in *B* and *C* would tend to indicate that the effects observed in *A* are not the result of current spread to neighbouring tracts.

Location of dorsal column stimulation

The characteristic effects of stimulating the different fasciculi of the dorsal columns are summarized in Fig. 2. All these data were derived from the same APTN neurone but very similar observations were made with another eleven cells. One hundred stimuli at 2 times threshold, 5 Hz for 20 s applied to the contralateral gracile fasciculus, potently increased the firing rate of the cell. The baseline firing rate

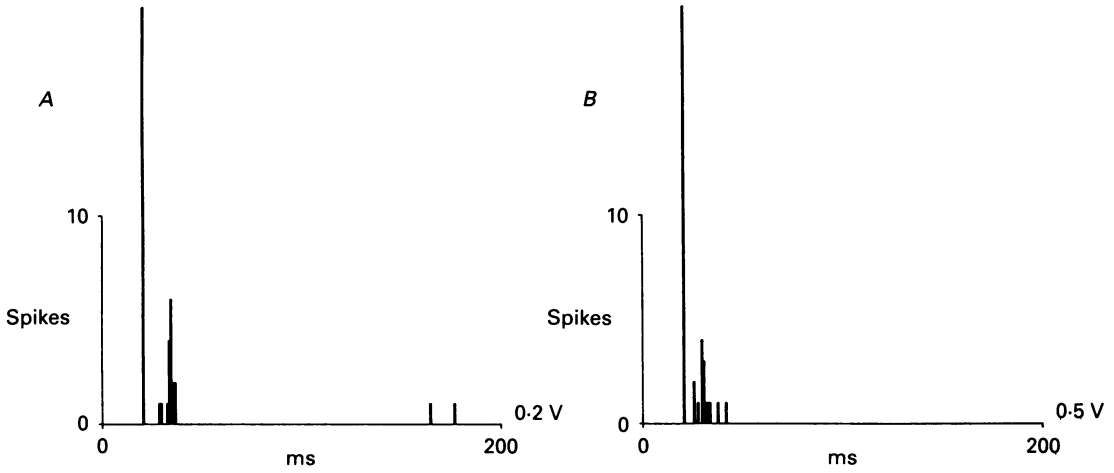

Fig. 3. Two PSTH's taken from the same APTN neurone. At 20 ms a single dorsal column stimulus occurred each trial. The column recorded at 20 ms is caused by the stimulus artifact. *A* shows the effects of stimulating the contralateral gracile fasciculus at the threshold intensity for A fibres. The latency to onset of potentials was 8 ms and the peak response was at 13 ms. *B* shows a PSTH recorded from the same cell when the stimulus was 2·5 times A fibre intensity. A similar number of action potentials were recorded over the thirty trials but the latency to onset was reduced to 5 ms. Similarly the latency to peak response was reduced to 9 ms. The result was typical of APTN neurones responding to threshold stimulation.

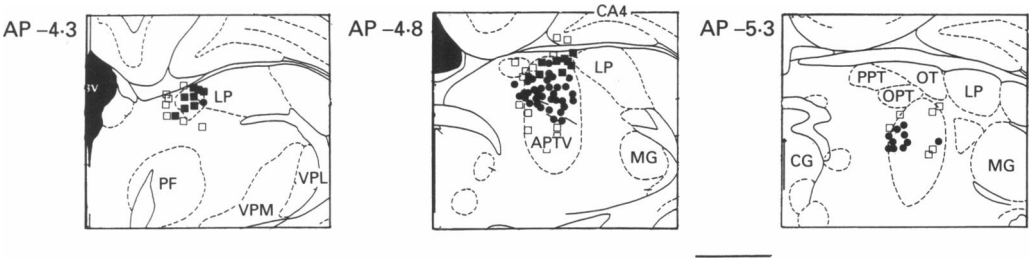

Fig. 4. Three coronal sections of the rat brain taken from Paxinos & Watson (1983). The symbols □ show sites of recordings from cells which failed to respond to stimulation of the contralateral gracile fasciculus at 2 times A fibre threshold ($n = 26$). ■ shows cells which increased the firing rate to gracile stimulation but did not closely follow each stimulus (see text; $n = 16$). ● shows the location of cells which were driven with a short latency by gracile stimulation ($n = 46$). All AP values are calculated from bregma. Abbreviations: APTV, anterior pretectal nucleus ventralis; CG, central grey; LP, lateral posterior thalamic nucleus; MG, medial geniculate nucleus; OPT, olivary pretectal nucleus; OT, nucleus of the optic tract; PF, parafasicular nucleus; PPT, posterior pretectal nucleus; VPL, ventrolateral posterior thalamic nucleus; VPM, ventromedial posterior thalamic nucleus. Calibration bar: 100 μV.

was $9{\cdot}6 \pm 1{\cdot}43$ and increased to $31{\cdot}4 \pm 2{\cdot}83$ spikes s^{-1}. A peristimulus time histogram of the response of the neurones to each of the stimuli showed a burst of action potentials lasting about 10 ms following each stimulus.

Similar stimulation of the ipsilateral gracile fasciculus had weaker effects on the

firing rate of neurones (baseline: $9{\cdot}6 \pm 1{\cdot}43$ spikes s^{-1}; response: $24{\cdot}6 \pm 3{\cdot}40$ spikes s^{-1}. However, only a slight indication of a response to individual stimuli could be seen on the histograms and the extremely long latency of about 30 ms suggests that any effect could be secondary to many central or even peripheral effects of the stimulation. Stimulation of the contralateral cuneate fasciculus had very little effect on the firing rate of the cells either in the short or the long term.

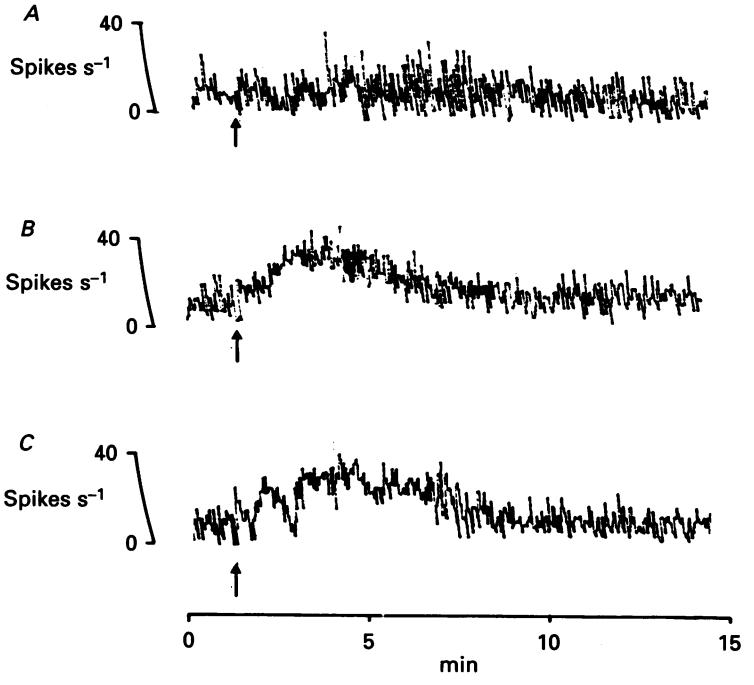

Fig. 5. The increase in the discharge rate of an APTN neurone in response to microinjection of the excitatory amino acid DL-homocysteic acid (DLH) into the contralateral gracile nucleus. In all traces the arrow indicates DLH application. *A* shows the minimal effects of an application of 2·5 μg DLH. *B* shows that a dose of 5 μg increases the discharge rate of the APTN neurone. A similar result is seen in *C* following administration of 7·5 μg. In this instance the increase in discharge rate is more prolonged. In all cases DLH was administered in a volume of 0·5 μl during a 3 min period.

In all the studies reported above the intensity of stimulation was constant at 4·0 V (2 times A fibre threshold). However, with three cells, a relationship could be determined between the intensity of contralateral gracile stimulation and the response latency. As shown in Fig. 3, there was little change in the total number of spikes evoked by stimulating just above threshold or at 2·5 times threshold but the latency to the first spike was reduced from 8 to 5 ms.

Location of responding neurones

Cells were encountered throughout the rostrocaudal and dorsoventral aspects of the APTN as defined by Paxinos & Watson (1982). Their locations are shown in Fig. 4. Nearly all of the cells which gave short-latency, brief, excitatory responses to stimulation of the contralateral gracile fasciculus were located in the medial portion

of the APTN which is named 'anterior pretectal nucleus dorsalis' by Paxinos & Watson (1982). A few of these 'driven' cells were found in the posterior parts of the APTN also. Only one cell from the anterior pole of the APTN was driven by dorsal column stimulation, although most of these rostral APTN cells were excited but with no clear, short latency. Most of the cells which failed to respond to dorsal column stimulation were located outside the borders of APTN or in its ventral or posterior parts.

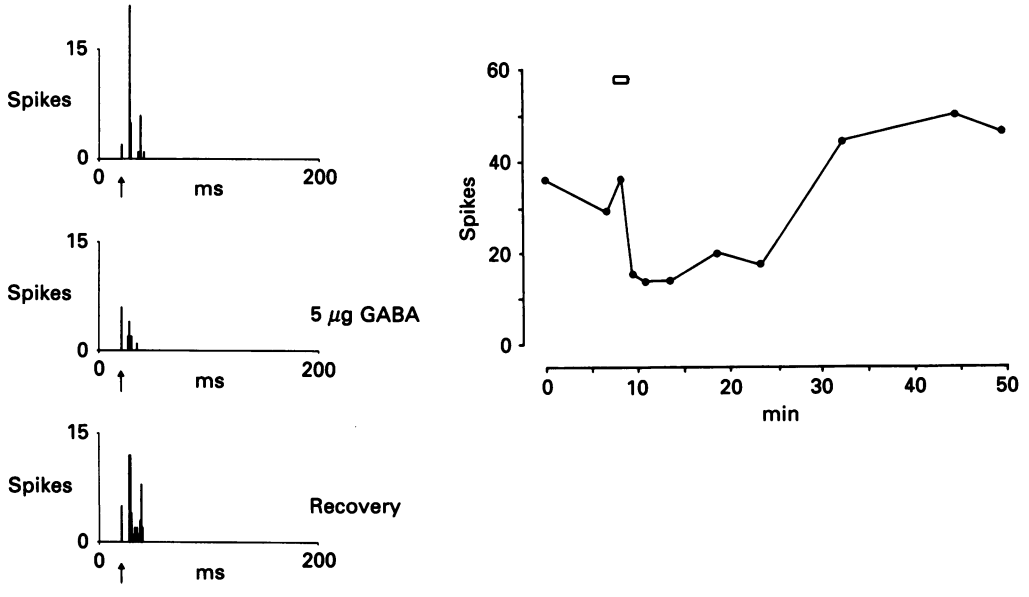

Fig. 6. The effects of 5 μg of the inhibitory amino acid GABA on the evoked response of an APTN neurone. The PSTHs (left) show the response of an APTN neurone to stimulation of the contralateral gracile fasciculus. The cell was normally quiescent and only fired in response to stimulation. Application of 5 μg GABA into the gracile nucleus reduced the response to stimulation by 50%. Recovery was seen after 30 min. This is illustrated in the graph, the bar at the top indicating the time of GABA administration.

It is clear from Figs 2 and 4 that the responses of APTN cells to dorsal column stimulation were dependent upon both the location of the stimulation site and upon the recording site. Cells in APTN dorsalis were driven by just-suprathreshold stimulation of the contralateral gracile fasciculus but the same cell could be weakly excited with a long latency to onset by stimulation ipsilaterally or of the cuneate fasciculus. Contralateral gracile stimulation, however, only weakly excited cells in the rostral pole of the APTN and was ineffective upon cells in APTN ventralis or on cells outside the borders of the nucleus.

Amino acids applied to nucleus gracilis

The effects of 2·5, 5·0 and 7·5 μg of the excitatory amino acid DL-homocysteic acid (DLH) microinjected into the dorsal surface of the contralateral nucleus gracilis are shown in Fig. 5. In five animals cells of the APTN dorsalis were recorded during these

microinjections and excitatory responses were recorded in all. Increasing doses of DLH caused increased amplitude of the response and reduced the latency to onset.

Microinjections of GABA into the gracile nucleus had very little effect on the firing rate of APTN cells but in all of the five animals studied profound inhibition of the

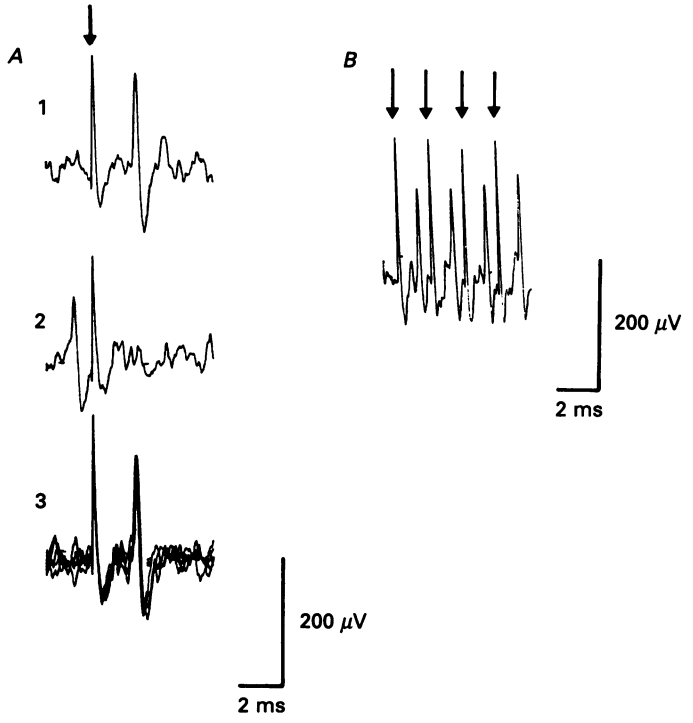

Fig. 7. Action potentials recorded from the gracile nucleus in response to stimulation of the APTN. A1 shows the antidromic spike occurring 2·2 ms after the stimulus. When a spontaneous action potential occurred less than 2·2 ms prior to stimulation, no antidromic spike was recorded (*A*2). *A*3 shows five superimposed traces with the antidromic spike being recorded at a very constant latency. *B* demonstrates that the same cell is able to follow high frequencies of APTN stimulation in excess of 300 Hz. The arrows above the trace indicate the stimulus artifacts. Each is followed by an action potential. Calibration bars: 2 ms, 200 μV.

response of these cells to dorsal column stimulation was observed. The effects on one cell are shown in Fig. 6. Three minutes after the microinjection of 5 μg GABA, the response of the cell decreased from an average of one variable latency spike per stimulus to about half this response probability. Recovery was complete about 1 h after the injection. The mean inhibition of the response to stimulation of dorsal columns was 56·3% and the mean recovery time was 14·6 min.

Antidromic activation of gracile nucleus cells by APTN stimulation

Studies were made to determine if the projection from gracile nucleus to APTN was direct (Fig. 7). A small concentric bipolar stimulating electrode was positioned in the APTN dorsalis and a recording electrode in the gracile nucleus was slowly

moved while stimulating the APTN repeatedly with 0·1 ms square-wave pulses. Extracellular action potentials were regularly encountered which followed the stimulation with a fixed latency of 2·52 ms ± 0·31 (mean ± S.E.M.). These cells also followed high-frequency stimulation of the APTN beyond 300 Hz. The appearance of a spontaneous action potential recorded from the cell body in nucleus gracilis a few milliseconds before the stimulus was applied to APTN caused collision of the orthodromic and antidromic action potentials so that no response to the stimulation was recorded. The distance between stimulating and recording electrodes was usually close to 10 mm and the mean conduction velocity of the thirteen cells was 3·89 m s^{-1}. All thirteen gracilis cells responded to low-threshold cutaneous stimulation.

DISCUSSION

These results have demonstrated a direct but crossed projection from nucleus gracilis which excites cells in the APTN dorsalis. These fibres conduct at a velocity of 3·9 m s^{-1}. Stimulation of the contralateral gracile fasciculus also excites cells in APTN dorsalis with a latency suggesting a monosynaptic pathway. The low-threshold dorsal column fibres which were activated by this stimulation conduct at a velocity of 21·7 m s^{-1}. The latency to onset of the APTN cell responses was 4–6 ms. The distances between the stimulating electrodes on the dorsal columns and the recording electrodes in the APTN were known and the conduction velocity of the fibres had been calculated with the result that the synaptic delay of 1·4 ms could be estimated. This was insufficient for more than two synapses. It is likely that amino acids act on cell bodies rather than fibres, and the effects of DLH and GABA microinjected into gracilis suggest that the relay is located here. Recordings made from cells in nucleus gracilis showed them to be antidromically driven by stimulation of APTN, confirming that the projection to APTN is direct.

These observations are relevant to the reported effects of APTN stimulation which inhibits the responses to intense cutaneous stimuli of both intact animals and spinal dorsal horn neurones (Rees & Roberts, 1987*a*). Very similar analgesic effects of dorsal column stimulation have been reported in man (Shealy *et al.* 1967; Nashold & Friedman, 1972) and other animals (Lindblom *et al.* 1977). Dorsal column stimulation is known to operate a spinal segmental gating of responses to intense noxious stimuli as well as activating an undefined supraspinal mechanism (Melzack & Wall, 1965; Foreman, Beall, Applebaum, Coulter & Willis, 1976). In the present experiments, only the ascending effects of dorsal column stimulation explain the driving of APTN cells because the dorsal columns were cut below the stimulation site. It is a reasonable postulate, which remains to be tested, that the driving of APTN cells by dorsal column stimulation explains some of the analgesic effects of this stimulation. It should be noted, however, that the strongest and most long-lasting analgesia from APTN stimulation is seen from sites in the rostral pole of the APTN (Roberts & Rees, 1986). Stimulation at more posterior sites in APTN dorsalis are not as effective. In the present study, cells in the rostral pole of the APTN were excited by dorsal column stimulation but with a much longer latency to onset. Neuroanatomical studies have demonstrated that cells in the rostral pole of the APTN receive inputs from the ipsilateral caudal APTN dorsalis, ipsilateral caudal APTN ventralis and also the

contralateral APTN (Foster *et al.* 1989). It is possible that cells in any of these regions mediate the excitation of rostral pole neurones but it is also possible that this excitation is mediated by a separate pathway.

Some of the characteristics of the dorsal column fibres responsible for driving APTN cells are revealed by the stimulation parameters. Neither discrete nor widespread low-threshold cutaneous stimuli reliably excited APTN cells. However, clear responses were easily obtained to dorsal column stimuli which were just above threshold. This suggests that large diameter fibres were activated to drive APTN cells and such fibres are dorsal root collaterals or postsynaptic dorsal column fibres (Uddenburg, 1968; Rethelyi & Szentagothai, 1973). Both of these convey information from low-threshold cutaneous receptors. Probably the most relevant difference between natural cutaneous stimulation and electrical activation of dorsal columns at A fibre threshold is the degree of synchronization of the afferent barrage. Cells in APTN responded when many dorsal column fibres discharged simultaneously but did not apparently do so when their activity in response to cutaneous stimulation was temporally dispersed. All of the cells recorded in the gracile nucleus responded to cutaneous stimulation and these same cells were driven antidromically by stimulation of the APTN. It is likely therefore that APTN cells receive considerable convergent input from nucleus gracilis. This would explain the effect of increased intensity of dorsal column stimulation on the responses of APTN neurones. Cells discharged in response to just suprathreshold stimulation and increasing the intensity of stimulation shortened the latency of the response. It is unlikely that this is due to the recruitment of finer dorsal column fibres as these would have a lower conduction velocity and a longer conduction time. It is more likely that the increased spread of stimulation current caused more low-threshold fibres to be activated and the convergence of these inputs onto the recorded APTN neurone enhanced its discharge. Of course, the implication is that APTN cells are not normally directly excited by natural low-threshold stimuli but that these would modulate the activity of APTN cells. However, the data on which this interpretation is based may well have been influenced by the anaesthetic.

The paucity of effects from stimulation of the cuneate fasciculus seems to imply that the APTN received little or no input from the cuneate nucleus. This may not be the case, however, as some degree of somatotopic representation may exist within the APTN and cells were only studied in the area which received input from nucleus gracilis. This possibility requires further study.

In the cat, postsynaptic dorsal column fibres are multireceptive and several authors have suggested that they may transmit information about high-threshold 'tissue damaging' stimuli (Angaut-Petit, 1975; Lu, Bennett, Nishikawa, Hoffert & Dubner, 1983; Noble & Riddell, 1988). It is possible that these postsynaptic fibres project to APTN but, being multireceptive, they should convey low- as well as high-threshold cutaneous information and their involvement should not explain the lack of effect of cutaneous stimuli. Furthermore, in the rat, Giesler & Cliffer (1985) failed to observe an unmyelinated primary afferent input to neurones of the postsynaptic dorsal column pathway and they suggested that it was not an important nociceptive pathway. However, the cells were multireceptive and presumably received an Aγ innervation.

Berkley, Budell, Blomqvist & Bull (1986) noted the termination of visceral primary afferents in the gracile nucleus and such fibres could mediate the driving of APTN cells by dorsal column stimulation. This could not explain completely the lack of cutaneous driving of these cells because the gracile cells which project to APTN are themselves driven by natural cutaneous stimuli. It is likely therefore that the fibres activated by dorsal column stimulation which drive APTN cells, were fibres which conduct responses to low-threshold cutaneous stimuli. They may, however, be multireceptive fibres which are driven by other inputs also.

In summary, it has been clear for some years that low-threshold cutaneous stimuli and dorsal column stimulation are analgesic due, in part, to an ascending influence which relays somewhere in the brain. The present study has demonstrated that low-threshold dorsal column fibres project to and excite cells in the APTN. The activation of cells in this nucleus has been shown elsewhere to reduce responsiveness to intense cutaneous stimuli.

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