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CONDUCTION VELOCITIES OF CORTICOSPINAL AXONS IN THE RAT STUDIED BY RECORDING CORTICAL ANTIDROMIC RESPONSES

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SUMMARY

1. The rat corticospinal tract was stimulated at the medullary pyramid and at different levels in the spinal cord (segments C2/3, T2, T12) and responses were recorded from the surface of the cerebral cortex and extracellularly from individual cortical neurones.

2. Irrespective of the site stimulated, the earliest surface and single unit responses had frequency-following and other characteristics which indicated they resulted from antidromic invasion of corticospinal neurones.

3. Synaptically mediated discharges with longer latency were also evoked in cortical neurones other than corticospinal neurones. At least in part these discharges probably resulted from stimulus spread to the dorsal column–medial lemniscus pathway.

4. Corticospinal neurones were almost all between 1·0 and 1·5 mm beneath the cortical surface while synaptically excited units were at all depths greater than 0·4 mm.

5. By stimulating at two sites, estimates of conduction velocity were obtained for single corticospinal axons. For those reaching at least as far as T12, velocities caudal to the pyramid ranged from 5 to 19 m/s (mean $11{\cdot}4 \pm 2{\cdot}9$ m/s; S.D.). Slow axons in the pyramid (antidromic latency > 2·5 ms) could rarely be excited from T12.

6. By stimulating at three sites (pyramid, T2, T12) most axons reaching T12 were found to have similar conduction velocities in the 'cervical' (pyramid–T2) and 'thoracic' (T2–T12) cord. However, in 15% of the axons the 'thoracic' velocity was at least 25% less than the cervical.

7. The results are discussed and related to those from previous investigations.

INTRODUCTION

The corticospinal tract in the rat is a substantial pathway which passes through the medullary pyramid and subsequently travels via the contralateral dorsal column for the whole length of the spinal cord (e.g. Dunkerley & Duncan, 1969; Brown, 1971; Ullan & Artieda, 1981).

It is clearly desirable that the conduction velocity of this important pathway should be established. However, although Porter & Sanderson (1964) and others

(Ohta, 1968; Stone, 1972) have investigated the latency and other characteristics (i.e. form and spatial distribution) of antidromic responses evoked in the cerebral cortex by electrical stimulation of the medullary pyramid, there have been no comparably detailed studies of responses evoked by stimulation of the corticospinal tract at spinal levels.

Porter & Sanderson (1964) found that the earliest cortical surface response to pyramidal stimulation had a latency to peak of 2 ms (approximately 1·2 ms to onset) and showed that it resulted from antidromic invasion of neurones contributing axons to the pyramid. However, it is not certain to what extent this and later responses were attributable to stimulation of corticospinal axons because the medullary pyramid also contains numerous corticobulbar axons. Indeed, the latter may outnumber the former by as much as two to one (McComas & Wilson, 1968).

McComas & Wilson (1968) recorded from six cortical neurones which were antidromically invaded both from pyramid and cervical cord and by measurement of the distance between the sites of stimulation the conduction velocity in the spinal portion of the axons was calculated to range between 7·6 and 10·8 m/s. More recently, however, Elger, Speckmann, Caspers & Janzen (1977) have concluded that the corticospinal tract in the rat contains numerous axons which conduct at approximately 60 m/s.

The large discrepancy between this result and that of McComas & Wilson prompted the present investigation. The approach used was to characterize the responses elicited in the cortex by stimulation at the pyramid and at different levels of the spinal cord. Measurements of antidromic latencies and of conduction distances then allowed the calculation of conduction velocities between the sites of stimulation (cf. McComas & Wilson, 1968). Stimulation was sometimes applied at the pyramid and at two spinal levels in order to determine the conduction velocity for two different portions of a single axon. Most of the results relate to axons descending at least to segment T12.

METHODS

Twenty-five albino rats (average weight 380 g) were used. Anaesthesia was induced with halothane vapour (Fluothane; I.C.I.), followed by intraperitoneal injection of 50 mg/kg sodium pentobarbitone (Sagatal; BDH). Subsequent maintenance doses (10 mg/kg) were given intravenously via a cannula in the femoral vein. Rectal temperature was maintained at 36–38 °C with a thermostatically controlled electric blanket and an infra-red lamp. The trachea was cannulated.

The animal was placed in a head holder (Kopf Instruments) in the orientation required for the stereotaxic system of Fifkova & Marsala (1967). The spinal column was extended and immobilized by clamps on the spinous processes of appropriate vertebrae. To allow stimulation of the corticospinal tract at spinal levels short laminectomies were carried out to expose the dura overlying the dorsal surface of the cord at one or two of segmental levels C2/3, T2 and T12. The dura was reflected and the cord surface was protected by a layer of paraffin oil at 37 °C.

A wide craniotomy was subsequently made to expose the left cerebral hemisphere and a burr hole was made in the occipital bone near the mid line to allow access for a pyramidal-stimulating electrode. The scalp edges were sutured to a metal ring above the animal's head, the dura was reflected at both skull openings and the exposed brain was covered with warm paraffin oil.

For stimulation of pyramid and cord, each cathode was a tungsten wire, 0·1 mm in diameter, etched to a taper and insulated with glass, except at the tip. The anode was a sprung silver ball which rested on the pia near the point at which the cathode penetrated the surface. Each anode/cathode pair was mounted on a Narishige micro-manipulator. The pyramidal electrode was advanced ventrally through the cerebellum to reach the left pyramid at stereotaxic co-ordinates

12·0 mm caudal and 11·5 mm ventral to the bregma (Fifkova & Marsala, 1967). The vertical position of the electrode tip was then slightly adjusted, if necessary, to maximize the short latency response (see Results) on the surface of the cerebral cortex. Electrodes at spinal levels were inserted into the right dorsal column and were similarly adjusted; the depth required to evoke maximal early cortical responses was approximately 1·7 mm which correlates well with the known location of the rat corticospinal tract in the deepest portion of the dorsal column (Dunkerley & Duncan, 1969).

Stimulation was accomplished with 0·1 ms rectangular pulses supplied from a constant current stimulator with a range of 0–1000 μA. Single stimuli or trains at frequencies up to 1000 Hz could be delivered.

Potentials evoked on the surface of the cerebral cortex were recorded differentially between a roving silver ball (0·5 mm diameter) held in a micro-manipulator and resting lightly on the cortical surface and a second ball resting on reflected dura. The animal was earthed via a silver plate in the mouth. Recording band width was 50 Hz to 5 kHz and responses were displayed on a storage oscilloscope equipped with a Polaroid camera.

Cortical single units were recorded extracellularly using glass micropipettes filled with 4 M-NaCl (impedance 5–10 MΩ at 1000 Hz) which were positioned using a hydraulic microdrive. Pulsations of the cortex were reduced by light pressure of a small Perspex plate on the pial surface and the micro-electrode was introduced into the cortex via a pore (1·5 mm diameter) in the centre of the plate. Responses were recorded differentially between the micro-electrode and a silver ball resting on the cortical surface close to the point of micro-electrode entry. Recording band width was 300 Hz to 20 kHz.

At the termination of each experiment the animal was killed by anaesthetic overdose and the lengths of cord between the different stimulating electrodes were measured *in situ*.

RESULTS

Responses to pyramidal stimulation were first characterized to establish comparability with findings of previous workers and responses to stimulation at different levels of the cord were then investigated.

Cortical responses to stimulation of the medullary pyramid

(*a*) *Responses on the cortical surface.* Responses recorded from the surface of the cerebral cortex following single shocks delivered to the ipsilateral medullary pyramid were similar in general form to those reported by previous investigators (Porter & Sanderson, 1964; McComas & Wilson, 1968; Ohta, 1968). The largest potentials were recorded within an area which extended in a wide strip between a point 4·0 mm lateral to the bregma and a point 4·0 mm posterior and 1·5 mm lateral to the bregma. This distribution appears to agree with the findings of Porter & Sanderson (1964).

As may be seen from Fig. 1 *A–C* the earliest event was a surface positive deflexion with a peak at 2·0 ms ($\pm$0·16 ms S.D.; six experiments), onset at 1·3 ms ($\pm$0·1 ms S.D.) and duration approximately 1·4 ms. The latency and amplitude of this response were constant between trials and following the nomenclature of Porter & Sanderson it was denoted wave (1). It was followed by a negativity (cf. wave (3) of Porter & Sanderson) which was especially evident when later events were small in amplitude as in Fig. 1 *D*. Porter & Sanderson reported that the falling phase of wave (1) was frequently notched by the presence of a second small positive wave (latency 3 ms) which was denoted wave (2). No sign of this response was observed in the present experiments with the possible exception of one case when the falling phase of wave (1) displayed a point of inflexion (see Fig. 1 *C*), but a small positive wave with latency 4 ms to peak was frequently superimposed on the negative wave (3) (see Fig. 1 *A–C*).

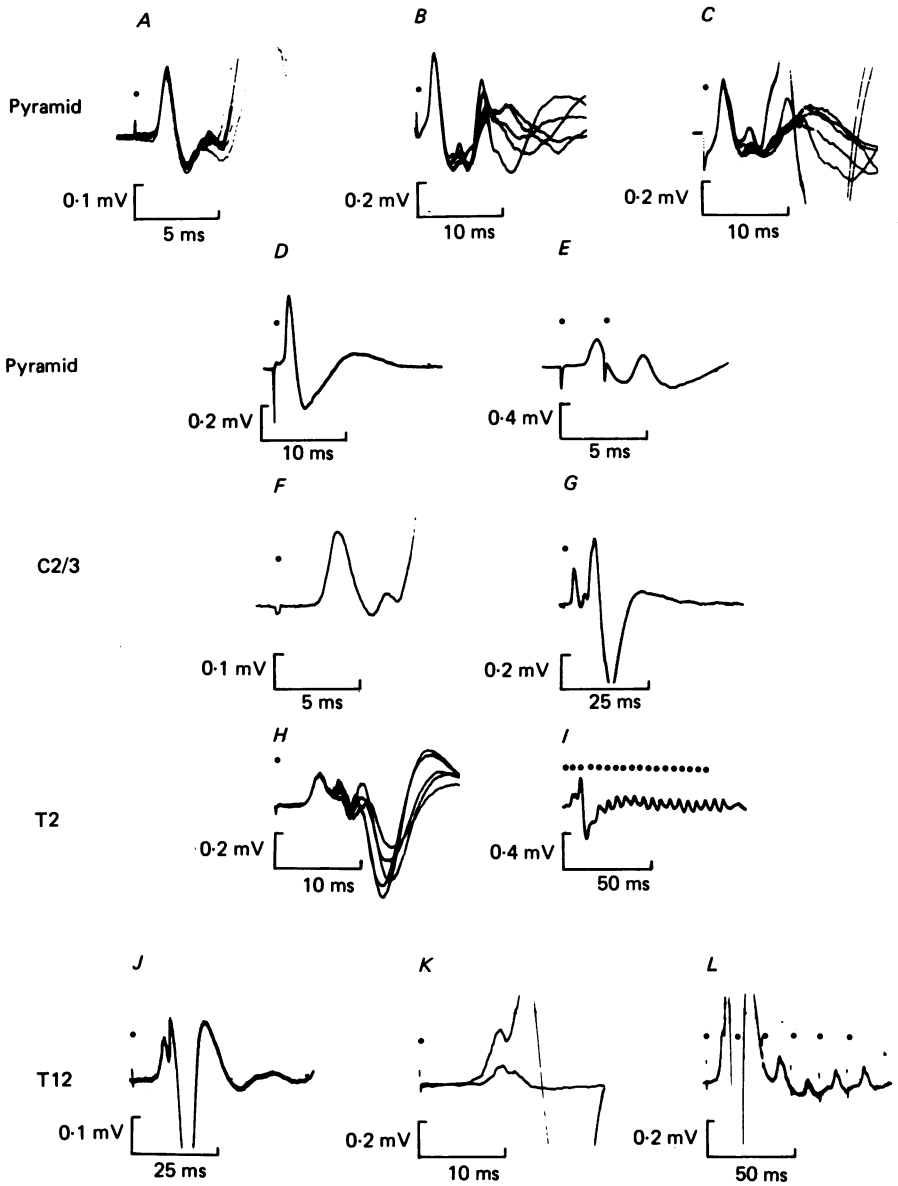

Fig. 1. Field potentials evoked on the cortical surface by supramaximal stimulation at the pyramid and at different spinal levels of the corticospinal tract. Positive up in all records. Stimuli, marked by small filled circles. *A* and *B*, five superimposed responses to single pyramidal stimuli at 1 Hz. *C*, seven superimposed responses. *A*, *B* and *C* from different animals. *D*, single response. *E*, responses to two stimuli 2·5 ms apart. *F* and *G*, single responses to stimulation at C2/3. *H*, five superimposed responses to stimulation at T2. *I*, responses to repetitive stimulation at 200 Hz. *J*, responses to one stimulus at T12. *K*, two superimposed responses to stimulation at 10 Hz; smaller response was evoked by second stimulus. *L*, stimulation with 6 pulses at 60 Hz.

It showed variations in amplitude and small variations in latency between trials and appears to correspond with wave (3P) of Porter & Sanderson. It was followed by a third positive peak with latency 7–9 ms. This large response showed very marked fluctuations in latency and amplitude (see Fig. 1*B* and *C*) and undoubtedly corresponds to wave (4P) of Porter & Sanderson. It was succeeded by a negativity which showed similar variations and this in turn was frequently followed by another wave (5P: latency to peak approximately 20 ms, not illustrated) after which the record returned to the base line.

Threshold for wave (1) ranged from 20 to 60 μA in different experiments but was constant in any one experiment. As stimulus intensity was increased the response recorded at the best point on the hemisphere reached a plateau amplitude of approximately 0·5 mV at intensities of 600–700 μA.

Fig. 1*E* shows that when two stimuli were delivered only 2·5 ms apart wave (1) was undiminished and in fact it was capable of following trains of many stimuli at 400 Hz. By contrast waves (3P), (4P) and (5P) failed completely at rates in excess of 10 Hz.

Further evidence that the different peaks were generated by different mechanisms was provided by the effect of maintenance doses of sodium pentobarbitone (5–10 mg/kg) administered to lightly anaesthetized animals; wave (1) remained constant in amplitude whilst all later events underwent a marked temporary decline which was evident within a few seconds. In addition, the potentials differed markedly in their response to anaesthetic overdose. After breathing ceased the time for the potentials to decline to zero amplitude was: wave (1), 50 sec; (3P), 25 sec; (4P), 10 sec. When, in another experiment, asphyxia was produced by tracheal occlusion the times were: wave (1), 30 sec; (3P), 15 sec; (4P), < 5 sec.

In light of this evidence there seems no doubt that as claimed by Porter & Sanderson (1964) wave (1) signals antidromic invasion of pyramidal tract neurones whilst (3P), (4P) and (5P) are generated synaptically as a result of stimulus spread to the nearby medial lemniscus and/or activation of a recurrent pathway involving axon collaterals of pyramidal tract neurones (see Discussion).

(*b*) *Single unit responses.* When micro-electrodes (see Methods) were inserted into the cortex in the region where surface potentials were largest, extracellular single unit recordings were readily obtained. The spikes were usually monophasic negative or diphasic negative–positive (see Fig. 7 for two examples) though diphasic positive–negative potentials were sometimes encountered.

Recordings were made from a total of 246 units and in respect of their responses to pyramidal stimulation they fell clearly into two groups. Units in the first group (218) yielded a single action potential which displayed a fixed threshold and a short latency which was invariant even at near threshold stimulus intensities. Such responses were invariably capable of following each of two stimuli separated by 2·5 ms. They were assumed to signal antidromic activation of pyramidal tract neurones. The frequency distribution for the latencies of the antidromic action potentials in these units is shown by the filled areas in the histogram of Fig. 2*A*.

According to Porter & Sanderson (1964) these events, occurring near synchronously in a large population of pyramidal tract neurones, give rise to wave (1). This identification was made partly on the grounds that the modal latency for single unit

responses coincided with the latency to the peak of wave (1). Fig. 2*A* shows that precisely the same finding was made in the present experiments.

A second population of twenty-eight units, encountered in the same electrode tracks, responded differently. They yielded a single action potential with variable threshold and variable (and usually longer) latency, and all failed to follow at any frequency higher than 2 Hz. These responses were presumably synaptically (i.e. orthodromically) generated. The open areas of Fig. 2*A* show the latency distribution for responses of this kind. Note that the latency range (3–9 ms) spans the period during which waves (3P) and (4P) were present on the cortical surface. When a maintenance dose of pentobarbitone was administered, synaptically driven responses rapidly (but temporarily) disappeared, a pattern of behaviour which parallels that found for waves (3P) and (4P). By contrast, like surface wave (1), antidromic single unit responses were not suppressed.

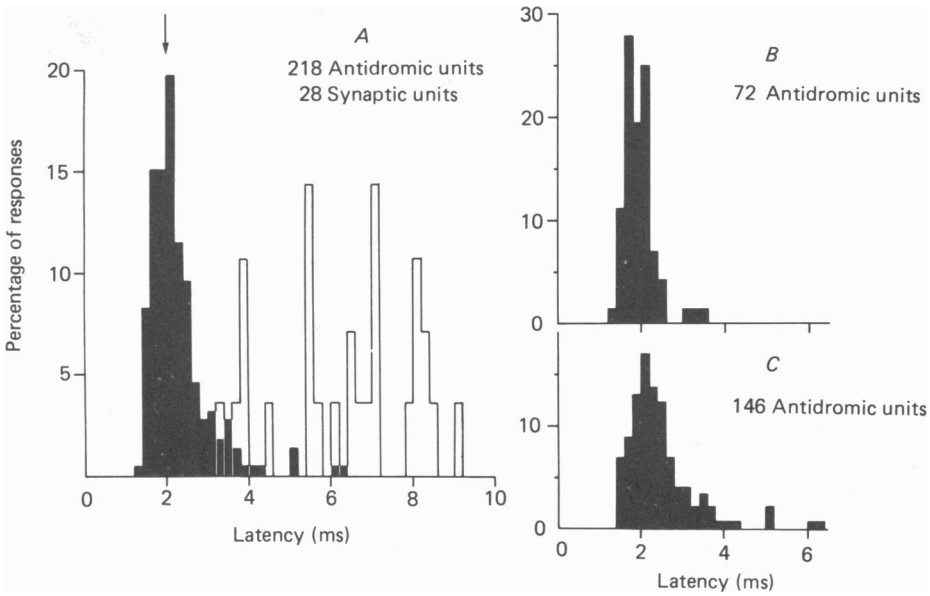

Fig. 2. Normalized latency distributions for cortical units responding to pyramidal stimulation. *A*, filled areas, antidromic responses; open areas, synaptically driven responses. Latency to peak of surface wave (1) is arrowed. *B*, latencies of antidromic responses to pyramidal stimulation for those units which were shown to project to T12. *C*, latencies of antidromic responses to pyramidal stimulation in units not tested for a projection to T12 (see text for further explanation).

Some pyramidal neurones were also tested for the presence of antidromic responses to stimulation at spinal levels (see also below) and Fig. 2*B* shows the distribution of pyramidal latencies for those units which were shown to project to T12 (i.e. cortico-lumbosacral neurones). Fig. 2*C* shows for comparison the latencies of those units recorded in experiments in which stimuli were applied at the pyramid only. This distribution presumably includes not only corticospinal axons reaching T12 but also an admixture of corticobulbar axons and corticospinal axons terminating at more rostral levels of the cord. Despite the likely presence of some cortico-lumbosacral

axons in Fig. 2*C* two differences are apparent. Firstly, the peak of the distribution in Fig. 2*B* is slightly earlier suggesting that fast axons are relatively more numerous in the cortico-lumbosacral than the 'mixed' population. Secondly, only 4% of units excitable from T12 had pyramidal latencies longer than 2·5 ms, as compared with 28% in Fig. 2*C*. This suggests that the more slowly conducting axons in the pyramid only rarely project as far caudally as T12.

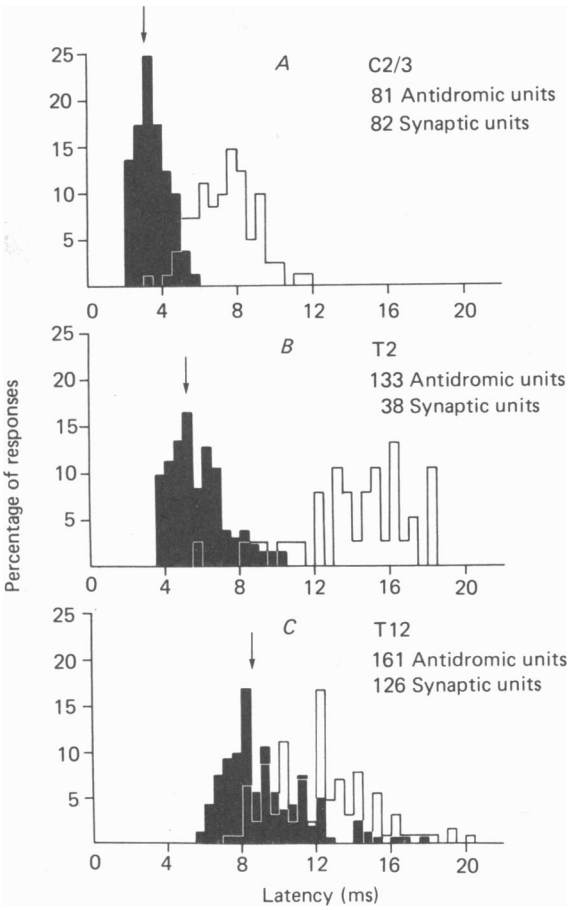

Fig. 3. Normalized latency distributions for cortical unit responses to stimulation at three spinal levels *A*, C2/3; *B*, T2; *C*, T12. Filled areas, units discharged antidromically; open areas, synaptically driven units. Latency to peak of wave (1) for each level is arrowed.

Cortical responses to stimulation in the spinal cord

(*a*) *Response latencies for surface potentials and single unit discharges.* Single shocks delivered via an electrode in the contralateral dorsal column at segmental level C2/3 evoked cortical responses very similar to those following pyramidal stimulation except that the latencies were longer (see Fig. 1*F* and *G*). From its frequency following characteristics, constant latency and amplitude, and cortical distribution

the earliest response was identifiable with wave (1). The subsequent waves, (3P) and (4P) were variable in latency and amplitude. They had latencies to peak of 6 ms and 8–10 ms respectively and failed to follow frequencies in excess of 10 Hz.

When single cortical units were recorded the results were again similar to those of pyramidal stimulation inasmuch as two distinct populations were encountered, one responding antidromically, the other driven synaptically. The frequency distribution of latencies for eighty-one antidromically driven and eighty-two synaptically driven units is shown in Fig. 3*A* by the filled and open areas respectively. Note that the mode for antidromic latencies was between 3·0 and 3·4 ms which compares well with the latency (arrowed) of the peak of wave (1) which was 3·1 ms (±0·7 ms S.D.; five experiments). Likewise the majority of synaptically driven responses occurred during the period of waves (3P) and (4P).

In many respects the results of stimulation at more caudal levels of the cord (i.e. T2 and T12) were similar to those obtained from C2/3. Fig. 1*H* shows typical responses recorded from the cortical surface following stimulation at T2 and Fig. 1*I* shows the earliest component, wave (1), following a train of stimuli at 200 Hz (it was capable of following up to 400 Hz) whilst the others are evoked only by the first stimulus. At this spinal level the latency of wave (1) was 5·2 ms (±0·7 ms S.D.; five experiments). This agrees well with the mode of the latency distribution for 133 units driven antidromically (see filled area of Fig. 3*B*), which was at 5·0–5·4 ms.

Similarly, for stimulation at T12 the latency to peak of the potential identified as wave (1) (see Fig. 1*J*) was 8·6 ms (±0·8 ms S.D.; eleven experiments) whilst the mode of the latency distribution for 161 antidromically identified units was 8·0–8·4 ms (see Fig. 3*C*). It is therefore evident that for each of the three cord levels stimulated there was a good temporal association between the peak of wave (1) and the modal latency amongst the antidromically driven cortical units. A similar association also existed between the latency to *onset* of wave (1) and the timing of the earliest antidromic responses of single units. These correlations were established by pooling the data from several experiments but they were also present in each individual experiment. This is demonstrated by Fig. 4*A* in which the latency to peak of wave (1) for each of twelve animals is plotted against the mean latency for the population of units antidromically invaded in the same experiment. The diagonal line is the regression line for this set of points and is very close to the line of equal latency.

Although the temporal correlation present at levels C2/3 and T2 between wave (1) and the antidromic unit responses was maintained at level T12 it must be emphasised that at this level the earliest response recorded from the cortical surface was not entirely attributable to antidromic invasion of corticospinal neurones. In all experiments the use of repetitive stimulation, which suppresses synaptically mediated responses, produced considerable diminution in the earliest surface potential evoked from T12. This is illustrated in Fig. 1*K* where two superimposed sweeps show the responses evoked by two trials 100 ms apart. Fig. 1*L* illustrates the further finding that the residual response was capable of following long trains of stimuli at high frequency.

The observation that the earliest response was reduced by repetitive stimulation received clarification when single unit recordings were made. As shown in the histogram of Fig. 3*C*, with T12 stimulation the latency distributions for synaptically

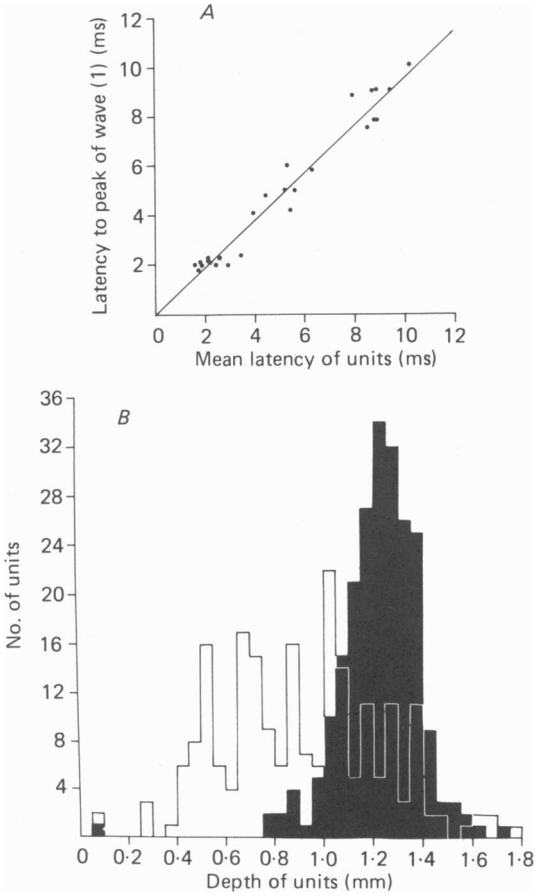

Fig. 4. *A*, temporal correlation between the latency to peak of wave (1) and the mean latency for antidromic single unit responses. Each point represents data collected during stimulation at a single site and in a single animal. Note that there is a wide range of latencies as data is represented from ten cases of pyramidal stimulation, two cases of stimulation at C2/3, six cases of stimulation at T2 and eight cases of stimulation at T12. Diagonal line is calculated regression line (gradient 0·95; vertical intercept 0·04; coefficient 0·98). *B*, depth of all cortical units responding to spinal stimulation (includes data for stimulation at C2/3, T2 and T12). Filled areas, 224 antidromic units; open areas, 215 synaptically driven units.

and antidromically mediated spikes overlap much more than for more rostral levels. Thus the first surface response is in part due to antidromic invasion of corticospinal neurones and in part to synaptically mediated events.

The most likely explanation for this change relative to the findings for more rostral stimulation is that synaptic responses to cord stimulation are mediated at least in part via an ascending path which is stimulated along with the corticospinal tract and which includes some axons with a higher conduction velocity. The dorsal column–medial lemniscal pathway is an obvious candidate and this candidature is supported by two observations. Firstly, with the cathode resting on the dorsal surface of the

cord at T12 large and variable surface potentials similar to those already described were evoked by low stimulus currents (50–100 μA) which failed to evoke wave (1). These responses completely failed at repetition rates in excess of 10 Hz. Secondly, when the electrode was advanced ventrally wave (1) first appeared at a depth of 0·7 mm. Further advance led to growth of wave (1) but to decline of the variable waves suggesting that they were evoked from structures more dorsal than those yielding wave (1).

(*b*) *Distribution and amplitude of antidromic responses on the cortical surface.* Some evidence was obtained for a topographical localisation in the origin of the corticospinal projection. When the amplitude of wave (1) was measured at many points on the cortical surface and isopotential maps were prepared (not illustrated) it was clear that large response (i.e. > 0·1 mV) to stimulation at T12 were restricted to the caudomedial part of the larger area which responded to stimulation of the pyramid. This accords well with the somatotopical organization revealed by the spatial distribution of corticospinal neurones retrogradely labelled after injection of horseradish peroxidase into different segments of the spinal cord in the rat (Ullan & Artieda, 1981).

It was evident also that wave (1) is not evoked at equal amplitude from all spinal levels. The peak amplitude of the largest responses to supramaximal stimulation was approximately 0·5 mV for pyramidal stimulation but only 0·3 mV for stimulation at T2. When wave (1) was evoked from T12 and isolated for measurement by repetitive stimulation as in Fig. 1*K* and *L*, the largest responses were only 0·15 mV. This progressive reduction in amplitude for stimulation at successively more caudal levels may reflect progressive loss of axons from the corticospinal tract along the length of the cord. A further possibility is temporal dispersion of the antidromic volley with increasing conduction distance.

(*c*) *Depth distribution of cortical unitary responses.* For each unit the depth of the micro-electrode tip at which the action potential was largest in amplitude was read off from the microdrive and the frequency distribution of depths for units recruited by spinal stimulation is plotted in Fig. 4*B*. The dark area represents antidromic responses whilst synaptically driven units are represented by the open areas. It is evident that antidromic units were in the deeper layers of the cortex, only one being less than 0·75 mm below the pial surface and most being between 1·0 mm and 1·5 mm. Synaptically driven units were more widely distributed. They were quite common as little as 0·5 mm below the surface though also present in the deepest layers.

For all stimulation sites there was no correlation between the depth of an antidromically driven unit and the latency of its response (Fig. 5; ●). This is illustrated for pyramidal stimulation (Fig. 5*A*) and also for neurones stimulated at C2/3 and T12 (Figs. 5*B* and *C* respectively). A similar observation applies to the synaptically driven units (○).

Conduction velocity of corticospinal axons

The latency of wave (1) evoked from T2 was 3·6 ms to onset and 5·2 ms to peak whilst the corresponding values for the pyramid were 1·3 ms and 2·0 ms. Since the straight-line distance between the two sites was 36 mm ($\pm$1·7 mm S.D.; six experiments) these latency values correspond to approximate conduction velocities in the 'cervical' cord of 15·7 m/s for the fastest corticospinal fibres and 11·3 m/s for

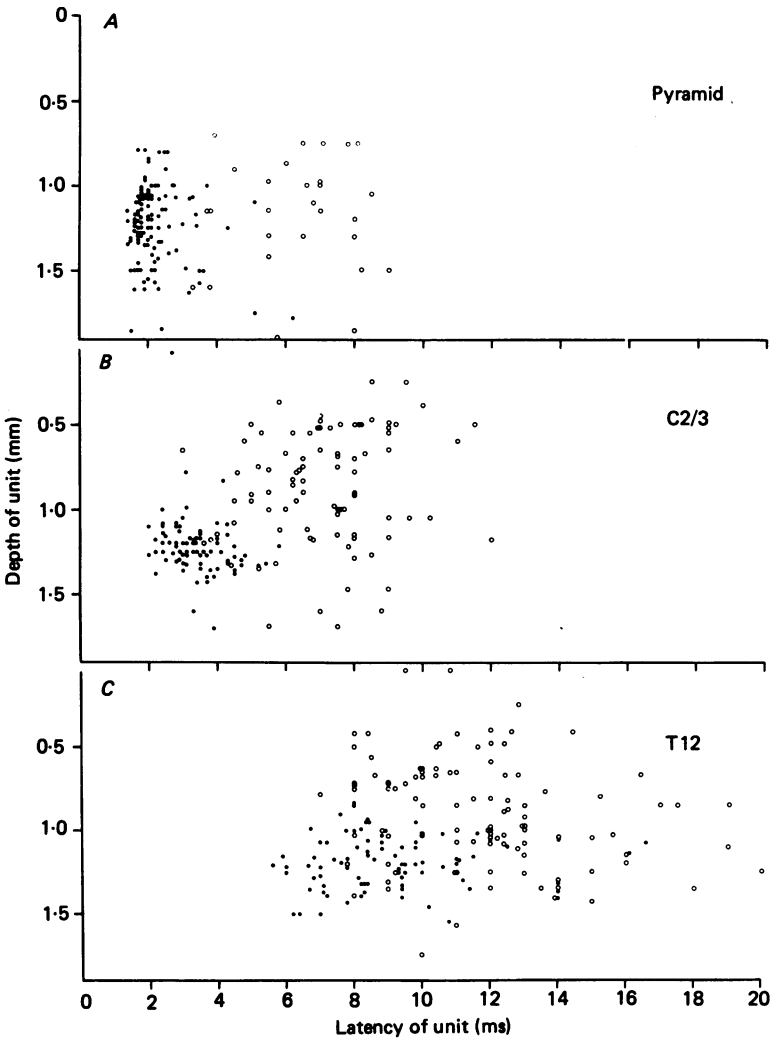

Fig. 5. Depth of cortical units plotted with respect to their latency of response. Stimulation at three sites. *A*, pyramid; *B*, C2/3; *C*, T12. ●, antidromic units; ○, synaptically driven units.

those whose activity gave rise to the peak. The corresponding values for the 'thoracic' cord (T12 to T2) were 13·7 ms and 11·0 m/s respectively.

Values for individual corticospinal axons could also be obtained when a cortical unit was antidromically activated both from the pyramid and the cord.

Care was taken in such cases to ensure that the same neurone was being activated. The spikes evoked from both sites were the same amplitude and shape and underwent parallel changes in amplitude when the position of the micro-electrode tip was changed. Sometimes the cell could be damaged with the micro-electrode and this always abolished both responses.

Fig. 6 shows frequency distributions for the conduction velocities of individual axons. Fig. 6*A* shows the values for sixty-five axons excited at both T2 and the

pyramid. The mean conduction velocity between these two sites was 11·5 m/s (±2·7 m/s S.D.). By comparison Fig. 6*B* shows the values for eighty-three axons which were excited at both T12 and T2; the mean is slightly lower at 10·5 m/s (±3·1 m/s S.D.). The over-all conduction velocity between T12 and the pyramid is shown for seventy-two axons in Fig. 6*C*; mean 11·4 m/s (±2·9 m/s S.D.). The experimental procedure employed was to begin by searching the cortex for antidromic units responding to stimulation at T12. When such a unit was encountered, and its latency determined, the latencies of its response to stimulation at T2 and the pyramid were also determined. As a result most of the values for the T2–pyramid portion of the cord (Fig. 6*A*) are for corticospinal axons which descended at least as far as T12.

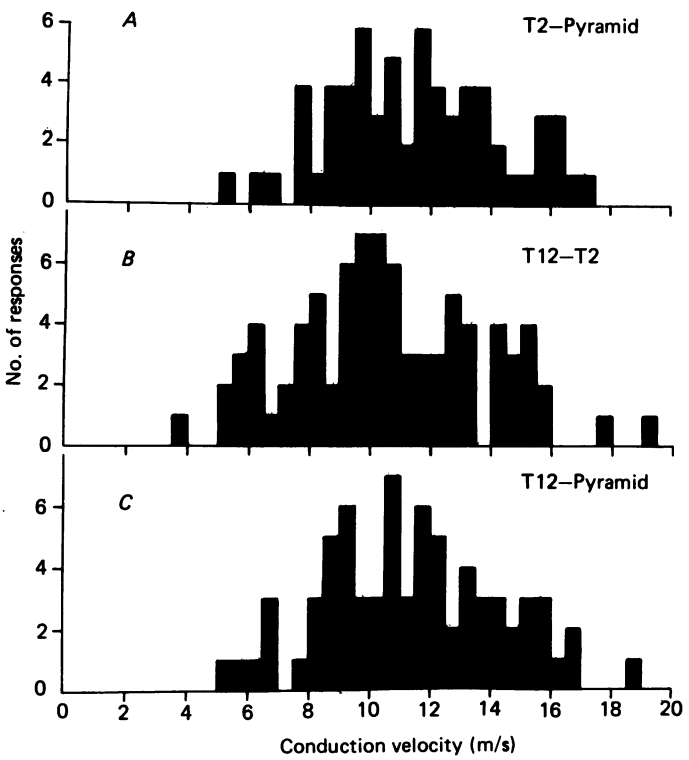

Fig. 6. Conduction velocities of single axons between *A*, T2 and the pyramid (sixty-five axons); *B*, T12 and T2 (eighty-three axons); *C*, T12 and the pyramid (seventy-two axons).

However, twelve of the sixty-five axons in Fig. 6*A* could not be recruited by stimulation at T12 and therefore probably terminated between T2 and T12. Their conduction velocities ranged from 8·4 to 17·1 m/s and therefore fell within the range for the other (i.e. cortico-lumbosacral) axons in Fig. 6*A*.

In fifty-three units excitable from T12 separate conduction velocities were calculated for the T2–pyramid and T12–T2 portions of the axon. Fig. 7*A* shows one such unit responding to a single shock delivered (in descending order) to pyramid, T2 and T12 and Fig. 7*B* shows that at each level responses could be evoked by each of 2 shocks, 2 ms apart. In this unit the conduction velocity between T12 and T2 (12·5 m/s) was almost the same as that between T2 and the pyramid (13·1 m/s).

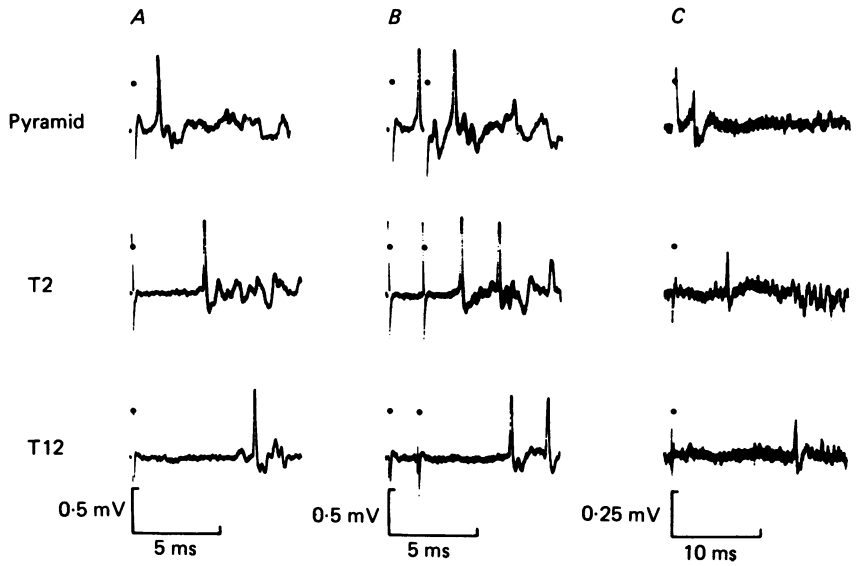

Fig. 7. *A* and *B* show responses of one antidromically driven cortical unit when stimulated at the pyramid, T2 and T12. *A*, responses to single stimuli; *B*, responses to paired stimuli with separation 2 ms. Conduction velocity calculated for the axon between T2 and the pyramid was similar to that between T12 and T2. *C*, responses of a second unit to single stimuli; conduction velocity calculated for T12–T2 was considerably slower than that for T2–pyramid (see test for further explanation). Negative up.

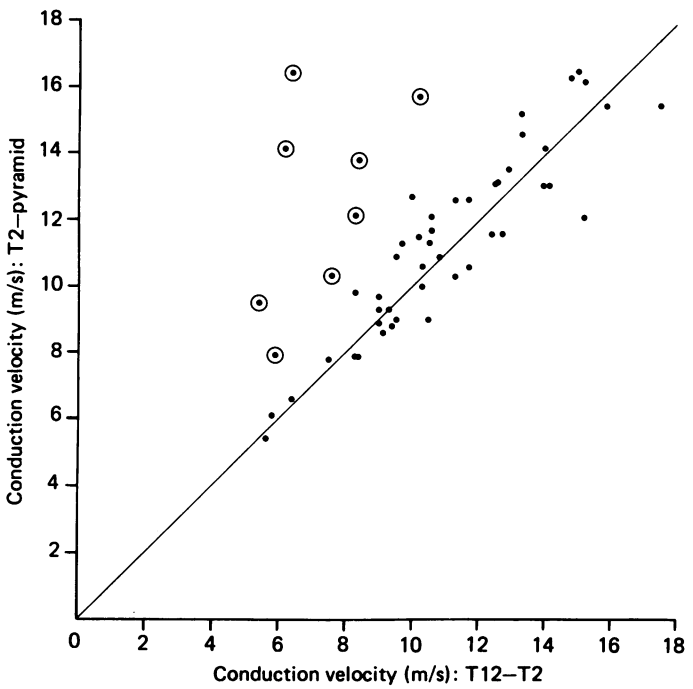

Fig. 8. Conduction velocity between T2 and pyramid plotted against conduction velocity of same axons between T12 and T2. The eight encircled points represent axons for which the conduction velocity was over 25% slower in the more caudal portion of the cord. Diagonal is line of equal velocity.

However, the different unit shown in Fig. 7*C* conducted considerably more slowly in the 'thoracic' cord (T12–T2: 5·4 m/s) than in the 'cervical' cord (T2–pyramid: 9·5 m/s).

In Fig. 8 the 'cervical' and 'thoracic' conduction velocities are compared for each of the fifty-three units and it is clear that in the majority of cases the values fall on or close to the line of equality. However, the conduction velocity for eight axons was at least 25 % slower in the 'thoracic' cord and in these cases (encircled points) it seems likely that real slowing occurred as the axons descended.

Small departures from equality are probably ascribable to the inevitable inaccuracies which attend the measurement of conduction distances. In particular no allowance was made for the deviation from a straight-line course which must occur in the pyramidal decussation. It is likely, therefore, that the calculated conduction velocities are underestimates and the degree of underestimation will be greater for the 'cervical' values. However, the errors are unlikely to be substantial because the conduction distances were considerable (means of 36 mm for T2–pyramid and 41 mm for T12–T2).

DISCUSSION

Cortical responses to pyramidal stimulation

The cortical surface response evoked from the pyramid in these experiments was very similar to that recorded by Porter & Sanderson (1964) with the small exception that little sign was seen of their wave (2). Results from single unit recordings were consistent with their hypothesis that wave (1) signals antidromic invasion occurring near-synchronously in a large number of pyramidal tract neurones. Porter & Sanderson reported wave (2) to be a small positive peak at a latency of about 3 ms which notched the downstroke of wave (1), followed repetitive stimulation at 200 Hz and coincided in latency with single unit antidromic spikes. In the experiments reported here single units with appropriate latencies were recorded (Fig. 2*A*) despite the absence of wave (2). However, both Porter & Sanderson (1964) and Ohta (1968) found that wave (2) was not invariably present and in the rabbit, Chang (1955) encountered an analogous wave only when the cerebral cortex was cooled to 20–23 °C; at physiological temperatures it was obscured by the negativity which follows wave (2).

Ohta (1968) recorded the mass antidromic response at different depths in the rat cortex and found that wave (2) reversed polarity at a depth of 1·6 mm whilst wave (1) reversed at 2·0 mm. He considered that wave (2) was caused by antidromic invasion of pyramidal tract neurones with slower axons and was situated more superficially in the cortex. A similar conclusion was reached by Towe, Patton & Kennedy (1963) who made single unit recordings in the cat and found that the shortest latency antidromic responses occurred in layer V and that longer latency responses occurred in layer III. However, in the present experiments there was no such correlation between the depth and the latency of units driven antidromically from either the pyramid (i.e. pyramidal tract neurones) or the spinal cord (i.e. corticospinal neurones). It is consistent with our observations that Ullan & Artieda (1981) have reported that rat corticospinal neurones retrogradely labelled using horseradish peroxidase were found only deep in the cortex (in layer Vb). Similarly, Deschenes Labelle & Landry (1979) have found pyramidal tract neurones are restricted to layer V in the cat.

Regarding the late and variable waves on the cortical surface, Porter & Sanderson (1964) demonstrated that they coincided with synaptically mediated discharges in cortical neurones other than pyramidal tract neurones and we have confirmed this finding. These authors also discussed the possible mechanisms which might generate such discharges. They include cortical activation via intracortical recurrent collaterals of the pyramidal axons and via pyramidal collaterals to ascending pathways. Alternatively, the medullary stimulus may spread to excite the medial lemniscus. The importance of this last possibility was later emphasised by the work of Stone (1972) who selectively diminished the late waves by sectioning the medial lemniscus in the medulla. It is also reinforced by the present experiments because apparently identical late waves could be evoked by stimulation in the dorsal part of the dorsal columns at intensities too weak to evoke a wave (1) response. By contrast, when the same stimuli were delivered deeper in the cord, where they succeeded in evoking wave (1), the late waves were smaller.

Conduction velocities in the corticospinal tract

Our most important findings relate to the conduction velocities of corticospinal axons. Stimuli applied to the medullary pyramid inevitably excite corticobulbar axons so that measurements of antidromic latency from this site allow deduction only of a limit above which corticospinal axons are unlikely to conduct. Moreover, estimates of the conduction distance from pyramid to cortex are necessarily very approximate. As a result, little evidence has previously existed concerning corticospinal velocities in the rat. The only direct measurements are of a few axons in the upper cervical cord (McComas & Wilson, 1968) and these results differ markedly from those of Elger *et al.* (1977), who deduced a velocity of 60 m/s for the fastest fibres (see below). Both from the latency of the antidromic response on the cortical surface and on the basis of single unit recordings we conclude that the fastest fibres conduct at somewhat less than 20 m/s whilst the fibres contributing to the peak of wave (1) conduct at about 11 m/s. The value for the fastest unit we encountered was 19·1 m/s.

It is evident that our results are in reasonable agreement with those of McComas & Wilson (1968) who found a range of 7·6 m/s to 10·8 m/s but conflict directly with those of Elger *et al.* (1977). It is therefore necessary to discuss the results obtained by the latter group to determine whether reconciliation is possible.

Following cortical stimulation Elger *et al.* (1977) recorded a field potential from the cord dorsum at L3/4 which had a latency of 1·7 ms to peak and which followed repetitive stimulation at 300 Hz. Conversely, when the dorsal surface of the cord was stimulated at L3/4 a cortical evoked potential was recorded with similar latency and frequency-following characteristics. In addition, Janzen, Speckmann, Caspers & Elger (1977) recorded excitatory post-synaptic potentials (e.p.s.p.s) (apparently monosynaptic) in lumbar motoneurones with latencies as short as 1·7 ms following cortical stimulation. Elger *et al.* concluded that an uninterrupted corticospinal pathway exists to the lumbar cord in which the fastest fibres conduct at about 60 m/s. However, as they noted, electron microscopy indicates that the tract consists of axons no larger than 3·7 μm in diameter (Dunkerley & Duncan, 1969) and application of the Hursh factor (6 m/s per μm; Hursh, 1939) to such fibres would yield maximum velocities of about 22 m/s. Elger *et al.* therefore suggested that the Hursh factor is

not applicable to corticospinal axons and that some much higher factor is required. However, a study in the cat by Towe & Harding (1970) has suggested that the Hursh factor errs on the high side and that a factor of 4·72 is more appropriate. It may be noted here that the Hursh factor gives a maximum conduction velocity of 22 m/s whilst the factor proposed by Towe & Harding would yield a value of 17·5 m/s. Both these values are close to the velocity for our fastest fibres. However, the mode of the fibre diameter spectrum for the rat pyramid occurs at 0·5–1·0 μm (Dunkerley & Duncan, 1969) which corresponds to approximate conduction velocities of 3–6 m/s (Hursh) or 2·4–4·7 m/s (Towe & Harding). These values are substantially lower than the mode of the velocities in the present study, but this discrepancy can be accounted for if the micro-electrode technique exhibits substantial bias towards cells with large diameter axons. This is indeed likely to be the case as the existence of a large bias has invariably been inferred in electrophysiological studies of the pyramidal tract in the cat (e.g. Towe & Harding, 1970). Since very similar values of conduction velocity were obtained in the present experiments from the latencies of the antidromic field potentials a similar bias presumably exists for this type of response.

Though the above suggests that our estimate of maximum conduction velocity is substantially correct it does not of course account for the results of Elger *et al.* (1977). It may be noted however, that these workers employed computer averaging techniques capable of resolving very small signals recorded from the brain surface. It is therefore possible that the antidromic potentials they recorded from the cortical surface were in fact generated at a distance (i.e. beneath the cortex) and signalled transmission in another pathway (e.g. rubrospinal or reticulospinal). This suggestion gains support from a recent study (Armstrong & Drew, 1980) which has shown that, in the small brain of the rat, tract waves generated in the medulla can easily be recorded from the surface of the cerebellum even without averaging.

As regards the tract waves which Elger *et al.* recorded from the cord surface following stimulation of the cortical surface, it is possible they were generated by synaptic or direct excitation of a descending pathway subcortical in origin and conducting substantially faster than the corticospinal tract. Such paths do exist, for Shapavolov & Gurevitch (1970) stimulated the medullary reticular formation and recorded a tract wave from the dorsal surface of the lumbar spinal cord with a latency of 1·3–2·1 ms to peak which followed repetitive stimulation at up to 500 Hz. This path conducted at a mean velocity of 65 m/s and evoked monosynaptic e.p.s.p.s in lumbar motoneurones with latencies short at 1·6 ms (cf. the 1·7 ms of Elger *et al.* 1977).

Eight out of fifty-three of our corticospinal axons (i.e. approximately 15 %) showed substantially slower 'thoracic' (T12–T2) than 'cervical' (T2–pyramid) conduction velocities. Such a change presumably reflects a decrease in axonal diameter and in this connexion it may be noted that in the cat, Shinoda & Yamaguchi (1978) have provided electrophysiological evidence that corticospinal axons in the cat may provide collaterals to different segmental levels and that the provision of branches can be associated with a reduction in the conduction velocity of the stem axon. Future studies should show whether the slowing we have demonstrated in some axons in the rat is due to a similar phenomenon or whether tapering can occur even in the absence of collateralization.

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REFERENCES

ARMSTRONG, D. M. & DREW, T. (1980). Responses in the posterior lobe of the rat cerebellum to electrical stimulation of cutaneous afferents in the snout. *J. Physiol.* **309**, 357–374.

BROWN, L. T. (1971). Projections and terminations of the cortico-spinal tract in rodents. *Exp. Brain Res.* **13**, 432–451.

CHANG, H.-T. (1955). Cortical response to stimulation of medullary pyramid in the rabbit. *J. Neurophysiol.* **18**, 332–352.

DESCHENES, M., LABELLE, A. & LANDRY, P. (1979). Morphological classification of slow and fast pyramidal tract cells in the cat. *Brain Res.* **178**, 251–274.

DUNKERLEY, G. B. & DUNCAN, D. (1969). A light and electron microscopic study of the normal and the degenerating cortico-spinal tract in the rat. *J. Comp. Neurol.* **137**, 155–184.

ELGER, C. E., SPECKMANN, E.-J., CASPERS, M. & JANZEN, R. W. C. (1977). Corticospinal connections in the rat. I. Monosynaptic and polysynaptic responses of cervical motoneurons to epicortical stimulation. *Exp. Brain Res.* **28**, 385–404.

FIFKOVA, E. & MARSALA, J. (1967). Stereotaxic atlas of the rat. In *Electrophysiological methods in biological research*, ed. Bures, E. J., Petran, M., Zachar, J. & Hahn, P. London: Academic Press.

HURSH, J. B. (1939). Conduction velocity and diameter of nerve fibres. *Am. J. Physiol.* **127**, 131–139.

JANZEN, R. W. C., SPECKMAN, E.-J., CASPERS, H. & ELGER, C. E. (1977). Corticospinal connections in the rat. II. Oligosynaptic and polysynaptic responses of lumbar motoneurons to epicortical stimulation. *Exp. Brain Res.* **28**, 405–420.

MCCOMAS, A. J. & WILSON, P. (1968). An investigation of pyramidal tract cells in the somatosensory cortex of the rat. *J. Physiol.* **194**, 271–288.

OHTA, M. (1968). Cortical motor function and the antidromic cortical response to stimulation of the medullary pyramidal tract in the rat. *Jap. J. Physiol.* **18**, 100–124.

PORTER, R. & SANDERSON, J. H. (1964). Antidromic cortical response to pyramidal-tract stimulation in the rat. *J. Physiol.* **170**, 355–370.

SHAPAVOLOV, A. I. & GUREVITCH, N. R. (1970). Monosynaptic and disynaptic reticulospinal actions on lumbar motoneurons of the rat. *Brain Res.* **21**, 249–263.

SHINODA, Y. & YAMAGUCHI, T. (1978). The intraspinal branching patterns of fast and slow pyramidal tract neurons in the cat. *J. Physiol. (Paris)*, **74**, 237–238.

STONE, T. W. (1972). Cortical responses to pyramidal tract stimulation in the rat. *Expl. Neurol.* **35**, 492–502.

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

TOWE, A. L., PATTON, M. D. & KENNEDY, T. T. (1963). Properties of the pyramidal system in the cat. *Expl. Neurol.* **8**, 220–238.

ULLAN, J. & ARTIEDA, J. (1981). Somatotopy of the corticospinal neurons in the rat. *Neurosci. Lett.* **21**, 13–18.