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SYNAPTIC LINKAGE BETWEEN AFFERENT FIBRES OF THE CAT'S HIND LIMB AND ASCENDING FIBRES IN THE DORSOLATERAL FUNICULUS

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In contrast with the very large amount of work carried out on the synaptic mechanisms of motoneurones, relatively few investigations have been made into the properties of the synapses which interrupt afferent pathways, although the latter junctions have long been known to possess distinctive properties (Marshall, 1941; Therman, 1941; Grundfest & Campbell, 1942; Lloyd & McIntyre, 1950; Amassian, 1953; Bishop, 1953; Rose & Mountcastle, 1954). Of the afferent junctional systems previously studied, the linkage between hind-limb primary afferent fibres and neurones projecting rostrally in the ipsilateral dorsolateral funiculus is of special interest because low-threshold (Group I) afferent fibres serving muscle effect monosynaptic connexions with neurones of this projection system (Clarke's column cells) as well as with motoneurones (Lloyd & McIntyre, 1950). Thus a favourable situation is provided for comparing the properties of an afferent with those of the well-known motoneurone synaptic system. The object of the experiments to be described was to explore more fully the differences between these two synaptic systems, and to examine the response patterns evoked in single dorso-lateral tract neurones by different forms of peripheral stimulation. Many of our results are in substantial agreement with those of Laporte, Lundberg & Oscarsson (1956*a*, *b*) and Laporte & Lundberg (1956), which became available when this investigation was at an advanced stage. Some of our findings have already been reported briefly (McIntyre, Mark & Steiner, 1956; Mark & McIntyre, 1956).

METHODS

Adult cats were used in all experiments, usually anaesthetized with pentobarbitone (Nembutal; Abbott Laboratories) in initial dosage of 40 mg/kg given intraperitoneally. Anaesthesia was maintained by intravenous administration of additional pentobarbitone as required. In a few experiments the animals were used in the acutely decapitate state after initial ether anaesthesia. Laminectomy was performed in order to expose the spinal cord from the lumbosacral to the upper thoracic segments; rigid fixation of the vertebral column and pelvis was secured by a series of clamps attached to a heavy base-plate. In

some experiments, electrical activity of the dorsolateral tract was recorded in volume by a surface lead, as in a previous study (Lloyd & McIntyre, 1950); in others, monophasic records of the tract discharge were made from a length of the dorsolateral funiculus in continuity caudally, but severed rostrally and dissected from the cord for several centimetres. This method was suggested by the work of Rudin & Eisenman (1951), and has been used extensively by Lundberg and his colleagues (Laporte *et al.* 1956*a*; Oscarsson, 1956, 1958). Nerves or spinal roots pertaining to the ipsilateral hind limb were dissected for recording or stimulation, and all exposed tissues were covered with warm mineral oil equilibrated with 95% oxygen and 5% carbon dioxide and retained by skin flaps in the usual way. Body temperature was maintained between 36 and 39° C by heating the experimental room and by the use of an infra-red lamp and an electrically-heated table. When 'natural' stimulation of cutaneous or muscle receptors was employed, denervation of most of the hind limb except for the chosen receptive fields was usually practised.

Responses of individual tract neurones were recorded by means of Ling–Gerard type glass capillary micropipettes filled with 3 M-KCl, with tip diameters of 0·5 μ or less. They were inserted by means of a rigidly mounted micromanipulator either into an otherwise undisturbed region of the dorsolateral tract usually in the 8th, 9th or 10th thoracic segment, or into more caudally situated regions of the grey matter containing the parent cell bodies of tract fibres. The usual cathode-follower input stage and standard dual-channel amplifying and display equipment were used, as described in other publications from this laboratory (Brock, Coombs & Eccles, 1952; Mark & Steiner, 1958; McIntyre, Bradley & Brock, 1959). Permanent photographic records were made with a Grass automatic camera. Electrical stimulation was effected either by thyratron-controlled condenser discharges and an isolating transformer, or by 'square-wave' pulses from a Grass stimulator and a radio-frequency stimulus isolation unit. For 'in-volume' stimulation of the spinal cord, pairs of fine steel needles, insulated except for the tips, were employed; otherwise, platinum or silver hook electrodes were used for stimulating or recording from peripheral nerves, spinal roots or the dissected dorsolateral tract. In some experiments contractions of hind-limb muscles were recorded by a strain gauge, the output of which drove one beam of the display unit by way of a direct-coupled amplifier. Muscle stretch was applied by a hand-operated rack and pinion device carrying the strain gauge, and the skin was stimulated by means of a blunt-ended glass rod or a fine probe.

'Input' was monitored either triphasically by a wick lead in contact with the appropriate dorsal root fibres at their entry into the spinal cord, together with an indifferent electrode placed on nearby muscle, or in the case of cutaneous nerves, diphasically by two electrodes located central to the stimulating pair (Mark & Steiner, 1958). Throughout this account, the terminology for cutaneous afferent fibres recently adopted by Lloyd (1957) will be used, namely, Group II for the band of larger myelinated fibres of about 6 μ and upwards in diameter (alpha and beta in the terminology of Gasser), and Group III for the smaller myelinated fibres or delta pile (Gasser, 1941).

RESULTS

Responses of the whole tract

Pattern and latency of responses. Figure 1 shows examples of the potentials evoked in the dorsolateral funiculus upon stimulating primary afferent fibres in lumbosacral dorsal roots. The most prominent feature is the large monosynaptically generated initial deflexion, which represents the nearly synchronous discharge of many tract fibres of rapid conduction velocity (Lloyd & McIntyre, 1950). The remainder of the response, or

after-discharge, is revealed most clearly by the monophasic method (*C* and *D*); it continues with declining amplitude for at least 10 msec.

In view of differences in conduction distance to the recording station, latency of the initial monosynaptic response varies, of course, from preparation to preparation; the range for maximal dorsal root volleys in these experiments was 1·7–2·8 msec. In a given preparation little variation in latency is observed when maximal volleys are used; however, when the

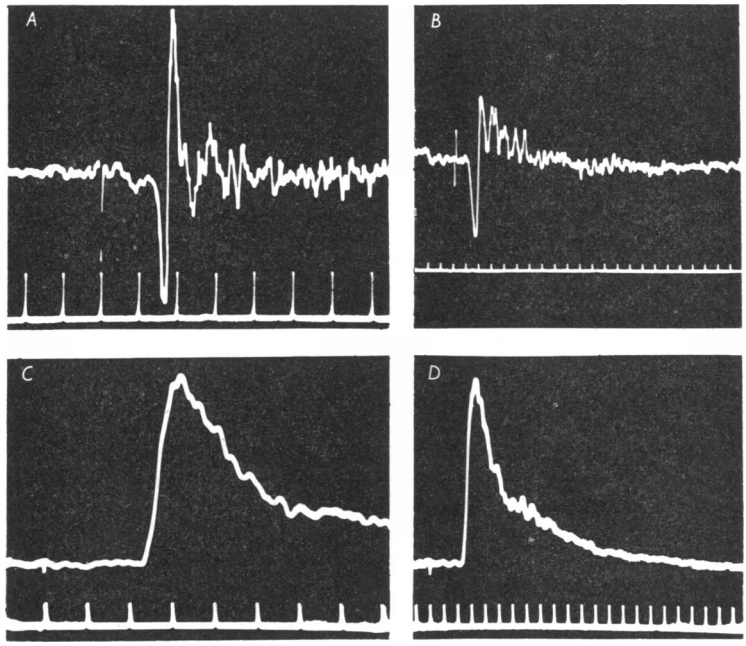

Fig. 1. Responses of dorsolateral tract to stimulation of combined L7 and S1 dorsal roots. *A* and *B* recorded by surface lead from the undisturbed tract in the 9th thoracic segment; two different preparations. *C* and *D*, monophasic records at different sweep speeds from the dissected dorsolateral funiculus in another preparation, at the 8th thoracic segmental level. *A* and *B* retouched. Time marker, msec.

input volley is reduced in size latency increases and becomes more variable. Graphical expression of this finding is presented in Fig. 2, in which the ordinate represents latency, and the abscissa, amplitude of the input dorsal root volley expressed as percentage of maximum.

Figure 3 gives examples of responses recorded from the whole dorsolateral funiculus upon stimulation of nerves in the hind limb. The response to a muscle afferent volley (*A*, *B*, *C*) is seen to consist of a well synchronized deflexion some 2–4 msec in duration, with very little after-discharge. Figure 3*D* demonstrates that a volley in a cutaneous nerve also sets up a substantial response in the dorso-lateral tract, in agreement with

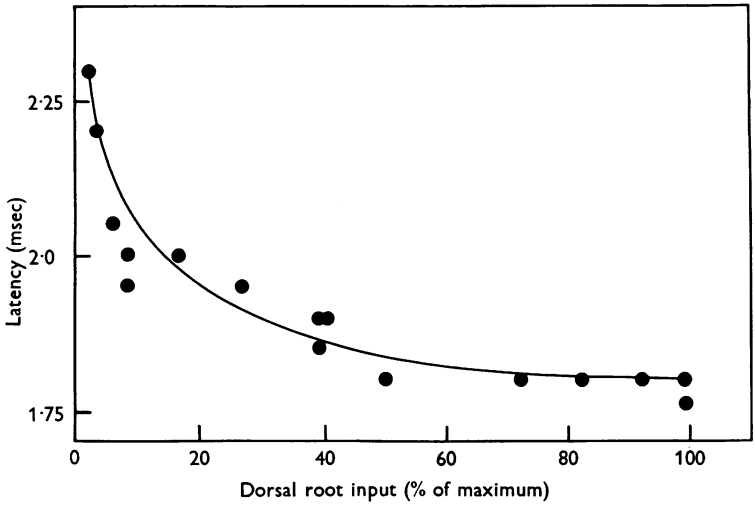

Fig. 2. Latency of tract response to stimulation of the combined L7 and S1 dorsal roots plotted against size of afferent volley. Ordinate, latency measured from the moment at which the afferent volley enters the cord. Abscissa, amplitude of dorsal root volley expressed as percentage of maximum.

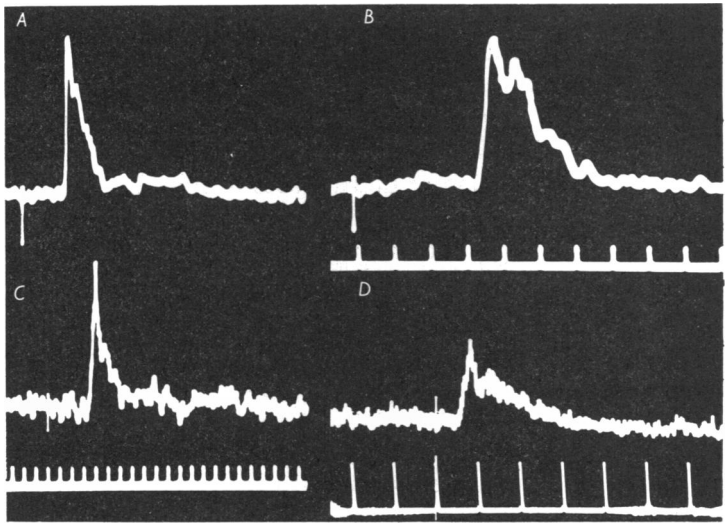

Fig. 3. Responses evoked by stimulation of hind-limb nerves and recorded monophasically from the ipsilateral dorsolateral funiculus. *A* and *B*, response recorded at two different sweep speeds to a volley in the combined nerves of triceps surae, plantaris and flexor digitorum longus, stimulus intensity being adequate to excite Group II as well as Group I fibres. *C*, response to similar stimulation of triceps surae nerves alone. *D*, response to stimulation (maximal for Group II fibres) of peroneal cutaneous nerve. Amplification for *C* and *D* twice that for *A* and *B*. Time scale below record *D* shows 10 msec intervals, and applies only to this record. Other time marks show milliseconds, and apply to the tracings above them. *A* and *C* recorded at the same sweep speed.

Laporte *et al.* (1956*a*). In comparison with the response to a muscle afferent volley, latency is longer, the initial deflexion is smaller and less well synchronized, and there is a prominent delayed discharge. It therefore appears that the after-discharge elicited in the tract by a dorsal root volley must largely be generated by the action of impulses in primary afferent fibres pertaining to cutaneous nerves, and not (or to a much smaller extent) by those in afferent fibres serving muscle. The tract response evoked by the combined action of a skin and a muscle-nerve volley timed to arrive simultaneously at the cord resembles the pattern of discharge evoked by dorsal root stimulation, and the combined potential approaches in magnitude and contour the sum of the tract responses to skin and muscle volleys in isolation. Thus excitatory convergence of cutaneous and muscle afferent fibres on to common tract units does not appear to be a prominent feature of the synaptic mechanisms concerned.

Although the latency of tract responses to cutaneous nerve stimulation is longer than that for a muscle afferent volley, measurement shows latency within the cord to be about the same, the additional delay in the case of cutaneous nerve volleys being the result of slower peripheral conduction velocity. Thus the earliest portion of the tract deflexion to be expected if cutaneous fibres could be stimulated in isolation at dorsal root level would appear early enough to contribute to the initial tract spike actually set up by a dorsal root volley, and it follows, too, that at least some of the cutaneous afferent fibres activating neurones projecting rostrally in the dorsolateral funiculus must do so by way of a single synaptic relay.

Upon repetitive stimulation of dorsal roots or hind-limb nerves, many tract neurones continue to respond even at fairly high frequencies of presynaptic drive. Surprisingly little reduction in the amplitude of individual tract responses takes place at a stimulation rate of 100/sec or even higher, in contrast with the monosynaptic discharge of motoneurones which is heavily depressed or abolished at such rates of presynaptic activation. However, the tract after-discharge suffers considerable reduction during a period of tetanic primary afferent stimulation.

Input–output relations. Input–output curves for the triphasically recorded monosynaptic initial tract deflexion in response to a dorsal root volley have previously been described (Lloyd & McIntyre, 1950). However, it is possible with monophasic recording to assess total tract output, including the after-discharge, by measuring area of the response. Figure 4 presents curves from an experiment in which measurements of discharge area (○) as well as amplitude of the initial spike-like deflexion (●) have been made from monophasic records of the tract discharge at various levels of dorsal root afferent input. Under the conditions of this experi-

ment, maximum input represents the summed activity of the Group I and Group II fibres in the stimulated dorsal roots (Lloyd, 1943*a*, *b*). Both curves rise steeply from their origin in expression of the fact that the smallest input volleys evoke measurable responses in the tract. From this it can be concluded, in confirmation of earlier studies, that dorsal root fibres of the lowest threshold excite some neurones of the tract by way of synaptic junctions of high transmitter potency, little or no summation being required to secure post-synaptic discharge. The curves stand in striking contrast with those defining amplitude of monosynaptic ventral

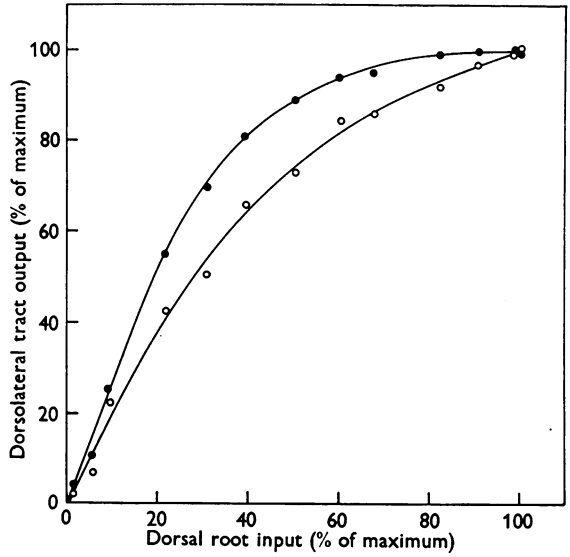

Fig. 4. Input–output curves relating amount of monophasically-recorded dorsolateral tract discharge to size of causative afferent volley, secured by stimulation of the combined L 7 and S 1 dorsal roots. Ordinates, tract output expressed as percentage of maximum; abscissa, amplitude of dorsal root volley also expressed as percentage of maximum. ●, amplitude of initial tract deflexion; ○, area of total tract discharge (potential-time integral). Each point the average of 8–12 observations.

root reflex discharge in response to various levels of dorsal root input, the sigmoid form of which expresses the need for summation in this simplest of spinal reflex paths (Lloyd, 1943*a*).

With monophasic recording we have found that amplitude of the initial spike tends to reach a plateau when the afferent volley attains about 70–80 % of maximum. Total tract discharge, however, continues to grow until the input reaches 100 % (Fig. 4, ○). Together these curves show that dorsal root fibres of all threshold values represented on the input scale (Groups I and II) effect excitatory connexions with neurones projecting by way of the dorsolateral funiculus, but that only the larger fibres of

lower threshold are concerned in evoking the early responses which sum to form the prominent initial component of the tract discharge. Of these larger fibres, those in the Group I category are clearly of prime importance. However, the larger Group II fibres of cutaneous origin must also participate in setting up the initial tract deflexion evoked by dorsal root stimulation, in view of their low threshold, and the fact that cutaneous afferent volleys can elicit tract responses of similar central latency (Fig. 3*D*).

The increase in total response of the tract (curve defined by open circles in Fig. 4) through recruitment of the higher-threshold Group II fibres to the input must obviously affect only its later portion. Indeed, progressive growth in the amount of late discharge can be observed by simple inspection of monophasic records as the input volley is increased above 50 % and approaches its maximum value. No such growth is usually apparent in triphasic records made from the cord surface, an observation which suggested to Lloyd & McIntyre (1950) that the Group I band of fibres alone is responsible for the delayed as well as for the initial tract discharge. This difference may be a result or the tendency towards mutual cancellation of asynchronous unit potentials recorded in volume.

Figure 5 plots the input–output relation for the amplitude of the tract discharge evoked by muscle afferent volleys in four experiments, the abscissa showing size of Group I volley as percentage of maximum. It can be seen that the relation is essentially linear, some response of the tract being detectable with quite small Group I volleys, and that no plateau appears as is the case when a dorsal root provides the input channel. Increasing the stimulus strength to include afferent fibres of higher threshold does not augment amplitude of the evoked tract spike, but may add a small late component to the response. The curve in Fig. 5 thus provides confirmation of the conclusion from studies with dorsal root stimulation that fibres throughout the Group I range are effective in provoking discharge of tract neurones by way of synaptic junctions of high transmitting power. The curve contrasts with the relationship found when Group I input is plotted similarly against monosynaptic ventral root reflex discharge (Hunt, 1955), an example of which is shown by the interrupted line in Fig. 5.

The difference between the curve of Fig. 5 and the upper (amplitude) curve of Fig. 4 is presumably related in part to the absence, in the measured input for the former (Group I action only), of the Group II component which accounts for growth of a dorsal root volley from 50 to 100 % of maximum, and which has little effect on the initial tract discharge. Since the Group I component of a dorsal root volley is compressed into the region of the abscissa between threshold and about 50 % of maximum, a hypothetical curve defining growth of the fraction of tract response

caused by the Group I content of such a volley would obviously rise more steeply than is the case in Fig. 5. However, it is likely that discharge of tract units linked to the larger Group II fibres contributes towards bringing about the steeper ascent of curves showing growth of response to dorsal root volleys (Fig. 4), for the tract response to a cutaneous volley rises very abruptly with increase of the input above threshold (Fig. 6).

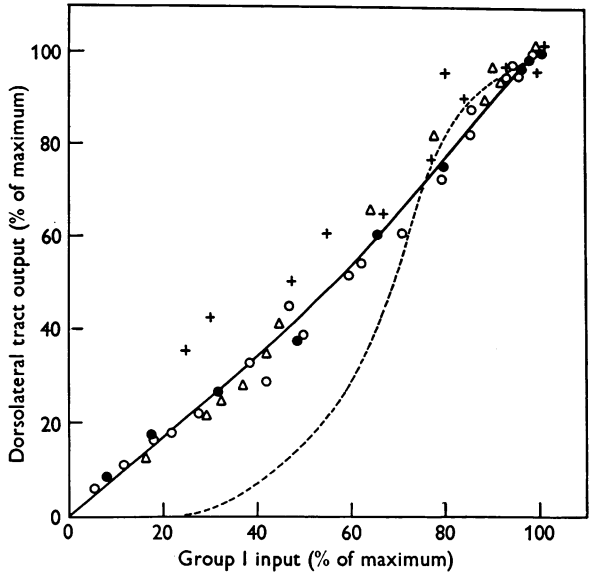

Fig. 5. Plotted points show for four experiments the amplitude of dorsolateral tract discharge (initial deflexion) expressed as percentage of maximum (ordinate) at various levels of Group I muscle afferent input, also expressed as percentage of maximum (abscissa). +, output measured triphasically from the undisturbed tract in response to input secured by stimulation together of the nerves to triceps surae, plantaris and flexor longus digitorum. ●, ○, two different preparations in which the same combination of muscle nerves provided the input, but output was recorded monophasically. △, another experiment with monophasic recording of output, but with input restricted to nerves supplying triceps surae. Each point the average of 10–20 observations. The interrupted curve shows the relationship obtained in another preparation between amplitude of Group I input and monosynaptic reflex discharge in the L 7 ventral root upon graded stimulation of the combined triceps surae, plantaris and flexor longus digitorum nerves (individual points not shown).

In one of the experiments plotted in Fig. 5, the Group I fibres stimulated were those of triceps surae alone (points shown by triangles), in contrast with the other three in which several muscle nerves were stimulated together. The points from the experiment with input restricted to a single synergic group do not appear to be distributed differently from those obtained by stimulation of the combined nerves of several muscles. This

observation, and the absence of a plateau in the curve, together suggest that there is not much convergent overlap of Group I afferent fibres from different muscles upon common tract neurones. Occlusion stemming from such convergence, if extensive, would be expected to find expression in a plateau, or at least an upward convexity, of the curve derived from the more massive input. Evidence from responses of single units in the tract favours the notion that on the whole individual muscles or synergic muscle groups are fairly discretely represented in the tract.

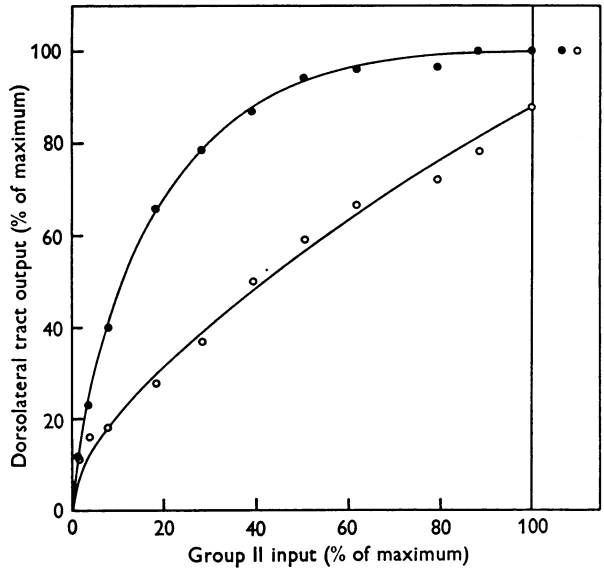

Fig. 6. Input–output curve for monophasically recorded tract discharge in response to graded stimulation of the ipsilateral superficial peroneal nerve. ●, amplitude of the initial deflexion; ○, area (potential-time integral) of whole tract discharge, both expressed as percentage of maximum (ordinate), against amplitude of afferent volley expressed as percentage of the maximal Group II (alpha-beta) spike. Points to the right of the vertical line at 100 % on the abscissa show the tract output evoked by stimulation strong enough to engage Group III (delta) fibres.

Figure 6 shows the input–output relation in an experiment with the peroneal cutaneous nerve serving as afferent channel, the tract response being recorded monophasically. The input scale represents amplitude of the cutaneous Group II volley in percentage of maximum; points to the right of the vertical line at 100 % show the effect of adding a substantial Group III component to the volley. As is the case with dorsal root stimulation, measurable responses of the tract appear with the smallest detectable cutaneous afferent volley, and increase steeply as the latter grow in size. The amplitude curve (●) reaches a plateau when the afferent volley is

about 70 % of maximum, and no further increase is observed when Group III impulses are added to the input. The curve for area, on the other hand, (○), shows after its steep initial portion a more gradual increase which continues throughout growth of the input volley to include all Group II fibres; recruitment of Group III fibres brings about a further increment in the total amount of discharge.

The abrupt origin of the curves in Fig. 6 shows that the low-threshold dorsal root afferent fibres effecting powerful synaptic linkages with tract neurones include many of cutaneous origin in addition to Group I fibres. The steeper rise and upward convexity of these curves compared with the roughly linear relationship obtained with Group I input (Fig. 5) suggests that the manner of synaptic linkage between cutaneous afferent fibres and neurones of the tract differs in some respects from the arrangement obtaining for the low-threshold muscle afferents. Shape of the amplitude curve in Fig. 6 is consistent with the notion that individual cutaneous afferent fibres make excitatory connexions with a considerable number of tract neurones, powerful enough with one or a few to cause discharge, subliminal in action on the remainder; and that the synaptic scale of each tract neurone in this category is composed of endings derived from many different primary afferent fibres. Otherwise expressed, both divergence and convergence are prominent features of the synaptic mechanisms linking cutaneous afferent fibres with tract neurones, in contrast with the more discrete arrangement postulated for Group I muscle afferents. Such an arrangement could explain the 'amplification' indicated by the steeply rising portion of the upper curve in Fig. 6, for each additional afferent fibre recruited by progressively stronger stimulation would be able to fire more neurones than it could acting in isolation, by virtue of spatial summation in units of the subliminal fringe created by action of its fellow afferent fibres of lower threshold. The plateau is likely to be at least in part a result of occlusion. The existence of extensive functional convergence upon individual tract neurones is directly demonstrated by the unit responses to be described subsequently.

Post-tetanic potentiation. Figure 7 demonstrates that there is a striking difference between the degree of post-tetanic potentiation (PTP) detectable in a motoneurone pool (Lloyd, 1949) and a population of dorsolateral tract neurones. Above (○) is plotted the amplitude of a monosynaptic reflex discharge recorded from the L7 ventral root and elicited at four-second intervals by test stimulation (supramaximal for Group I fibres) of a group of muscle nerves. Below is plotted (●) the amplitude of the initial dorsolateral tract deflexion evoked by the same afferent volley and recorded simultaneously on the second oscilloscope beam. The tract response undergoes very little potentiation (peak 1·5 times control value)

in comparison with the motoneurone discharge which is increased twenty-fivefold. This result agrees with the findings of Holmqvist, Lundberg & Oscarsson (1956), and shows that there is a small subliminal fringe of tract neurones even with a maximal Group I volley, in contradiction of earlier experiments using the less sensitive 'in-volume' recording technique, in which no PTP could be detected (McIntyre, 1953). Figure 7

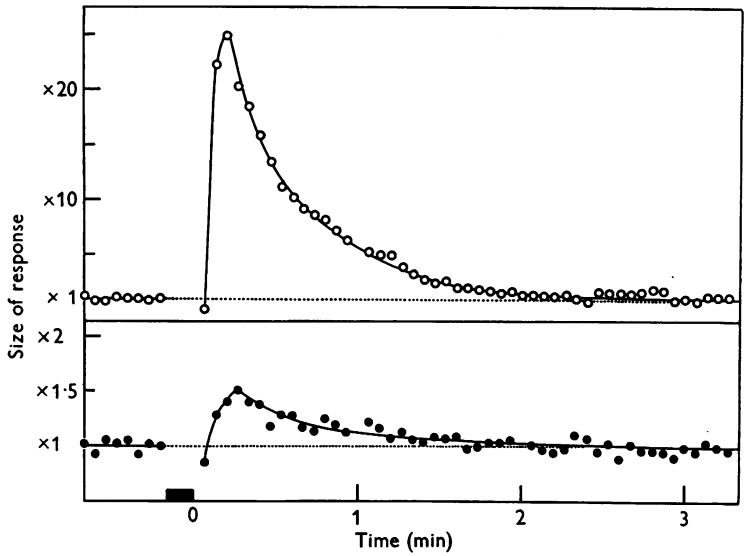

Fig. 7. Post-tetanic potentiation of responses to stimulation (supramaximal for Group I fibres) of the combined triceps surae, plantaris and flexor longus digitorum nerves. Ordinates, size of individual responses in multiples of pre-tetanic control amplitude (note different scales). Abscissa, time in minutes after cessation of tetanic stimulation for 10 sec at 450/sec, delivery of which is indicated by the black rectangle. Individual controls shown to the left of the latter. ○, monosynaptic reflex discharge in L7 ventral root. ●, amplitude of monophasically recorded dorsolateral tract response recorded simultaneously on the second oscilloscope beam.

demonstrates that the two sets of Group I presynaptic endings undergo qualitatively similar post-tetanic changes in transmitter potency, but the large discrepancy in magnitude of the effect emphasizes the difference between the two synaptic systems. Even less PTP has been seen in responses of the tract to maximal cutaneous afferent volleys, indicating that the subliminal fringe for the appropriate tract neurones must be very small indeed under these test circumstances.

Responses of single tract units

Response patterns. With Ling–Gerard micropipettes, responses can be recorded from single fibres in the dorsolateral funiculus, from cells of

Clarke's column in the upper lumbar segments, or more caudally from other cells in the grey matter, the units being identified in each case by their short-latency antidromic response to stimulation of the dorsolateral, funiculus in the mid or upper thoracic region. Most of our unit responses have been recorded from tract fibres, as in the work of Laporte *et al.* (1956*b*), with whose results our own are in general agreement. Figure 8 shows typical examples of single-tract unit responses to dorsal-root stimulation. The most striking characteristic of the responses to single afferent volleys is the common occurrence of repetitive firing, in contrast

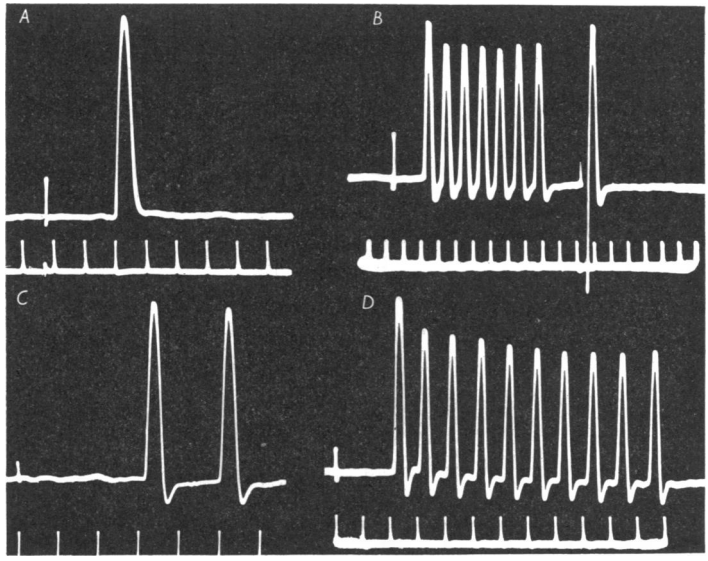

Fig. 8. Responses recorded by Ling–Gerard micropipettes of four different fibres in the dorsolateral funiculus to stimulation (maximal for Group I and Group II fibres) of the combined L7 and S1 dorsal roots. The last spike in record *B* is set up by direct stimulation of the tract several segments above the recording site; its short latency shows it to be an antidromically conducted response. Spikes retouched in *A*, *C* and *D*. Time marker, msec.

with the behaviour of motoneurones. Firing frequency was often as high as 800/sec and in many units initially exceeded 1000/sec. Such high frequencies might suggest injury, but this can be ruled out because no high-frequency bursts appeared spontaneously, and such neurones could be made to discharge single impulses by reducing the size of afferent volley (Figs. 10 and 11) or by antidromic activation (last spike in Fig. 8*B*). Furthermore, direct stimulation of such tract neurones by 'square-wave' current pulses 10–50 msec in duration induced repetitive firing throughout the stimulus, initially at high frequency, whereas a brief shock evoked but one impulse.

Thus there can be no reasonable doubt that the repetitive impulse trains are physiological at least in the sense that they can be evoked by way of essentially normal pre- and post-synaptic elements, and that they reflect some property of the synaptic junctions concerned which is absent from, or fails to manifest itself at, the synaptic junctions engaging motoneurones. Acceptance of these firing patterns as a normal manifestation of tract unit activity is further suggested by the prolonged shower of potentials recordable from the whole dorsolateral funiculus (Fig. 1), a ready explanation for which would be the occurrence of repetitive action in the undisturbed projection system.

By summing a series of unit discharge patterns, an approximate synthesis can be made of the total tract response which can be compared with an actual monophasic tract discharge. Figure 9 presents such a comparison carried out with the aid of certain simplifying assumptions explained in the legend. Peaks of the rectangles indicate contour of the summed response of 77 tract units; superimposed on this is a tracing of an actual whole-tract discharge recorded monophasically. Despite the relative crudity of the synthesis, correspondence between the actual monophasic response and the hypothetical discharge is sufficiently close to suggest not only that this small sample of 77 units is reasonably representative of the population, but also that repetitive firing of individual neurones is indeed an adequate explanation for the tract after-discharge.

Effects of grading volley size on unit responses. Figure 10 presents four responses of a tract neurone to a dorsal root volley of increasing amplitude, and demonstrates our regular finding with repetitively-firing units of reduction in latency and increase in number of discharges with increased presynaptic drive. Figure 11 shows graphically for another unit similar changes in latency (●) and spike number (▲), and it can be seen that these two effects are to some extent independent. Reduction in latency with augmentation of input is also seen in those units yielding only one impulse to a maximal afferent volley. It is obvious that these effects of grading the amplitude of afferent input on latency and on the number of post-synaptic impulses together demonstrate convergence of action by impulses in afferent fibres of different threshold upon individual tract neurones.

From experiments in which nerves in the hind limb rather than dorsal roots were stimulated it is clear that the majority of tract units responding to dorsal root stimulation with more than 2–3 impulses, and all those discharging long trains (e.g. Fig. 8*B*, *D*), are connected to afferent fibres of cutaneous nerves, whereas a large proportion of those with responses limited to 1 or 2 impulses are concerned with signals from muscle stretch receptors. This is in general agreement with the findings of Laporte *et al.* (1956*b*), and with the results of experiments upon the whole-tract dis-

charge (Fig. 3). Our experiments indicate that different muscles or synergic groups are fairly discretely represented in the tract, whereas widespread convergence takes place on units linked to cutaneous afferent fibres.

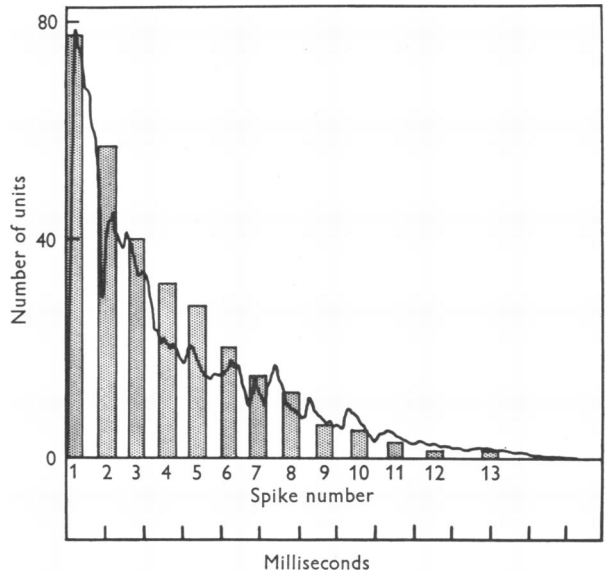

Fig. 9. Comparison of 'synthetic tract response', derived from firing patterns of 77 units, with actual monophasic dorsolateral tract discharge in response to maximal stimulation of L7 and S1 dorsal roots. Ordinate, number of units contributing to size of supposed summed potential at each of 13 intervals after onset of the initial spike, the intervals being set by the temporal sequence of the 13 impulses discharged by the unit giving the longest repetitive train (upper abscissa scale). Time (msec) after onset of first spike or whole tract discharge shown below. Stippled rectangles located on abscissa in accordance with the sequence of spikes in the unit firing 13 times; height of each is determined by the number of impulses appearing in that position were all 77 units to fire simultaneously with the same initial latency, and with the temporal sequence of subsequent spikes, if any, corresponding to that of the unit giving the longest train. Continuous line, tracing of an actual monophasic tract response to dorsal root stimulation on same time base and scaled so that its peak corresponds to height of the first rectangle. Impulses from different units are assumed to contribute equally to recorded potential.

Unit responses to receptor stimulation. Further subdivision of the tract neurones linked with Group I afferent fibres is indicated by their responses to stretch of muscles with intact innervation. In agreement with Laporte & Lundberg (1956), the majority exhibited spindle behaviour but some had the characteristics of tendon organs. Low mechanical threshold and 'in-parallel' behaviour during active muscle contraction (Matthews, 1933) together with, in the few instances in which it was tried, acceleration of

discharge by the action of succinylcholine or decamethonium (Granit, Skoglund & Thesleff, 1953) served to identify spindle-controlled tract units (Fig. 12*A*); the tendon-organ type of unit was so designated because of high mechanical threshold and 'in-series' behaviour (Fig. 12*B*). In our experiments no evidence was obtained suggesting convergence of the two

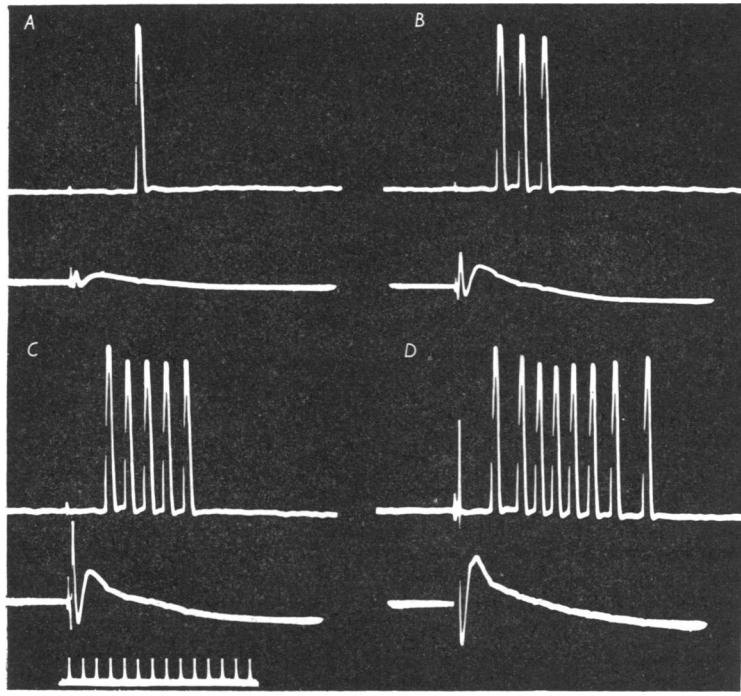

Fig. 10. Responses of a single unit in the dorsolateral funiculus to four different levels of afferent input secured by stimulation of the ipsilateral L7 dorsal root. Upper tracings, unit discharge recorded by Ling–Gerard micropipette; lower records, afferent volley recorded by surface lead at its entry into the cord. *D*, volley maximal for Groups I and II; *A*, *B*, *C*, volley 4·5%, 17% and 42% of maximum respectively; spikes retouched. Time marker, msec.

types of Group I fibre upon common tract neurones (but cf. Lundberg & Oscarsson, 1956). We conclude that the dorsolateral tract not only provides for discrete representation of synergic muscle groups, but within each group separate lines of communication are available for impulses from the two types of stretch receptor.

Tract units fired by electrical stimulation of skin nerves (Fig. 13*A* respond also to low-intensity mechanical stimulation of the integument or its appendages (Fig. 13*B*). The receptive fields serving such units have varied greatly in extent, some measuring many hundreds of square millimetres, whereas others, especially on the foot or toes, were only a few

millimetres across. Bending of hairs, or pressure exerted on the skin, were effective in setting up discharge of tract units linked to the area in question. The initial burst of impulses in response to natural stimulation may be at very high frequency, as is shown in Fig. 13*B*, *C*. Thus it appears that the rapid repetitive firing set up by electrically-initiated nerve volleys is not entirely unnatural, almost as high rates of firing being evoked by receptor-initiated activity, presumably in converging primary afferent fibres serving the same skin area.

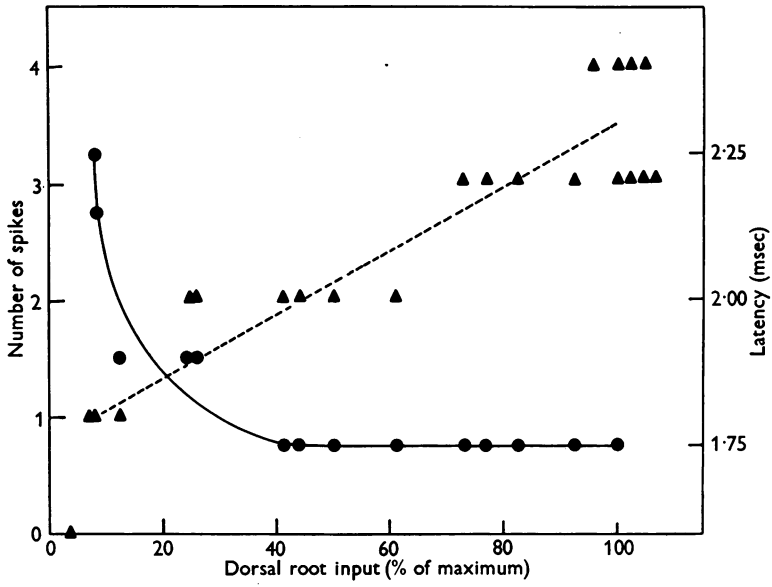

Fig. 11. Latency of first spike msec; (● and continuous line, right-hand ordinate scale), and number of spikes appearing (▲ and interrupted line, left-hand ordinate scale) are plotted for a dorsolateral tract unit at various levels of afferent input evoked by stimulation of the L 7 and S 1 dorsal roots and expressed as percentage of maximum (abscissa).

Inhibition. In addition to the powerful excitatory effects of afferent impulses on neurones of the dorsolateral tract, inhibitory action can also be observed, as described by Laporte *et al.* (1956*b*) and Laporte & Lundberg (1956). Inhibition of tract units with excitatory drive from a given muscle may be exerted by Group I impulses from its antagonist, or by action in afferent fibres of higher threshold in other deep or superficial nerves. Although impulses from different cutaneous nerves converging upon a tract neurone commonly exert excitatory effects, inhibitory interaction may also be observed. The experiment with natural stimulation illustrated in Fig. 13*D* may indicate the significance of such inhibition. This unit, fired by stimulation of the superficial peroneal nerve, showed

some background discharge and responded to pressure on the lateral toe (upper record). It was readily inhibited by light pressure on the neighbouring toe or the plantar cushion (lower record). Such inhibition appears to be of the kind reported for other afferent pathways such as the dorsal column system (Mountcastle & Powell, 1959), and could serve to sharpen spatial discriminative ability.

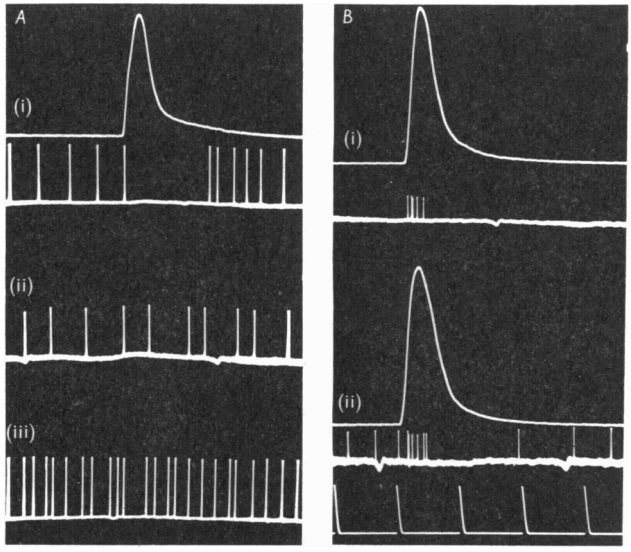

Fig. 12. Responses of tract units linked to stretch receptors in triceps surae, the afferent innervation of which was intact. *A*, unit showing muscle spindle behaviour: (i) lower record shows unit discharging to slight stretch of the muscle (about 15 g) and pausing during contraction brought about by a single weak stimulus to the peripheral end of the severed S 1 ventral root—upper trace is strain gauge record of tension developed at the tendo Achillis; (ii) resting discharge of the same unit with similar slight tension on the tendon; (iii) the same unit a few minutes after intravenous injection of 200 μg of decamethonium bromide, muscle length unchanged; alterations in spike size due to slight movement of micro-electrode tip. *B*, records similar to those of *A* (i), from another unit showing tendon organ characteristics: (i) at moderate initial tension; (ii) after increasing tension on the tendon to the point of evoking discharge of the unit. Time marker, 100 msec.

DISCUSSION

The origin, destination and physiological role of all the elements contributing to the responses recorded from the dorsolateral funiculus at present remains speculative. However, there can be little doubt that at least a major fraction of the neurones responding to impulses of muscle receptor origin belong to the classical dorsal spinocerebellar or dorsolateral tract of Flechsig, with cell bodies in the column of Clarke and end-stations in the cerebellum. Indeed, unit responses in the region of Clarke's column

to antidromic and orthodromic stimulation have been recorded in a few experiments of the present series, and recently by Curtis, Eccles & Lundberg (1958), which confirm this view, though the great susceptibility to injury of the cells in this nucleus makes systematic study very difficult. The significance of the neurones connected to afferent fibres of cutaneous

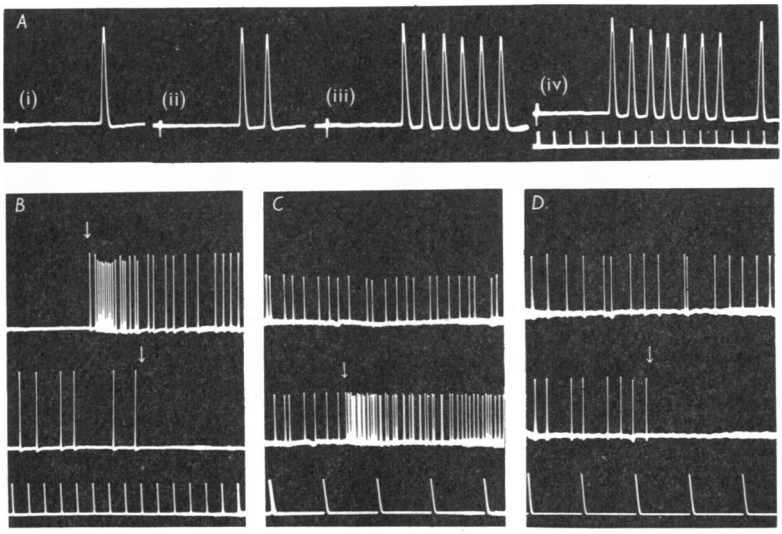

Fig. 13. Responses of units in the dorsolateral funiculus to cutaneous nerve or skin receptor stimulation. *A* (i)–(iv), a series of responses of a unit to stimuli of increasing strength applied to the intact peroneal cutaneous nerve; stimulus in (iv) strong enough to engage some Group III fibres. Time marker, msec. *B*, discharge of the same unit to light touch in the centre of its receptive field (skin in front of ankle joint); arrow in upper record signals onset of stimulation; in lower record, arrow shows cessation of stimulus some seconds later. Time marker, 10 msec. *C*, another unit, showing spontaneous discharge in the absence of stimulation (upper record); arrow in lower record shows onset of tactile stimulus to receptive field as in *B*. Time marker, 100 msec. *D*, another unit showing some spontaneous discharge, and responding to pressure on the lateral surface of the 4th digit with a well-maintained discharge (upper record); arrow in the lower record signals the onset of tactile stimulation of the plantar cushion, which inhibited the unit's firing. Time marker, 100 msec.

origin is, however, not yet apparent. The large measure of independence of tract neurones fired by muscle and cutaneous receptors respectively suggests that each belongs to a separate functional system, and this view is reinforced by our failure to record from the region of Clarke's column any of the long repetitive trains of impulses characteristic of skin-controlled units, even with maximal stimulation of dorsal roots. However, such firing patterns are encountered in the grey matter of segments between the level of afferent volley entry and the caudal end of Clarke's column. Thus

there is good reason to suppose that many of the tract neurones linked to cutaneous afferent fibres do not belong to the dorsal spinocerebellar system. Whether they pertain to the spino-olivary tract described by Grundfest & Carter (1954), the fast lateral-column system with eventual projection to the cerebral cortex (Morin, 1955; Mark & Steiner, 1958), or are simply long propriospinal neurones cannot at present be decided with certainty. Lundberg & Oscarsson (1959) have recently reported that some dorsolateral tract fibres linked to cutaneous afferents have their cell bodies below the level of Clarke's column and do not project to the cerebellum, but according to these authors other skin-controlled fibres do belong to the dorsal spinocerebellar system. At any rate, there appears to be agreement that fibres with a diversity of function course rostrally in the anatomical field of Flechsig's tract.

Despite the probable functional non-homogeneity of the various neurones contributing to the responses we have studied in the dorsolateral funiculus, certain similarities in their behaviour to synaptic activation stand out in comparison with the more extensively studied synaptic responses of motoneurones. Outstanding amongst the properties common to these afferent synapses is the small amount of summation required to discharge the post-synaptic neurones as compared with motoneurones, as shown by the input–output relationship at low levels of input. Another difference (doubtless related to the last) between the synapses of motoneurones and those of the tract neurones is the much smaller subliminal fringe detectable in the latter with maximal presynaptic volleys, a difference revealed by comparing the curves of post-tetanic potentiation (Fig. 7). The remarkable resistance of the afferent synapses to anaesthetic agents may be cited as a third characteristic contrasting with the much greater susceptibility of motoneurone synapses, and the capacity of post-synaptic tract neurones to continue responding during relatively high-frequency repetitive presynaptic stimulation constitutes a fourth distinctive property not apparent in the responses of motoneurones.

Although the various tract neurones we have studied are linked with primary afferent fibres by synapses which are similarly powerful according to the above criteria, nevertheless some differences appear to exist between the junctions made by afferent fibres of muscular and those of cutaneous origin. The apparently steeper rise and plateau of input–output curves for cutaneous nerve volleys as compared with the approximately linear relation for muscle afferent input suggests an even closer and more powerful linkage of the former with the appropriate tract neurones. Though other factors are doubtless involved in the genesis of this difference, a similar conclusion is indicated by the very small amount of post-tetanic potentiation detectable in the tract response to a maximal cutaneous nerve volley,

and by the prominence of repetitive discharge in the post-synaptic unit responses engendered by such afferent input. It appears likely that convergence of cutaneous afferent fibres upon common post-synaptic neurones is much more extensive than in the case of muscle afferent fibres, at least of those in the Group I range. An outstanding impression of our experience with tract unit responses elicited by stimulation of muscle nerves or stretch receptors is the infrequency with which such units can be fired from muscle afferents outside those belonging to a synergic pair or group. It seems likely that such muscles or synergic groups on the whole enjoy a fairly discrete representation in the tract, so that the projection system can convey to higher levels topographically organized information concerning the moment-to-moment patterns of posture or movement in the limb. In view of the remarkable giant synaptic contacts described by Szentágothai & Albert (1955) between primary afferent fibres and Clarke's column cells, which presumably are the actual junctions yielding the tract discharges evoked by Group I afferent input, it would be of great interest to know the morphological characteristics of the junctions between cutaneous afferent fibres and the tract neurones which they activate so powerfully.

Mechanism of repetitive firing. It is of interest to examine possible ways in which the rapid repetitive discharge of dorsolateral tract neurones may be brought about. It has already been pointed out that these repetitively firing cells have in all cases responsed with a single impulse when activated antidromically (Fig. 8*B*), or by just supra-threshold synaptic drive (Fig. 10*A*). These findings not only help to exclude injury as a factor in the genesis of multiple firing, but demonstrate conclusively that the mechanism responsible is not inherent in the post-synaptic cells themselves nor dependent upon self re-excitation by neurone chains driven by recurrent collaterals (Bishop, Jeremy & McLeod, 1953). In short, the observations demonstrate that the mechanisms responsible for repetitive firing are presynaptically located. Similar conclusions have been reached for repetitively-firing spinal internuncials by Hunt & Kuno (1959) and by Wall (1959). However, it is not easy to decide just what presynaptic machinery is responsible, for several factors could operate to prolong synaptic action. Simple dispersion of presynaptic impulses through differences in conduction velocity could lead to a relatively prolonged bombardment of second-order neurones, even with single-shock stimulation, and this almost certainly contributes to prolongation of action, especially with a volley set up in Group II or III fibres at some distance from the cord. However, with stimulation of dorsal roots near the cord this dispersion would be very much less, yet repetitive firing is very striking with afferent volleys set up in this way. Furthermore, we have

found that repetitive firing can be evoked by stimulation of primary afferent fibres in the dorsal column, and it does not seem possible to find a locus for such stimulation at which the repetitive firing is effectively reduced, though for a given tract unit such stimulation should, when near the site of synaptic relay, achieve minimal presynaptic dispersion. Thus, while admitting that simple dispersion may play a part in prolonging presynaptic action, especially when the afferent volley is set up in nerves of the limb, it does not seem possible to explain it fully in this way. The 'dorsal column relay' of Hursh (1940) is another possible mechanism which could prolong presynaptic action at these afferent synapses; however, with the spinal cord at 38–39° C Hursh's phenomenon is greatly reduced, yet repetitive firing is just as prominent as it is at lower cord temperatures.

The most likely possibilities are either repetitive presynaptic bombardment through delay-paths provided by presynaptic systems of internuncial chains (Lorente de Nó, 1938) or prolonged transmitter action by impulses in individual presynaptic terminals. The latter hypothesis could involve a prolongation of electrical action in the ultimate presynaptic ramifications (Lloyd & McIntyre, 1949), with consequent maintenance of transmitter action for considerably longer than the duration of an impulse in the parent axon, presumably by sustained delivery of a chemical agent; or the enduring transmitter action could be the result of glial or other juxta-synaptic barriers maintaining effective concentrations of chemical transmitter agent after its initial release over a relatively short time course. Evidence to hand does not permit proof or refutation of either of these suggestions, nor of the occurrence of repetitive bombardment via internuncial chains. However, the similar and very striking repetitive firing of Renshaw cells (Renshaw, 1946; Eccles, Fatt & Koketsu, 1954; McIntyre *et al.* 1956) in response to single antidromic volleys in motoneurones, a situation in which it seems unlikely that impulse-circulation in internuncial chains could play a part, inclines us to favour the view that prolonged transmitter action is an important part of the mechanism leading to multiple firing at afferent synapses. This hypothesis, and the postulate of repetitive bombardment through internuncial action, are by no means mutually exclusive; indeed, there is good reason to suppose that the latter mechanism, together with dispersion of primary afferent impulses (especially when conduction distance is long) also play a part in prolonging the synaptic drive. Hunt & Kuno (1959), for example, present evidence favouring the occurrence of a prolonged barrage of impulses upon repetitively-firing internuncials, which in many respects behave like the afferent neurones studied in this investigation. It seems likely to us that the later spikes of our repetitive trains may depend largely upon the

delayed arrival of presynaptic impulses, but that the initial burst of high-frequency post-synaptic discharge is more probably brought about mainly by prolonged intense transmitter action initiated by relatively synchronous impulses in many converging afferent terminals. Interjection of a directly-evoked (Wall, 1959; Hunt & Kuno, 1959), or an antidromic impulse into a synaptically-elicited train does not lead to 'resetting' of the rhythm, and this has been cited as evidence supporting the internuncial chain hypothesis (Wall, 1959). However, in the case of the repetitive trains studied by us, failure of an antidromic impulse to upset the spike rhythm only demonstrates the presynaptic locus, but not the nature, of the driving mechanism. Antidromic stimulation of our tract neurones, such as the one giving the responses of Fig. 8*B*, does not reset the rhythm, but firing rate is so high that the temporal sequence of impulses in the early part of the train is determined solely by recovery from refractoriness.

It is of interest that we have been able to elicit similar trains of impulses in tract neurones by direct stimulation with square-wave current pulses; in other words, these neurones show very little accommodation. The observation is consistent with the view that prolonged depolarization of post-synaptic cells by the sustained transmitter action postulated above could be the immediate agent for generating repetitive discharge, much in the manner shown for crustacean stretch receptor neurones by Eyzaguirre & Kuffler (1955). Apart from the presynaptic mechanisms, the ability to discharge at high frequencies shown by central neurones such as the one yielding the responses in Fig. 13*A*, *B*, or the internuncials studied by Haapanen, Kolmodin & Skoglund (1958), Wall (1959) and Hunt & Kuno (1959), provides another striking contrast with motoneurones, which seldom if ever respond in this way. The difference is probably due to the presence of a prolonged phase of subnormality in the latter which greatly limits their capacity to fire repetitively at high rates. This post-activation subnormality is associated with a well developed after-hyperpolarization, which is absent from internuncials (Hunt & Kuno, 1959), and probably from fusimotor neurones (Hunt & Paintal, 1958) which latter also tend to fire repetitively. One interpretation of the difference could be that repetitively-firing neurones do not exhibit post-activation hyperpolarization and associated subnormality because the impulses, initiated in or near the initial portion of the axon, do not invade the dendritic processes, the most likely site of the prolonged recovery processes in motoneurones which are so invaded (Lloyd, 1951).

The physiological significance of repetitive firing by neurones of the dorsolateral funiculus remains at present a matter for speculation. However, its common occurrence in second or third-order neurones of other afferent systems (e.g. Amassian, 1953; Bishop *et al.* 1953; Rose &

Mountcastle, 1954), and in spinal internuncials, cortical and reticular neurones (Amassian, 1953; Amassian & de Vito, 1954; Hunt & Kuno, 1959) suggests that the phenomenon may be of considerable importance in central nervous function, for example, through temporal expansion and hence intensification of post-synaptic action, or by synaptic transformation of spatial into temporal patterns of signals. The occurrence of repetitive action at so many central synapses, and the contrasting behaviour of motoneurones, suggest that the latter may represent an exceptional case, in keeping with the unique function of final-common-pathway cells.

SUMMARY

1. Responses of neurones projecting rostrally in the field of Flechsig's tract have been set up by stimulating primary afferent fibres or receptors pertaining to the ipsilateral hind limb, and recorded singly or *en masse*.

2. In the whole-tract response to dorsal root stimulation the initial spike-like component is monosynaptically evoked by impulses in Group I and low-threshold Group II fibres, and the after-discharge results largely from action in the smaller myelinated afferent fibres, especially those of cutaneous nerves.

3. Input–output curves demonstrate that the synaptic linkages between tract neurones and afferent fibres both of skin and muscle origin are powerful, little or no summation being required to secure post-synaptic discharge. Little post-tetanic potentiation is evident at these junctions, and transmission is well maintained during repetitive presynaptic stimulation.

4. Unit recording shows that a large proportion of tract neurones fire more than once in response to a single afferent volley, those fired by cutaneous impulses yielding the longest repetitive trains. Correspondence between an actual whole-tract response and a synthetic tract discharge constructed from unit firing patterns indicates that this repetitive firing accounts for the after-discharge.

5. Most of the tract neurones responding to cutaneous nerve volleys or stimulation of skin receptors are distinct from those fired by muscle afferent volleys; of the latter units, most are linked with muscle spindles but some with tendon organs. Synergic muscle groups appear to be fairly discretely represented in the tract.

6. In addition to the powerful excitatory synaptic effects, inhibitory actions also take place at the junctional mechanisms serving neurones of the dorsolateral tract.

7. The mechanism and significance of the repetitive firing phenomenon are discussed.

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