J. Physiol. (1980), **305**, *pp.* 433–449
With 9 text-figures
Printed in Great Britain

THE PROJECTION OF JOINT RECEPTORS TO THE CUNEATE NUCLEUS IN THE CAT

By D. J. TRACEY

From the Department of Physiology, Monash University, Clayton, Victoria, Australia 3168

(*Received 29 November 1979*)

SUMMARY

1. Records were made from axons in the dorsal columns and cells in the cuneate nucleus which responded to stimulation of the wrist joint nerve.

2. A sample of twenty-five axons activated by the wrist joint nerve was recorded in the dorsal columns at the level of the third cervical segment. All twenty-five were post-synaptic fibres as judged by response latency, burst length, and maximum frequency of following. Nineteen of the twenty-five had convergent inputs from the wrist joint nerve and the cutaneous superficial radial nerve.

3. While no primary wrist joint afferent fibres were recorded in the dorsal columns, their presence was demonstrated by recording single units in the wrist joint nerve which were antidromically activated by microstimulation in the cuneate fasciculus.

4. The majority of cells recorded in the cuneate nucleus were activated not only by stimulation of joint afferents, but also by skin and muscle afferent fibres.

5. About half of the cells in the cuneate nucleus responded to wrist movement in animals with partially denervated forelimbs, where the intact wrist joint nerve was the only afferent channel providing information about natural, imposed wrist movements. The majority of the cells had phasic responses, which were weak and irregular in comparison with the responses of primary wrist joint afferents to the same movements.

6. Only two of thirty-four cells tested could be shown to project directly to the ventrobasal thalamus, using collision of antidromic and peripherally activated impulses as the criterion.

INTRODUCTION

The fact that afferent fibres from the joints project to the cerebral cortex in the cat has been known since the work of Gardner & Noer (1952), who demonstrated a projection of hind-limb afferents to the contralateral sensory cortex SI, and to SII on both sides. This work has been confirmed and extended, and it is now known that low threshold joint afferents of both knee and elbow project to cytoarchitectonic areas 3, 1 and 2 of the posterior sigmoid gyrus, while elbow joint afferents also appear to project to area 4γ (Clark, Landgren & Silfvenius, 1973). But there is little data available on the pathways by which information from joint afferents reaches the cerebral cortex. Studies using lesions of the dorsal columns and dorsolateral fasciculus suggest that both fibre tracts are involved for the hindlimbs, while the dorsal

0022-3751/80/1370-0135 $07.50

columns are mainly implicated for the forelimbs (Clark *et al.* 1973). It is known that cells in the gracile nucleus (Williams, BeMent, Yin & McCall, 1973) and somatosensory thalamus (Yin & Williams, 1976) respond to movements of the knee joint after surrounding skin and muscle have been denervated; these responses are almost entirely rapidly adapting. This is consistent with the finding that the few knee joint afferents which reach the dorsal column nuclei are rapidly adapting (Burgess & Clark, 1969). It appears that slowly adapting knee joint afferents make synaptic contact with cells of Clarke's column (Lindström & Takata, 1972) and project via the dorsal spinocerebellar tract and its collaterals to nucleus *z*, just rostral to the gracile nucleus – although cells in nucleus *z* which receive joint input do not appear to relay to the ventrobasal thalamus (Johansson & Silfvenius, 1977). How slowly adapting joint afferents from the hind limb project to the thalamus is not known.

Still less is known about the central projections of forelimb joint afferents. As already mentioned, lesion experiments implicate the dorsal column-medial lemniscus pathway, and single units have been reported in the cuneate nucleus which respond to stimulation of the elbow joint nerve (Millar, 1979*a*) and project to the ventrobasal thalamus (Millar, 1979*b*). However, more information is still needed.

In the experiments to be described, an attempt was made to define the properties of cells in the cuneate nucleus activated by joint afferents. In particular, how do these cells respond to wrist movement in the absence of muscle or skin innervation? Are these cells also activated by muscle and skin afferents? Do they project to the ventrobasal thalamus? Are they monosynaptically activated by primary afferents? This study was carried out in order to try to answer these questions.

METHODS

Successful experiments were carried out in twenty-four cats, anaesthetized with Na pentobarbitone or halothane. Blood pressure was monitored via a carotid cannula. If systolic blood pressure fell below 80 mm Hg, the experiment was terminated. End-tidal CO_2 was also monitored, and kept below 5% by increasing the concentration of O_2 in the inspired air where necessary.

Dissection. The median, ulnar, medial cutaneous and musculo-cutaneous nerves were all cut in the upper forelimb. This deafferented carpal and digital flexor muscles, as well as the skin on the ulnar side of the forearm and the radial side of the ventral surface of the forearm. The superficial radial nerve was cut distally, taking care to include all twigs from branches on either side of the cephalic vein. All carpal and digital extensor muscles had their tendons of insertion cut, so that wrist movements could not excite muscle afferents running in the radial nerve, which was left intact. The wrist joint branch of the dorsal interosseous nerve was exposed and freed from surrounding muscle for a length of 10–20 mm.

The cat was fixed in a frame with its head in a stereotaxic apparatus. The hips were held higher than the head in order to increase central venous pressure and reduce the possibility of air or paraffin embolism. The forelimb was arranged horizontally so that the wrist was free to move over its whole range, and the radius was clamped near the junction of the supinator and abductor pollicis longus muscles. Movements of the paw about the wrist joint were carried out by hand. Skin flaps were tied up to form a pool over the forelimb, and the pool was filled with paraffin at 37 °C.

Single units. Experiments were carried out on the cuneate nucleus in fourteen cats, twelve of which were anaesthetized with Na pentobarbitone. The remaining two cats were anaesthetized with halothane delivered in a mixture of nitrous oxide and oxygen. The responses of 'joint' cells in the cuneate nucleus appeared to be the same regardless of the anaesthetic used, and the data have therefore been treated together.

The head was flexed to allow better access and improve the stability of the medulla. The cuneate tubercle was exposed by removing some of the occipital bone and the arch of the atlas. Skin flaps were tied up to form a paraffin pool. The dura was reflected, and the posterior part of the cerebellar vermis was carefully retracted to expose the obex, which was used as a reference point for subsequent recording. Glass micropipettes filled with 4 M-NaCl (impedances 2–7 MΩ) were inserted through holes made in the pia with watchmakers' forceps.

Preliminary experiments were carried out to map the distribution in the medulla of field potentials evoked by stimulation of the wrist joint nerve. Such field potentials were found through most of the mediolateral and dorso-ventral extent of the cuneate nucleus, and in the reticular area ventral to the cuneate, from 1 mm caudal to the obex to 3 mm rostral to the obex. Single unit recordings were concentrated in the middle part of the cuneate, near the obex, where the greatest proportion of cells relaying to the thalamus is situated (Hand & Van Winkle, 1977; see also Gordon & Seed, 1961, for the gracile nucleus).

The micro-electrode was slowly advanced while stimulating the wrist joint nerve supramaximally at a rate of 1 Hz, until a single driven unit could be recorded extracellularly and clearly isolated from background activity. For each electrode track, the position with respect to the obex was accurately measured, and for each unit the depth below the surface of the medulla was noted. An attempt was made to examine the following properties of each unit: (1) latency and threshold of the response to stimulation of the wrist joint nerve; (2) whether or not the unit also responded to stimulation of superficial radial at supramaximal strength; (3) the response of the unit to movements of the wrist; (4) the response to pulling on the tendons of the following muscles: extensor communis digitorum, extensor lateralis digitorum and extensor carpi ulnaris. Pulling on tendons was found in preliminary experiments to be more effective and reliable in eliciting a response than electrical stimulation of small dissected muscle branches; (5) whether the unit could be shown to project to the nucleus ventralis posterolateralis (VPL) of the thalamus.

Recordings in the dorsal columns were made in five cats anaesthetized with Na pentobarbitone. A laminectomy was carried out at C3, and axons were recorded using tungsten micro-electrode insulated with glass (impedances 5–10 MΩ at 500 Hz). In order to achieve stable recordings, the animals were paralysed and artificially respired, and a pneumothorax was created. The distance of each electrode track from the mid line, and the depth of each unit below the surface of the cord was noted. Each axon was tested as described for cells in the cuneate nucleus.

Antidromic identification. The projections of cells recorded in the cuneate nucleus were examined using an antidromic stimulating electrode with its tip in VPL. Before the head was flexed for recording (see above), a Pt electrode (0·5 mm in diameter, insulated to the tip) was advanced stereotaxically into VPL at co-ordinates A8·0, L6·0 (Snider & Niemer, 1961; see also Andersen, Eccles, Schmidt & Yokota, 1964). Recordings were made from the electrode while it was advanced, and short latency, positive potentials could be recorded in response to stimulating the superficial radial and wrist joint nerves (Fig. 1*B*). When these potentials were maximal, usually close to the horizontal zero plane, the electrode was cemented to the skull and the stereotaxic microdrive removed so that the head could be flexed for recording. The electrode was then used as a cathode to stimulate the terminations of the medial lemniscus in VPL. In four experiments the position of the electrode tip in VPL was confirmed histologically.

Histology. At the end of each experiment, a glass micro-electrode was left in place in the cuneate nucleus or spinal cord as a marker, at a measured distance from the mid line. The medulla was then fixed *in situ* by the injection of 500 ml. formol saline via the carotid cannula. After 12 hr the medulla or cord was cut transversely rostral and caudal to the electrode. The cuts were made vertically using a scalpel blade held in the same stereotaxic microdrive which had held the micro-electrode. After removal, the tissue block was fixed for a week in formol saline, sectioned on a freezing microtome, and stained with cresyl violet or toluidine blue. The electrode tracks were reconstructed after the degree of shrinkage had been estimated using the distance of the marker electrode from the mid line.

RESULTS

When the wrist joint nerve was stimulated with single shocks (0·1–0·5 V, 0·1 msec) surface potentials could be recorded from the cuneate tubercle with a silver ball electrode (Fig. 1*A*). This suggests that axons in the wrist joint nerve project to the cuneate nucleus. When the surface of the cuneate nucleus was stimulated with single cathodal shocks (0·1–1·0 mA, 0·1 msec) an antidromic volley could be recorded

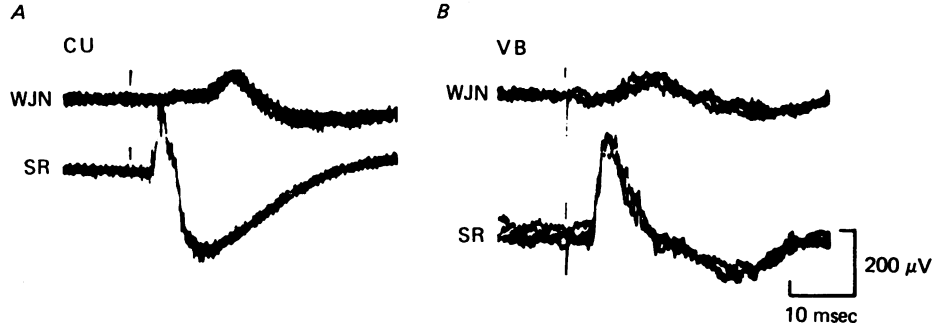

Fig. 1. Potentials evoked by stimulating the wrist joint nerve (WJN) (upper traces) and the superficial radial nerve (lower traces) in the same animal. *A*, shows responses recorded with silver ball electrodes from the surface of the cuneate tubercle. Stimulus strength 1·5 *T* for both wrist joint nerve and superficial radial (SR). *B*, shows responses recorded with a Pt electrode, insulated to the tip, in the ventrobasal complex of the thalamus. Stimulus strength *ca.* 1·1 *T* for WJN, 1·7 *T* for SR. Note that negativity is upwards in *A*, positivity upwards in *B*. Three sweeps are superimposed in each record. Two peaks are distinguishable in the cuneate surface potential evoked by the wrist joint nerve. The small early potential has a latency of 6·0 msec and is probably due to monosynaptically activated cells. The large late potential has a latency of 12 msec, and is probably due to polysynaptically activated cells. The thalamic response to stimulating the wrist joint nerve has a latency (7·5 msec) which suggests that cuneothalamic relay cells are monosynaptically activated by afferents in the wrist joint nerve.

peripherally in the wrist joint nerve (Fig. 2*B*). This volley disappeared when the dorsal columns were sectioned at C4. The lesion was confined to the dorsal columns, as confirmed histologically. This suggests that primary afferent fibres in the wrist joint nerve project to the cuneate nucleus via the dorsal columns.

However, the latency to onset of the major peak in the orthodomically evoked surface wave (12·0 msec, Fig. 1*A*) was considerably longer than the latency to onset of the antidromic volley (4·3 msec, Fig. 2*B*). This discrepancy suggests that the major peak in the cuneate surface potential is not due to the activity of cells monosynaptically excited by primary afferents. Such a discrepancy did not arise for cutaneous axons in the superficial radial nerve, where the latency of the orthodromic volley (3·0 msec, Fig. 1*A*) corresponds with that for the antidromic volley (3·2 msec, not shown).

Axons in the dorsal columns. The long latency of the cuneate surface wave evoked by joint afferents might be explained if cells in the cuneate nucleus were excited by synaptically activated fibres running in the dorsal columns (Uddenberg, 1968*b*). Recordings were therefore made from single axons in the dorsal columns at the level of the third cervical segment.

Axons were sought which responded to single shocks delivered to either the wrist joint nerve or superficial radial. Many axons could be recorded with properties expected for primary afferents from the superficial radial nerve: they responded to a single shock with a single, short-latency spike which followed repetitive stimulation at high frequencies (up to 500 Hz). However, in spite of persistent attempts, no

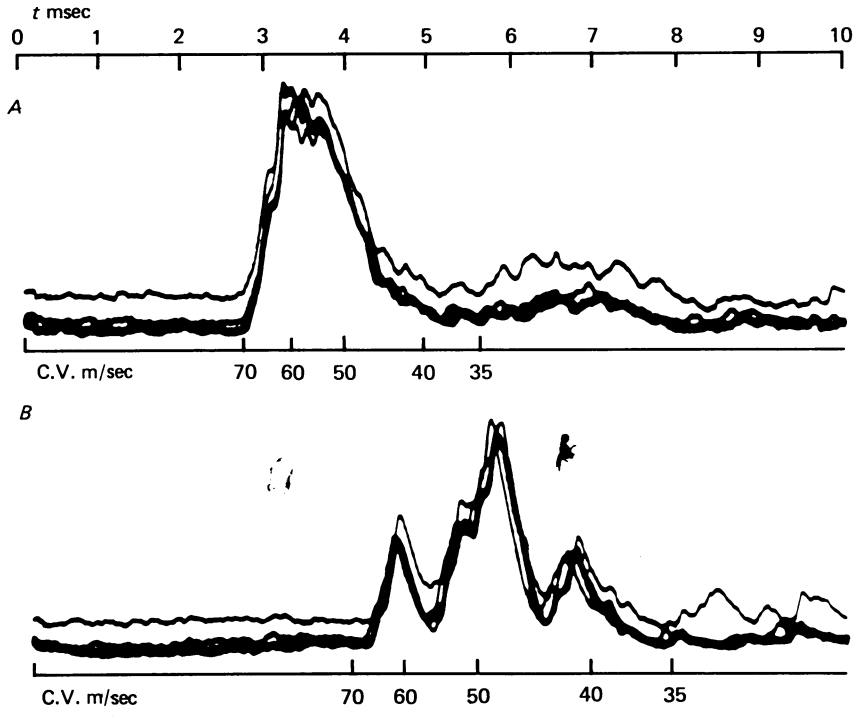

Fig. 2. Volleys recorded peripherally in the wrist joint nerve, elicited by stimulating (*A*) the dorsal root entry zone (C7 and C8, 0·1 msec, 1·2 mA) (*B*) the cuneate nucleus (obex level, 0·1 msec, 1·4 mA). The volley was made monophasic by crushing the nerve between the two recording electrodes. In both cases paired silver ball electrodes were used to deliver constant current stimuli at 10 times threshold for the antidromic volley. The time from the stimulus has been converted to a conduction velocity scale for each volley using the measured conduction distances of 195 mm (dorsal roots) and 273 mm (cuneate nucleus). Ten traces were superimposed at a stimulus repetition rate of 100 Hz.

primary afferents from the wrist joint nerve could be found, using insulated tungsten electrodes and glass micropipettes. Twenty-five axons were recorded which responded to volleys in the wrist joint nerve. But all twenty-five were judged to be synaptically activated fibres, since they had the following properties. (*a*) They responded to single shocks with a burst of spikes whose length was graded with stimulus strength. (*b*) They would not follow frequencies of stimulation higher than 10–20 Hz. (*c*) Many (19/25) were also activated by the cutaneous axons of superficial radial (Fig. 3). These fibres were evidently activated by low-threshold wrist joint mechanoreceptors – thresholds were less than twice the threshold for the nerve volley in all cases. Latencies of the first spike in a burst were 7–15 msec for the wrist joint nerve, and 4–5 msec for superficial radial. The majority of such fibres were found deep in the

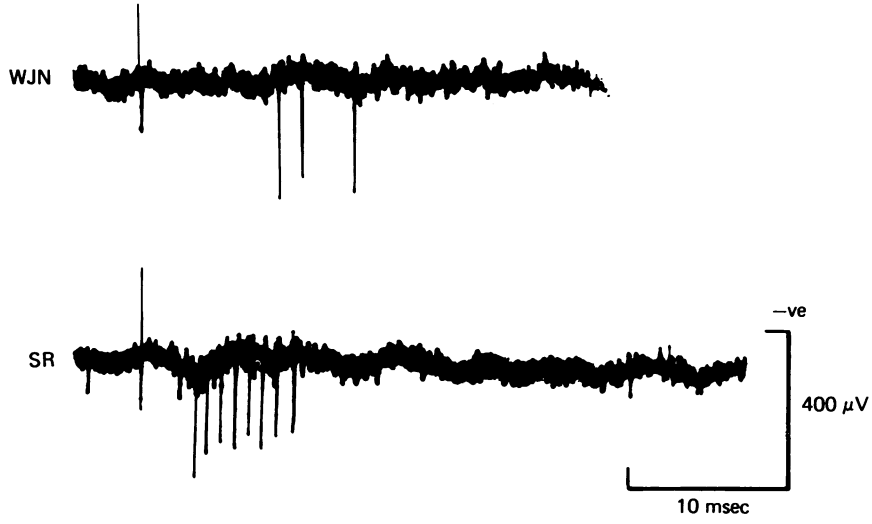

Fig. 3. Post-synaptic fibre recorded in the dorsal columns at C3. Upper trace: response to stimulating the wrist joint nerve. Lower trace: response to stimulating the superficial radial nerve.

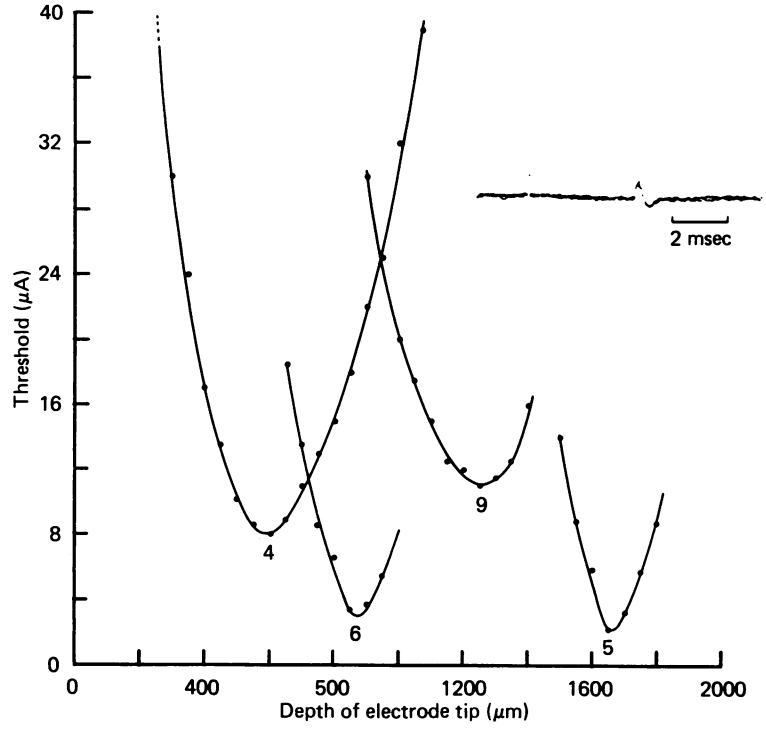

Fig. 4. Threshold (μA) is plotted against the depth of a stimulating electrode tip (μm from dorsal column surface) for four all-or-none units which could be clearly distinguished in records from the whole wrist joint nerve. The inset shows unit number 4: five sweeps were superimposed at 100 Hz. Conduction velocities were: 4–49·6 msec^{-1}, 5–49·6 msec^{-1}, 6–43·9 msec^{-1}, 9–58 msec^{-1}.

dorsal columns, as described by Uddenberg (1968*a*). Other postsynaptic fibres were also found which were activated by superficial radial but not by the wrist joint nerve.

While these findings are consistent with the idea that cells in the cuneate nucleus may be activated by second-order fibres in the dorsal columns, the apparent absence of axons from the wrist joint nerve in the dorsal columns is inconsistent with the observation that a significant volley in the wrist joint nerve can be evoked antidromically from the surface of the cuneate nucleus. An attempt was therefore made to demonstrate the presence of single primary afferent fibres from wrist joint receptors in another way. The wrist joint nerve is small in diameter, with only 200–300 myelinated axons (Tracey, 1979). Single fibre activity can therefore be detected even in recordings from the whole nerve. If a tungsten stimulating electrode (impedance 5–10 MΩ) was advanced into the dorsal columns at C3, cathodal pulses elicited an antidromic volley in the wrist joint nerve (cf. Millar, 1979*a*). The current strength from a constant current stimulator could be adjusted so that the volley consisted only of a single all-or-none unit (Fig. 4, insert). As the stimulating electrode was advanced towards single axons identified in this way, the threshold current decreased to a minimum, and then increased as the electrode tip moved further away. Threshold currents are plotted against depth of the electrode tip for four such axons in Fig. 4. The curves are roughly parabolic in shape, and in several cases the minimum threshold was close to 2 μA. Roberts & Smith (1973) in a study on fibres of the dorsal spinocerebellar tract found that threshold stimuli of less than 2 μA indicated that the electrode tip was within 200 μm of a node of Ranvier. Thresholds at sites midway between two nodes were often well over 20 μA. It is concluded that the stimulating electrodes were activating single axons, belonging to the wrist joint nerve and running in the dorsal columns. In several cases the electrodes were also used to record activity at the point of least threshold, and presumably closest approach to the fibre. Even then it was not possible to detect an orthodromically evoked action potential when the wrist joint nerve was stimulated electrically.

Thus there is good evidence that wrist joint receptors send axons to the cuneate nucleus, and that the axons also activate second-order fibres which run in the dorsal columns. However, axons of the wrist joint nerve could not be recorded in the dorsal columns, although axons of the superficial radial nerve and post-synaptic fibres activated by joint afferents were commonly found. Two factors may have contributed to this disparity. If axons of the wrist joint nerve are small in diameter relative to other axons in the dorsal columns, this would introduce a sampling bias (e.g. Towe & Harding, 1970; Whitehorn, Howe, Lessler & Burgess, 1974). This explanation seems unlikely since the conduction velocities of wrist joint axons over the path including the dorsal columns and peripheral nerve ranged between 35 and 65 msec^{-1} (Fig. 2*B*; see also individual values in Fig. 4). The diameter of these axons probably does not change appreciably from peripheral nerve to dorsal columns, since the same range of values was found for conduction in the peripheral nerve alone (Fig. 2*A*) and for single axons of the wrist joint nerve recorded from dorsal root filaments (Tracey, 1978, 1979). These values are somewhat smaller than those found for axons of the superficial radial nerve in the same experiments (45–80 msec^{-1}) and for non-primary afferents in the cuneate fasciculus (40–70 msec^{-1}; Uddenberg, 1968*b*) but it seems unlikely that the corresponding differences in fibre diameter contributed a significant sampling bias against recording axons of the wrist joint nerve in the dorsal columns.

A second factor which may have made it difficult to record axons of the wrist joint nerve in the dorsal columns is the small number of these axons in relation to the number of other myelinated fibres. There are approximately 200 myelinated fibres in the wrist joint nerve, and 3500 in the superficial radial nerve (Tracey, 1979; Matsumoto & Mori, 1975). If we assume that the same proportion of fibres projects as far as the recording site at C3 for both nerves, the ratio of superficial radial axons to wrist joint axons will be 18:1.

Single units in the cuneate nucleus. Relatively few single units could be found in the region of the cuneate nucleus which responded to afferent volleys in the wrist joint nerve. A typical yield was five units per experiment. The spike amplitude of such units was generally small (100–200 μV), in some cases too small to determine all the

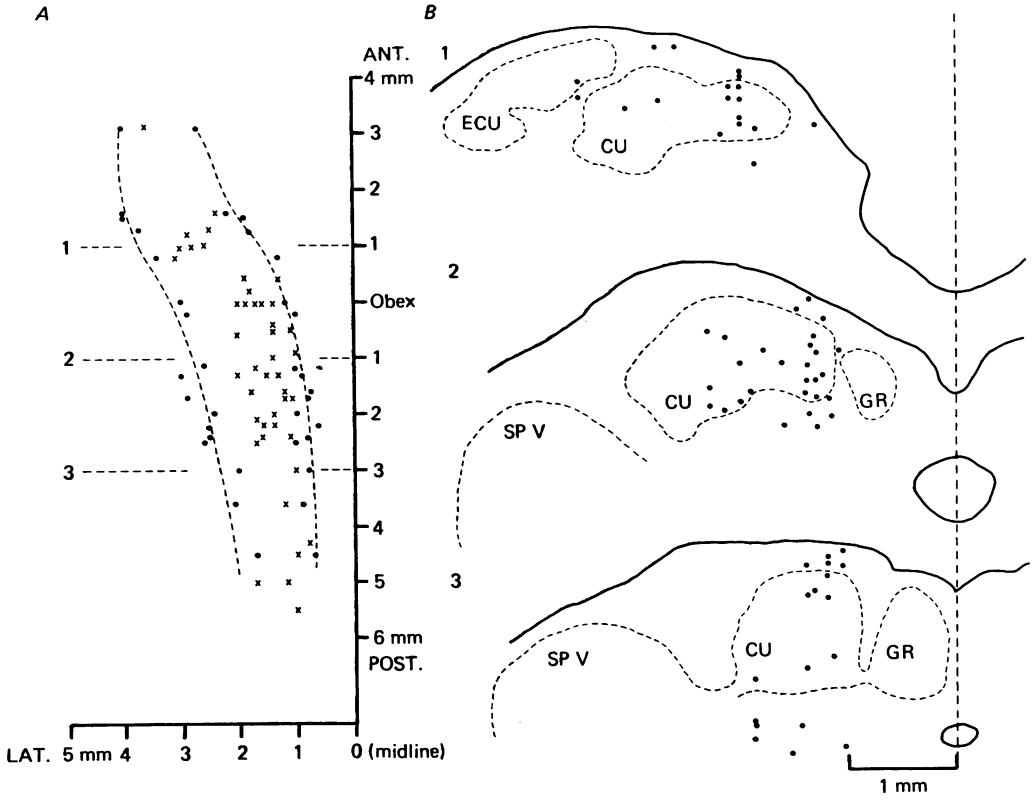

Fig. 5. Locations of cells and fibres recorded in the region of the cuneate nucleus. *A* shows the positions of all electrode tracks which encountered cells or axons activated by stimulating the wrist joint nerve (WJN). The positions (crosses) with respect to the obex are shown as noted during the experiment. Many electrode tracks encountered more than one unit. The boundaries of the cuneate nucleus (seen from above) are reconstructed from transverse sections containing the electrode tracks, and are shown by a pair of dots for each track. The dashed lines drawn through the dots thus represent the medial and lateral boundaries of the cuneate nucleus. *B* shows the positions of units activated by stimulating the wrist joint nerve. It is impractical to show the outlines of the cuneate for each unit, and so positions are shown on three representative sections (1, 2, 3) made at 1·0 mm anterior to the obex (A 1·0), 1·0 mm posterior to the obex (P 1·0) and 3·0 mm posterior to the obex (P 3·0). These levels are shown in *A*. The location of each unit on these composite diagrams bears the same relation to nuclear outlines as determined in the section carrying the electrode track. Level 1 shows those units recorded between A 0·1–A 2·0; level 2: P 1·9–A0·0 (obex); level 3: P 4·5–P 2·0. CU, cuneate nucleus. GR, gracile nucleus. ECU, external cuneate nucleus. SPV, spinal trigeminal nucleus.

characteristics of the unit. However, sixty-eight single units were studied whose location could be reconstructed histologically. Of these, thirty-nine were located within the confines of the cuneate nucleus, thirteen were found ventral to the cuneate, and fourteen were located in the remnants of the dorsal columns overlying the

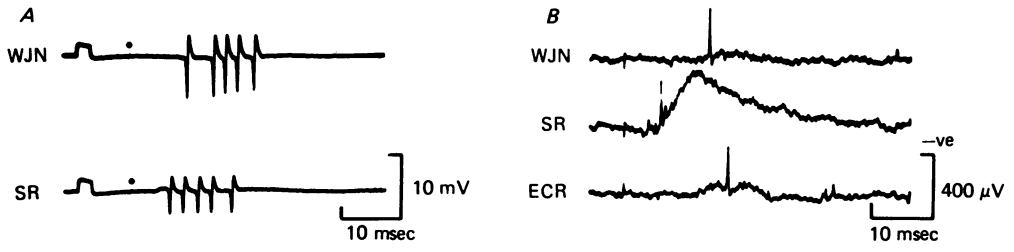

Fig. 6. Convergence of joint, cutaneous and muscle afferents onto two cells in the cuneate nucleus. *A*, this cell, activated by stimulating the wrist joint nerve (WJN) and the superficial radial nerve (SR) has an unusually large biphasic spike. The response pattern of a burst of spikes is typical. Stimuli marked by dots. The responses of this cell to muscle pull and wrist joint flexion are shown in Fig. 9. *B*, the response of a cell to stimulation of the wrist joint nerve, superficial radial nerve and the muscle nerve to extensor carpi radialis.

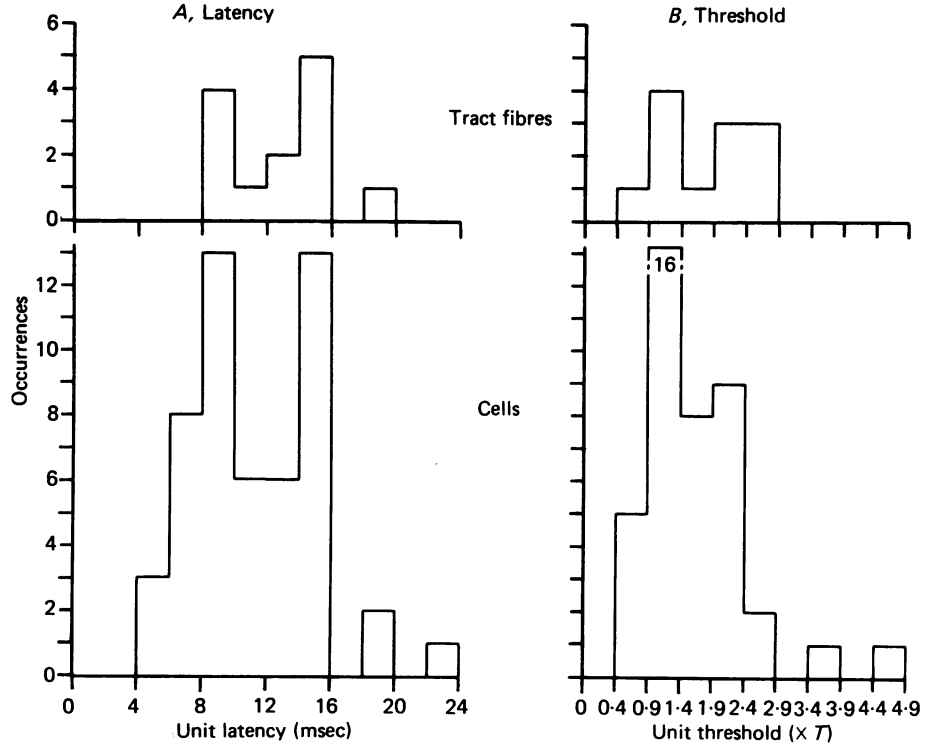

Fig. 7. Latencies and thresholds of cells and fibres activated by stimulating the wrist joint nerve. *A*, shortest latencies of the first spike in the evoked burst. *B*, thresholds of response, in relation to the threshold (*T*) for the cuneate surface potential elicited by stimulating the wrist joint nerve.

cuneate nucleus (Fig. 5). Units located within or below the cuneate nucleus had negative or biphasic spikes (Fig. 6) and were presumed to be cells rather than axons (Amassian & de Vito, 1957). Units found in the cuneate tract dorsal to the nucleus had positive going spikes and were presumed to be axons. All units, regardless of location, responded with a burst of one or more impulses to a single shock delivered to the wrist joint nerve. Occasionally the number of impulses in a burst could be

graded with stimulus strength; this gradation was more clearly marked in tract fibres than in cells. In other respects, the properties of cells and fibres were not different. Latencies were long, typically 8–15 msec (Fig. 7*A*). Threshold stimuli were mostly below twice threshold for the cuneate surface potential (Fig. 7*B*).

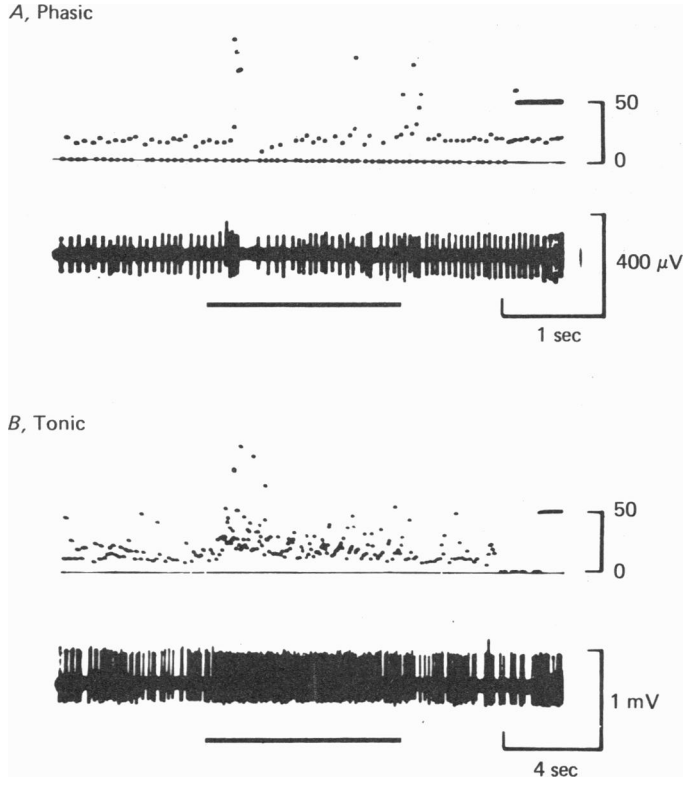

Fig. 8. Responses of two cells, activated by stimulation of the wrist joint nerve, to flexion of the wrist. Both cells were located in the cuneate nucleus. *A*, phasic response; *B*, tonic response. In both records, the upper trace shows the instantaneous frequency of firing (Hz), while the lower trace shows the unit response. Bar indicates flexion of the wrist from 90° (partial flexion) to 45° (full flexion). Note the different time scales.

Responses to wrist movement. In cats where the only source of afferent information about wrist movement was the wrist joint nerve, forty-one cells were tested for their responses to changing the angle of the wrist. Of these, nineteen showed increases in firing rate, although the responses were quite irregular in comparison with the rather regular firing rates found for primary afferent fibres from the wrist joint nerve (Tracey, 1979). The majority of responses were phasic (Fig. 8*A*) and lasted only while the wrist was being flexed or extended, not while it was held in any static position. Only three tonic cells whose response to extreme flexion lasted 10 sec or longer (Fig. 8*B*) were found. These cells also responded phasically to wrist extension. Three of the eleven fibres tested responded to wrist movement.

Convergence. As many cells as possible were tested to see whether they were activated, not only by wrist joint afferents, but also by skin and muscle afferents.

In preliminary experiments where the superficial radial nerve was left intact, responses were also found to hair movement or to touching the skin in the area of the wrist. This is consistent with the findings of Millar (1979*a*) who studied cells in the cuneate nucleus which responded to volleys in the elbow joint nerve. Many of these cells also had cutaneous or hair receptive fields.

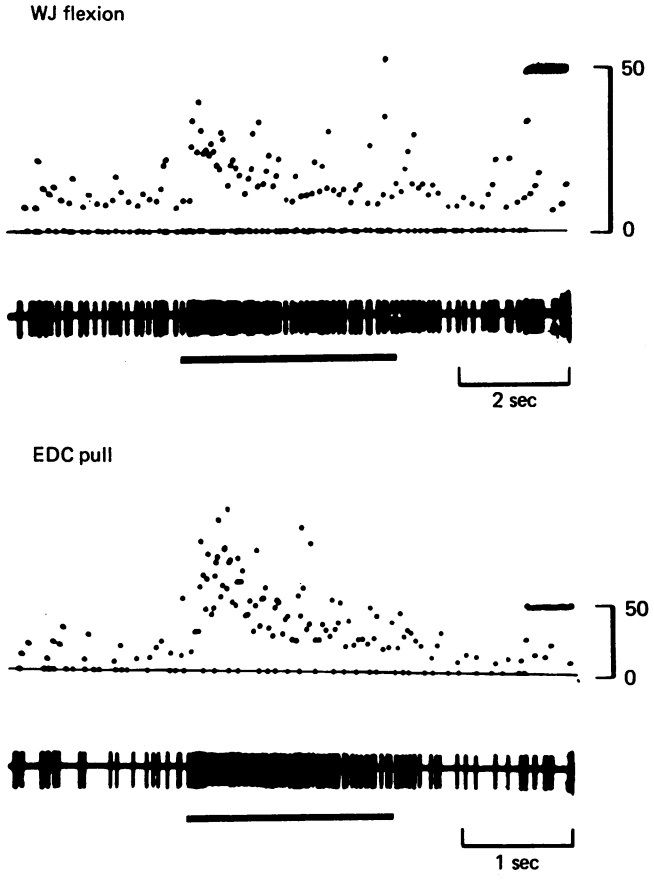

Fig. 9. Response of a cell, located in the cuneate nucleus to (*A*) flexion of the wrist (*B*) pulling on the tendon of extensor digitorum communis. In both records, the upper trace shows the instantaneous frequency of the unit (Hz), while the lower trace shows the unit response. Bar indicates flexion of the wrist in the upper record, pull on muscle tendon in the lower record. The responses of this cell to stimulating the wrist joint nerve and superficial radial are shown in Fig. 6*A*.

Fifty-three cells responding to the wrist joint nerve were tested to see whether they were excited by afferent volleys in the superficial radial. Thirty-seven of these cells responded to cutaneous volleys with a burst of 4–8 spikes (Fig. 6*A*). The latencies of the first spike in such a burst (6–8 msec) were always shorter than the latencies in response to volleys in the wrist joint nerve (8–15 msec). Seven of the eleven fibres tested also showed convergent input from cutaneous afferents.

Many of the cells excited by volleys in the wrist joint nerve were also excited by

muscle afferent fibres. Thus Fig. 6*B* shows a cuneate cell which responded to stimulation of the wrist joint nerve, superficial radial and the muscle nerve to extensor carpi radialis. In this record the electrode impedance was relatively low and the response of the neurone is superimposed on a field potential in each case. In most cases input from muscle receptors was tested not by stimulating the muscle nerve but by gently tugging on the distal tendons of carpal and digital extensor muscles (Fig. 9*B*). This ensured that the response was due to mechanoreceptors, although one could not decide whether the effect was due to muscle spindles or tendon organs. Twenty-five of forty-four cells tested responded to stretching one or more of the extensor muscles. These responses were mostly phasic and excitatory; the example in Fig. 9*B* shows a cell which responded to the wrist joint nerve, and had a tonic response to stretching extensor digitorum communis.

In thirty-three cells with wrist joint input, convergence from both cutaneous and muscle afferents could be tested. All thirty-three cells had convergent input from skin or muscle, while fifteen were activated by all three inputs.

Projections to the thalamus. An unexpected finding of this study was the lack of demonstrable projections from joint neurones in the cuneate nucleus to the ventrobasal thalamus. When the presumed endings of medial lemniscal fibres in VPL were stimulated with pulses 0·1 msec in duration and up to 10 V in amplitude, short latency potentials (about 1 msec) could be seen on the surface of the cuneate. In addition, units were often found which followed antidromic stimuli with latencies of 0·8–1·2 msec at stimulus frequencies up to 200 Hz. Other neurones were found which responded with longer latencies and lower following frequencies. Such cells were considered to be activated transsynaptically (Gordon & Seed, 1961). But of the thirty-four joint cells which could be adequately tested, using collision of antidromically and peripherally evoked action potentials as the criterion (Darian-Smith, Phillips & Ryan, 1963), only two could be demonstrated to project to VPL. (Both of these cells, from different experiments, responded phasically to movements of the wrist but not to muscle pull. Both were located ventral to the cuneate nucleus). None of the six fibres tested could be antidromically activated. To check the adequacy of the technique, a sample of cells activated by cutaneous axons was also examined (i.e., neurones driven by stimulation of the superficial radial but not by the wrist joint nerve). Of nineteen cells tested, nine could be shown to project to VPL using the same criterion. It is concluded that the axons of cuneothalamic relay cells were fired antidromically by the stimulus method used, but that very few neurones in the cuneate nucleus with afferent input from the wrist joint nerve relay directly to nucleus VPL of the thalamus.

DISCUSSION

Previous reports have indicated that afferent fibres from joint capsules project to the dorsal column nuclei (Kruger, Siminoff & Witkovsky, 1961; Winter, 1965; Williams *et al.* 1973). However, this identification has usually been made on the grounds that cells in the dorsal column nuclei respond to joint movement, but not to palpation of muscle bellies. It is now clear from the present study and the work of Millar (1979*a*, *b*) that forelimb joint afferents do project to the cuneate nucleus in the cat.

Three main points emerge from the data. These will be outlined briefly and then considered in more detail. (1) Wrist joint receptors project to the cuneate nucleus not only as primary afferents, but also via post-synaptic fibres. (2) Cells in the cuneate nucleus which receive input from wrist joint receptors also receive convergent input from receptors in skin and muscle. (3) Using the collision test no significant projection of joint-activated cells in the cuneate nucleus could be demonstrated to the ventrobasal complex of the thalamus.

Axons in the dorsal columns. Recordings from the wrist joint nerve during antidromic stimulation of the cuneate nucleus and cuneate fasciculus leave no doubt that primary wrist joint afferents project to the cuneate nucleus in the dorsal columns. This is consistent with the data of Millar (1979*a*) who showed that afferents in the elbow joint nerve could be antidromically excited from the cuneate nucleus.

In addition, there appears to be a substantial projection to the cuneate nucleus of non-primary afferent fibres activated by wrist joint receptors. Uddenberg (1968*a*, *b*) was the first to report the presence of post-synaptic fibres in the cuneate fasciculus, although Amassian & de Vito (1957) had found units with similar properties which they identified as ephaptically coupled primary afferents. In fact, Uddenberg (1968*b*) found that post-synaptic dorsal column units were often activated by bending of joints, in particular the wrist joint. However, he did not consider that specific joint receptors activated the units.

On the basis of antidromic testing, only a few primary afferent fibres from the knee joint in cat or monkey project to the cervical dorsal columns (Burgess & Clark, 1969). However, it is known that cells in the gracile nucleus are activated by afferents in the knee joint nerve (Williams *et al.* 1973). It may be that the hindlimb projection of joint receptors to the dorsal column nuclei also involves postsynaptic fibres, described for the gracile fasciculus by Anguat-Petit (1975*a*, *b*).

At first sight, this suggestion is inconsistent with the report by Whitsel, Petrucelli & Sapiro (1969). These authors searched the gracile fasciculus of the squirrel monkey for axons activated from the hindlimbs. While fibres activated by both deep and superficial receptors were found at lumbar levels, only cutaneous fibres could be recorded at cervical levels. However, as they were using natural stimuli, any post-synaptic fibre having convergent inputs from deep and superficial receptors would have had a cutaneous receptive field. Post-synaptic fibres activated by joint afferents might thus have been classified as cutaneous. In fact there is recent evidence that knee joint receptors excite non-primary afferents in the gracile fasciculus (Jankowska, Rastad & Zarzecki, 1979).

It would appear from the sizes of the antidromic volleys in the wrist joint nerve elicited respectively from the cuneate nucleus and the dorsal root entry zone that at least 90% of primary afferents project to the cuneate. This may be an underestimate, since the antidromic volley elicited from the cuneate nucleus is dispersed relative to that from the dorsal roots. This suggests that the second-order fibres are either excited by the small number of primary afferents which do not project to the cuneate nucleus, or that they are excited by collaterals from primary afferents which do project. In two experiments, it was found that stimulation of the cuneate nucleus resulted in bursts of spikes in second-order fibres, similar to the bursts evoked by peripheral stimulation. When primary afferents were examined, only single spikes

were found in response to single peripheral or antidromic shocks. It is possible that stimulating the cuneate nucleus results in a burst of spikes in a second-order fibre due to antidromic invasion of a primary afferent, and its collateral onto the second order fibre.

Responses of cuneate neurones. In order to judge whether cells in the cuneate are monosynaptically excited by primary afferents of the wrist joint nerve, one needs to know the time of arrival at the cuneate of the primary afferent volley. Such a volley could not be recorded from the surface of the cuneate. However, the maximal antidromic volley elicited from the cuneate indicated conduction times of 4–8 msec (Fig. 2*B*). Some cells in the cuneate nucleus had shortest latencies in the range 5–9 msec, and might have been monosynaptically activated. However, many cells had longer latencies than this, and were probably excited not by primary afferents of the wrist joint nerve but by second-order fibres of the kind recorded in the dorsal columns. Millar (1979*a*) reported the loci of a number of cells in the cuneate which were activated by stimulating the elbow joint nerve. In fact the cells were found by seeking for antidromically activated elbow joint efferents: since they were close to these afferents and had short latencies (3–8 msec) they were presumably monosynaptically activated. Cells were also found which were apparently activated polysynaptically (J. Millar, personal communication).

In animals where wrist joint receptors were the only source of information about wrist movement, the majority of units had rapidly adapting responses to wrist movement (of the twenty-four units which responded to wrist movement, only three had responses lasting 10 sec or longer, whereas an earlier study of the primary afferents of the wrist joint nerve showed that 28% were slowly adapting (Tracey, 1979)). Gordon, Landgren & Seed (1961), working on the spinal nucleus of the trigeminal nerve in barbiturate-anaesthetized cats, found that the slow adaptation which was so characteristic of primary fibres was uncommon among second order cells, and suggested that the difference might be due to the action of the general anaesthetic. In the present study, no differences were found in the speed of adaptation of cells whether the cats were anaesthetized with barbiturate or with halothane in N_2O/O_2, and it seems unlikely that the preponderance of rapidly adapting cells is an effect of anaesthesia.

Alternative explanations are (1) that the synapses interposed between the primary afferent and the cuneate cell introduce adaptation characteristics more rapid than those of the primary afferents; (2) that cells in the cuneate respond differently to wrist movement when receiving afferent input only from the joint, and when receiving convergent input from joint, muscle and skin.

Convergence. Neurones in the dorsal column nuclei are normally thought of as being modality specific (Kruger *et al.* 1961). A striking result of this study was that many neurones in the cuneate nucleus which receive input from joint afferents are also activated by cutaneous and muscle afferents. Schwartz (1965) has reported that numerous units in the cuneate respond phasically to hair movement as well as tonically to stimulation of muscle and joints, and Millar (1979*a*, *b*) also reported convergence of cutaneous and joint afferents onto neurones of the cuneate nucleus. Such convergence occurs not only onto second order dorsal column cells, but also onto cells in the cuneate nucleus monosynaptically activated by primary joint afferents

(Millar, 1979*b*). As a result, it is particularly difficult to decide how much of the response of higher order cells to joint *movements* is actually due to joint *afferents*. Unless a complete denervation of skin and muscle affected by the joint movement is carried out, it is impossible to know whether a response is due to joint, skin or muscle afferents.

The functional significance of such convergence is not clear. It may be that those afferents signalling a particular joint position or movement all converge on a common cell, regardless of their modality. But we need to know more about the types of afferents involved (e.g., muscle spindles or tendon organs) and about the pattern of convergence (whether cells excited by joint afferents which signal flexion have convergent inputs from extensor muscle afferents and from cutaneous receptors activated by joint flexion). If cells showing such a convergence of modalities could be shown to project to the cerebral cortex via the thalamus, it would be consistent with the growing body of evidence that joint, muscle and cutaneous afferents all play a role in kinaesthesia (see McCloskey (1978) for review).

Projections. However, one of the unexpected results of this study was that very few of the cells in the cuneate which were activated by joint afferents could be fired antidromically from VPL, although the ability to record wrist joint nerve potentials during electrode insertion, histological controls after the experiment, and the successful antidromic activation of a reasonable proportion of cutaneous cells in the cuneate all suggested that the electrode location and stimulus parameters were appropriate. This confirms an observation by Gordon & Seed (1961) in nucleus gracilis; none of the neurones which they classed as 'joint' cells could be fired antidromically from the medial lemniscus. The simplest explanation is that such neurones do not project directly to VPL and correspond to the 'interneurones' of Andersen *et al.* (1964). These authors found that interneurones were often activated from two or three afferent nerves in contrast to cuneothalamic relay cells, most of which were activated from only one. If joint neurones in the cuneate do not project to the thalamus, it is surprising that field potentials evoked from wrist joint nerve could regularly be recorded in VPL (Fig. 1*B*).

However, in a recent study on cells in the cuneate which were monosynaptically activated by elbow joint afferents, eighteen of thirty-five cells tested could be shown to project to the contralateral thalamus (Millar, 1979*b*). It is possible that cells activated directly by primary afferents project to the thalamus while cells activated by second-order afferents do not. It is also possible that second order fibres in the dorsal columns send collaterals to the thalamus as well as the dorsal column nuclei (Hayes & Rustioni, 1979).

This work was supported by grants from the Australian Research Grants Committee and the National Health and Medical Research Council. I should like to thank Professor A. K. McIntyre, Professor R. Porter and Dr Bruce Walmsley for valuable advice and constructive criticism of the manuscript. I should also like to thank Mr Greg Gordon for assistance with every aspect of this project.

REFERENCES

AMASSIAN, V. E. & DE VITO, J. L. (1957). La transmission dans le noyau de Burdach. *Colloques int. Cent. natn. Rech. Scient.* **67**, 353–393.

ANDERSEN, P., ECCLES, J. C., SCHMIDT, R. F. & YOKOTA, T. (1964). Identification of relay cells and interneurons in the cuneate nucleus. *J. Neurophysiol.* **27**, 1080–1095.

ANGAUT-PETIT, D. (1975*a*). The dorsal column system. I. Existence of long ascending postsynaptic fibres in the cat's fasciculus gracilis. *Exp. Brain Res.* **22**, 457–470.

ANGAUT-PETIT, D. (1975*b*). The dorsal column system. II. Functional properties and bulbar relay of the postsynaptic fibres of the cat's fasciculus gracilis. *Exp. Brain Res.* **22**, 471–493.

BURGESS, P. R. & CLARK, F. J. (1969). Dorsal column projection of fibres from the cat knee joint. *J. Physiol.* **203**, 301–315.

CLARK, F. J., LANDGREN, S. & SILFVENIUS, H. (1973). Projections to the cat's cerebral cortex from low threshold joint afferents. *Acta physiol. scand.* **89**, 504–521.

DARIAN-SMITH, I., PHILLIPS, G. & RYAN, R. D. (1963). Functional organization in the trigeminal main sensory and rostral spinal nuclei of the cat. *J. Physiol.* **168**, 129–146.

GARDNER, E. & NOER, R. (1952). Projection of afferent fibers from muscles and joints to the cerebral cortex of the cat. *Am. J. Physiol.* **168**, 437–441.

GORDON, G., LANDGREN, S. & SEED, W. A. (1961). The functional characteristics of single cells in the caudal part of the spinal nucleus of the trigeminal nerve of the cat. *J. Physiol.* **158**, 544–559.

GORDON, G. & SEED, W. A. (1961). An investigation of nucleus gracilis of the cat by antidromic stimulation. *J. Physiol.* **155**, 589–601.

HAND, P. J. & VAN WINKLE, T. (1977). The efferent connections of the feline nucleus cuneatus. *J. comp. Neurol.* **171**, 83–110.

HAYES, N. L. & RUSTIONI, A. (1979). Collateral branching of ascending spinal neurons in macaques. *Neurosci. Abstr.* **5**, 708.

JANKOWSKA, E., RASTAD, J. & ZARZECKI, P. (1979). Segmental and supraspinal input to cells of origin of non-primary fibres in the feline dorsal columns. *J. Physiol.* **290**, 185–200.

JOHANSSON, H. & SILFVENIUS, H. (1977). Input from ipsilateral proprio- and exteroceptive hind limb afferents to nucleus *z* of the cat medulla oblongata. *J. Physiol.* **265**, 371–393.

KRUGER, L., SIMINOFF, R. & WITKOVSKY, P. (1961). Single neuron analysis of dorsal column nuclei and spinal nucleus of trigeminal in cat. *J. Neurophysiol.* **24**, 333–349.

LINDSTRÖM, S. & TAKATA, M. (1972). Monosynaptic excitation of dorsal spinocerebellar tract neurones from low threshold joint afferents. *Acta physiol. scand.* **84**, 430–432.

MATSUMOTO, A. & MORI, S. (1975). Number and diameter distribution of myelinated afferent fibers innervating the paws of the cat and monkey. *Expl Neurol.* **48**, 261–274.

MCCLOSKEY, D. I. (1978). Kinesthetic sensibility. *Physiol. Rev.* **58**, 763–820.

MILLAR, J. (1979*a*). Loci of joint cells in the cuneate and external cuneate nuclei of the cat. *Brain Res.* **167**, 385–390.

MILLAR, J. (1979*b*). Convergence of joint, cutaneous and muscle afferents onto cuneate neurones in the cat. *Brain Res.* **175**, 347–350.

ROBERTS, W. J. & SMITH, D. O. (1973). Analysis of threshold currents during microstimulation of fibres in the spinal cord. *Acta physiol. scand.* **89**, 384–394.

SCHWARTZ, S. T. (1965). An Analysis of Resting Activity in the Cuneate Nucleus, Ph.D.Dissertation, Albert Einstein College of Medicine, 1965. Cited by NORTON, A. C. & KRUGER, L. (1973). *The Dorsal Column System of the Spinal Cord.* Los Angeles: Brain Information Service, U.C.L.A.

SNIDER, R. S. & NIEMER, W. T. (1961). *A Stereotaxic Atlas of the Cat Brain.* Chicago: University of Chicago Press.

TOWE, A. L. & HARDING, G. W. (1970). Extracellular microelectrode sampling bias. *Expl Neurol.* **29**, 366–381.

TRACEY, D. J. (1978). Joint receptors in the wrist of the cat. In *Studies in Neurophysiology: Presented to A. K. McIntyre*, ed. PORTER, R., pp. 75–86. Cambridge University Press.

TRACEY, D. J. (1979). Characteristics of wrist joint receptors in the cat. *Exp. Brain Res.* **34**, 165–176.

UDDENBERG, N. (1968*a*). Differential localization in dorsal funiculus of fibres originating from different receptors. *Exp. Brain Res.* **4**, 367–376.

UDDENBERG, N. (1968*b*). Functional organization of long, second-order afferents in the dorsal funiculus. *Exp. Brain Res.* **4**, 377–382.

WHITEHORN, D., HOWE, J. F., LESSLER, M. J. & BURGESS, P. R. (1974). Cutaneous receptors supplied by myelinated fibers in the cat. I. Number of receptors innervated by a single nerve. *J. Neurophysiol.* **37**, 1361–1372.

WHITSEL, B. L., PETRUCELLI, L. M. & SAPIRO, G. (1969). Modality representation in the lumbar and cervical fasciculus gracilis of squirrel monkeys. *Brain Res.* **15**, 67–78.

WILLIAMS, W. J., BEMENT, S. L., YIN, T. C. T. & MCCALL, W. D. (1973). Nucleus gracilis responses to knee joint motion: a frequency response study. *Brain Res.* **64**, 123–140.

WINTER, D. L. (1965). N. gracilis of cat. Functional organization and corticofugal effects. *J. Neurophysiol.* **28**, 48–70.

YIN, T. C. T. & WILLIAMS, W. J. (1976). Dynamic response and transfer characteristics of joint neurons in somatosensory thalamus of the cat. *J. Neurophysiol.* **39**, 582–600.