AFTER-POTENTIAL OF SPINAL AXONS IN VIVO*

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This investigation is concerned with certain properties of the action potential in tracts of the central nervous system. During the course of other studies (16, 3) it became important to know the after-potential sequence of rapidly conducting tract fibers in the intact spinal cord. This paper presents a method for obtaining this information and evidence for the existence in dorsal column axons of an after-potential sequence which is significantly different from that of peripheral nerve *A* fibers. In succeeding papers (17) the role of the dorsal column after-potential in producing intramedullary and dorsal root current flows is examined. Study of these currents affords an experimental test of predictions which follow directly from the conclusions of the present paper on the form of the dorsal column after-potential. Finally in another paper (3) are presented for comparison the results of a direct examination of the after-potential sequence of spinal funiculi *in vitro*. In addition, the findings of a general survey of the properties of spinal funiculi are presented there.

Technique

The cats (84 in all) used for this and the subsequent study (17) were, as a rule maintained under sodium pentobarbital anesthesia (27 mg./kilo) since suppression of transynaptic neural activity as well as of the dorsal column relay potential was desired. Critical experiments were also performed in unanesthetized cats not less than 1 hour following decapitation or decerebration under ether. After laminectomy, mineral oil was layered over roots and cord to a depth of several centimeters and maintained within 0.5° C. of rectal temperature (37.5 ± 2°C.) by means of radiant heating.

Electrodes of bright silver or chlorided silver were used. Monophasic rectangular stimulating pulses (0.1 to 0.5 msec. duration), isolated from ground by Schmitt radio frequency coupling units (Grass) were delivered as constant current through ⅓ to 1 megohm resistors in series with the preparation. When stimulating pulses were applied through two pairs of electrodes from two independent stimulators the circuits

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were checked to ensure that no interaction occurred between them. The preparation either was used ungrounded except through the 2 megohm input inpedance of the recording circuit or was grounded indifferently in muscle. The recording circuit, with push-pull RC coupled amplifiers, had a time constant of 2.2 seconds, a high frequency response with less than 10 per cent attenuation at 13,000 C.P.S., 50 per cent attenuation at 20,000 C.P.S., and an in-phase rejection of 700 up to 10,000 C.P.S.

Preliminary Considerations

Theoretical Basis of a Method for Identifying the After-Potential of Spinal Axons

Study of the recovery of excitability following impulse conduction has provided a successful method for determining by indirect means the form of peripheral nerve after-potentials in the intact state in which direct recording of potential is complicated by many factors (5, 6). However, satisfactory correspondence exists between excitability and after-potential following refractoriness only when there are present those labile properties of nerve related by Lorente de Nó to the L fraction of membrane potential (12).

Provided the effects of relayed activity can be controlled and if two important propositions are fulfilled, then a similar investigation becomes possible for tracts of the intact spinal cord. The propositions are: first, that variation of excitability in axons of spinal tracts is directly proportional to variation in membrane potential (*i.e.*, there is a large L fraction in central axons). Second, that there exists a region where spinal tract fibers are free from the polarizing action of externally developed currents during their recovery from a conditioning volley.

It may safely be concluded that the conditioning effects of activity relayed in the dorsal column fibers will be minimal since in a warm spinal cord under mineral oil and in the presence of sodium pentobarbital the dorsal column relay potential (9) is only a fraction of the size of the initial tract volley (see Fig. 1, right).

The validity of proposition 1 has been shown by Gasser and Grundfest (5), by Graham and Lorente de Nó (6), and by Lorente de Nó (12) for peripheral nerve. Grundfest and Magnes (7) have similarly demonstrated for dorsal root a close correlation between excitability and electrotonic potential. But more direct evidence is presented in this paper which shows that a satisfactory correspondence exists between dorsal column excitability and dorsal root electrotonus.[1] Finally, excellent correspondence between after-potential and recovery of excitability has been demonstrated directly for excised axons of the central nervous system (3). The first proposition is therefore strongly supported and attention may be turned to the second proposition.

[1] Since dorsal column excitability parallels dorsal root electrotonic potential which corresponds to dorsal root excitability (see section on Results), a most unlikely set of properties would have to be supposed to prevent a similar correspondence between dorsal column membrane potential variations and dorsal column excitability.

Whereas in blood-perfused peripheral nerve post-spike excitability changes can be directly assigned with assurance to corresponding changes arising in the conditioned axons, this cannot be done *a priori* in the spinal cord. In addition to the variation in excitability intrinsic to the recovery of the conditioned tract fibers there may occur excitability changes induced by activity in nearby structures. Success in avoiding such extrinsic effects can be assured only when a large tract spike can be obtained in the absence of subsequent slow potentials thus indicating that the recovery of the activated fibers is not being modified by extraneous current flows. The statements above follow directly from the theorems of Helmholtz as presented by Lorente de Nó (12–14). These emphasize that there must be a difference in membrane potential existing along a cell in order for it to generate external currents, but that even in the absence of such currents there may be large variations in membrane potential if the variations extend uniformly over the cell as do after-potentials.

Success in fulfilling proposition 2 could also be assured if there were anatomical evidence for the existence of a sufficient length (5 to 6 cm.) of tract having a simplicity of structure approaching that of peripheral nerve (*i.e.* lacking in collaterals whose activity could modify excitability of parent fibers directly, or indirectly through the activation of interneurons). Both anatomical and electrical evidence are available to indicate that thoracic dorsal columns fulfill the desired conditions.

Anatomical Evidence.—Anatomical evidence indicates that collaterals of ascending dorsal column fibers are given off in greatest density within a few segments of the level of root entry and are sparse in the thoracic region (2, 15). This is strikingly confirmed by the ease with which dorsal columns are peeled away from the underlying gray matter in the thoracic region (3, 16), whereas by contrast collaterization in the lumbar (and cervical) region is so dense that this procedure is virtually impossible there. Therefore, in the lumbar cord a significant area of afferent fiber membrane is devoted to the collaterals as well as the parent fibers. In the thoracic cord, however, the system will be far more homogeneous in its membrane properties.

Electrical Evidence.—Hughes and Gasser demonstrated in 1934 that the negative intermediary dorsal cord potential showed more rapid spatial decrement than the preceding spike potential when recorded at successively greater distances rostral to the root level of entry of the afferent volley (8). The fact that the slow cord potentials are more closely localized to a few cord segments about the region of root entry than is the spike is particularly striking since the spike potential, because of its short-wave length, will suffer greater reduction in size through temporal dispersion. In spite of this, one finds on examination that there is a limit 6 or more cm. above the root level of entry where there are no longer any recordable voltages developed by current flows at the cord dorsum after the spike potential is over.

Fig. 1 shows the result of recording several centimeters rostral to the point

of origin within the cord an afferent volley in lumbar cord (left) and in lower thoracic cord (right). In the lumbar region stimulation of the cord or of a lumbar dorsal root sets up large intermediary potentials (4) following the spike. These indicate that significant post-spike currents are flowing. In the thoracic region stimulation of the cord or of a lumbar dorsal root sets up a virtually pure tract volley with no sign of post-spike current flows. It can be concluded from this observation that in the thoracic cord, following conduction of a spike, events extrinsic to the dorsal column parent fibers are not applying significant currents to them and further that, to within the limits of detection, the acti-

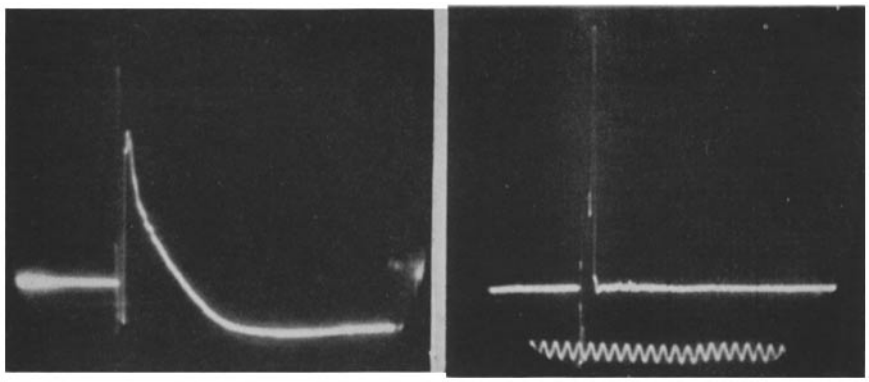

FIG. 1. Left: Maximal dorsal cord response following stimulation DRL_7. Recorded 1.5 cm. rostral to level of root entry. Note relatively large size of slow potentials compared to size of spike potential.

Right: Dorsal cord response led from dorsal columns at T_{10} following stimulation applied to lumbar cord. Post-spike potentials are absent although the tract volley is well developed. Also note the lack of significant relayed activity following the spike. Both recordings monopolar. Time: 1000 C.P.S. Left sweep approximately twice as slow as right.

vated fibers have uniform properties of membrane recovery. The second proposition, too, is therefore strongly supported.

Satisfactory evidence in support of these two propositions having been assembled, the following experimental design for study of post-spike excitability was established.

Experimental Methods

Two experimental methods were used. In the first, method A, two adjacent filaments of a lumbar (L_6 or L_7) or sacral (S_1) dorsal root cut distally were each placed on a pair of recording electrodes (diagram of Fig. 2A). One rootlet, hereafter called the active rootlet, was also placed on a pair of stimulating electrodes through which supramaximal conditioning stimuli were delivered at regular intervals (1/sec.) through-

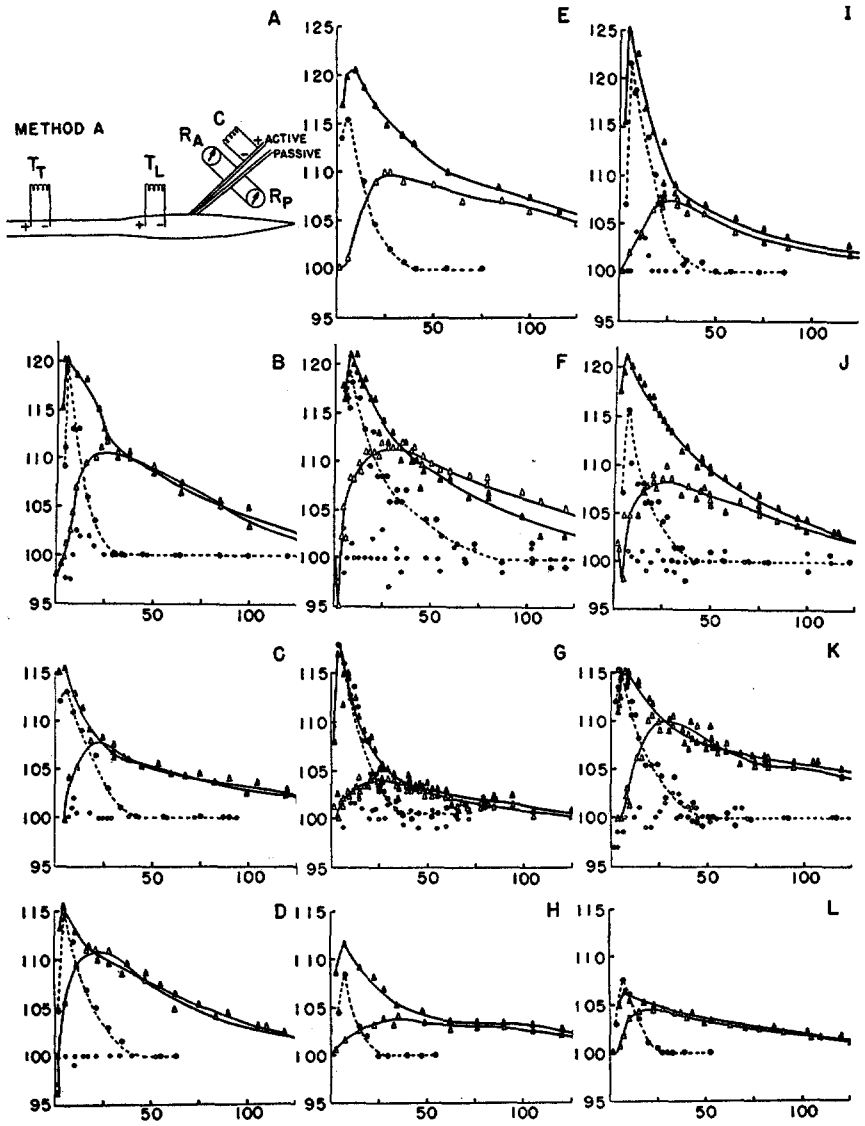

FIG. 2. Method A. In A is diagrammed the electrode placement on cord and roots to obtain the combinations for stimulating and recording described in the text. Thoracic region at left, lumbar intumescence with two entering rootlets at right. Plus and minus signs indicate respectively anode and cathode of stimulating circuit.

Solid triangles, recording from conditioned rootlet while testing excitability in lumbar cord; open triangles, recording from rootlet adjacent to that conditioned while testing lumbar cord; solid circles, recording from conditioned rootlet-testing thoracic cord; open circles, recording from adjacent rootlet-testing thoracic cord. Abscissa, time in milliseconds. Ordinate, per cent excitability with 100 equal to resting excitability. (These coordinates are used for all excitability data throughout this paper.) Each point is an average of 6 to 10 readings compared repeatedly with control value (but in F, G, J, and K every reading taken at 1/sec. is plotted). The data are uncorrected for differences in resting thresholds at the two testing sites.

out the experiment. Two additional pairs of stimulating electrodes were placed on the surface of the dorsal columns with their axes parallel to the longitudinal axis of the cord for purposes of testing the excitability of the longitudinally oriented fibers of the dorsal columns. The position of these electrodes was thus arranged in accordance with Rushton's calculations of the optimal angle for excitation between stimulating field axis and the axis of longitudinal axons (18).

One of these pairs of stimulating electrodes (T_L) was placed gently on lumbar dorsal column with the cathode proximal to the active root but 1.5 to 2 cm. above its level of entry into the cord in order to avoid any possible interference by electrotonic effects of root activity. The other pair (T_T) was placed on thoracic dorsal column with the cathode also proximal to the conditioned root but 6 to 12 cm. cranial to it.

A supramaximal conditioning volley was sent orthodromically into the spinal cord by a shock to the active rootlet (electrodes *C* of Fig. 2A). The changes in excitability produced in the dorsal column by this volley were determined in both lumbar and thoracic regions by sending small testing volleys (20 to 50 per cent of maximal elicited by stimulus pulses of constant current strength at electrodes T_L or T_T) antidromically down the dorsal column and measuring their variation in height at the rootlets. By recording the testing volleys from the rootlets which had been maximally conditioned (R_A Fig. 2A) the excitability changes were determined for the dorsal column axons which had carried the conditioning volley. By recording the testing volley from the rootlet adjacent to the one conditioned (R_P, Fig. 2A) excitability changes were determined for dorsal column axons which had not carried the conditioning volley.

For purposes of direct comparison each of the curves describing the relation between the time interval between conditioning and testing volleys and the change in the size of the testing volley was calibrated after the method of Graham and Lorente de Nó (6) in terms of a stimulus-response scale experimentally derived for each curve. The change in size of the testing volley was thereby converted into the change in current strength required to produce an equivalent change in volley size under conditions of constant resting excitability. Since the thresholds of the individual axons comprising the dorsal column are distributed in a narrow range relative to their mean value (3, 17) and since their action potential properties are homogeneous throughout the population (3, 17), the excitability change determined in this way is equivalent to that which occurs in the individual axons (see Lorente de Nó (12)[2]). Threshold change calibrated in this manner has been expressed conventionally as a per cent of control value ($\frac{\Delta T}{T} \times 100$ per cent). The per cent change in threshold is then independent of variations from one preparation to another in the fraction of stimulating current effectively delivered to the axons (*e.g.* resulting from differences of shunting or electrode placement). Excitability changes in this paper are therefore expressed in the conventional way as percentages.

While per cent excitability changes can be compared meaningfully within one homogeneous tissue at different times, such a direct comparison is not necessarily valid from one tissue to another. For in the latter case one must know the magnitudes of the mean control thresholds (the denominator T of the ratio $\frac{\Delta T}{T} \times 100$ per cent)

[2] Lorente de Nó (12), Vol. 132, p. 90.

relative to each other in addition to a knowledge of the per cent changes in excitability. The importance of this statement is apparent when it is realized that in this analysis we must compare the excitability changes of dorsal column axons at different places along their longitudinal extent (in lumbar and thoracic regions). Fortunately, there is much experimental evidence to show that the small to moderate decrease of fiber diameter and conduction velocity in the thoracic cord will result in a higher threshold there. Therefore an increase of excitability following conduction of an impulse in thoracic cord would be greater, relative to an increase in lumbar cord, than a direct comparison of the percental data would indicate. The significance of this will be discussed in the section on Results.[3]

A description of the second approach (method B) follows. Pairs of stimulating electrodes were placed on the dorsal columns of both thoracic and lumbar cord, and recording electrodes were placed a few centimeters away from each (Fig. 3). The excitability changes for lumbar or thoracic dorsal columns were then determined by sending conditioning and testing pulses through the same pair of stimulating electrodes and recording the variation in height of the testing volley at the neighboring recording electrodes. With a testing volley which at peak facilitation is smaller than the conditioning volley the total excitability change in the conditioned axons is observed. This consists both of excitability changes intrinsic to the recovery processes of these axons and also of those induced by activity in adjacent cells or in contiguous dissimilar portions of the same cell. However, by conditioning with an intensity sufficient to activate only a part of the neuron pool, a testing stimulus can be used sufficiently strong to fire not only all the conditioned fibers but also some of those in the immediate vicinity which have not been conditioned. The response to such a testing shock will vary only as the excitability of the unconditioned fibers since the testing shock is made to fire all the conditioned fibers (after recovery from refractoriness) and since the amplitude of response per unit axon remains constant whether or not the fiber has conducted the conditioning volley (6, 3). In general the smallest practical conditioning volley was used in thoracic cord while a moderately large one was used in lumbar cord. Again the data were calibrated in terms of equivalent stimulus current strength.

The only purpose of the analysis of method B is to serve as a rough check on method A. However, it is to be noted that while method A tested excitability changes in only those fibers of root origin, method B undoubtedly tested many propriospinals as well.[4]

[3] Since the fiber populations have a small scatter of thresholds in each of the cord regions a rough estimate of their threshold difference may be gained by comparing their maximum conduction velocities. The data of Lloyd and McIntyre (11), following cutaneous nerve stimulation, show up to a 12 per cent decrease in thoracic cord. The data of Gasser and Graham (4) and our own, following root stimulation, show up to 50 per cent decrease.

[4] As in all such excitability studies, there is contained the implicit assumption that change in spike height at the recording electrodes is roughly proportional to the number of axons carrying a spike potential. In addition it is assumed that there is no significant change in the size of the individual spike potential carried by each axon after refractoriness is over. This has been shown to be true for mammalian peripheral nerve (6) and for dorsal columns *in vitro* (3). Since in the present experi-

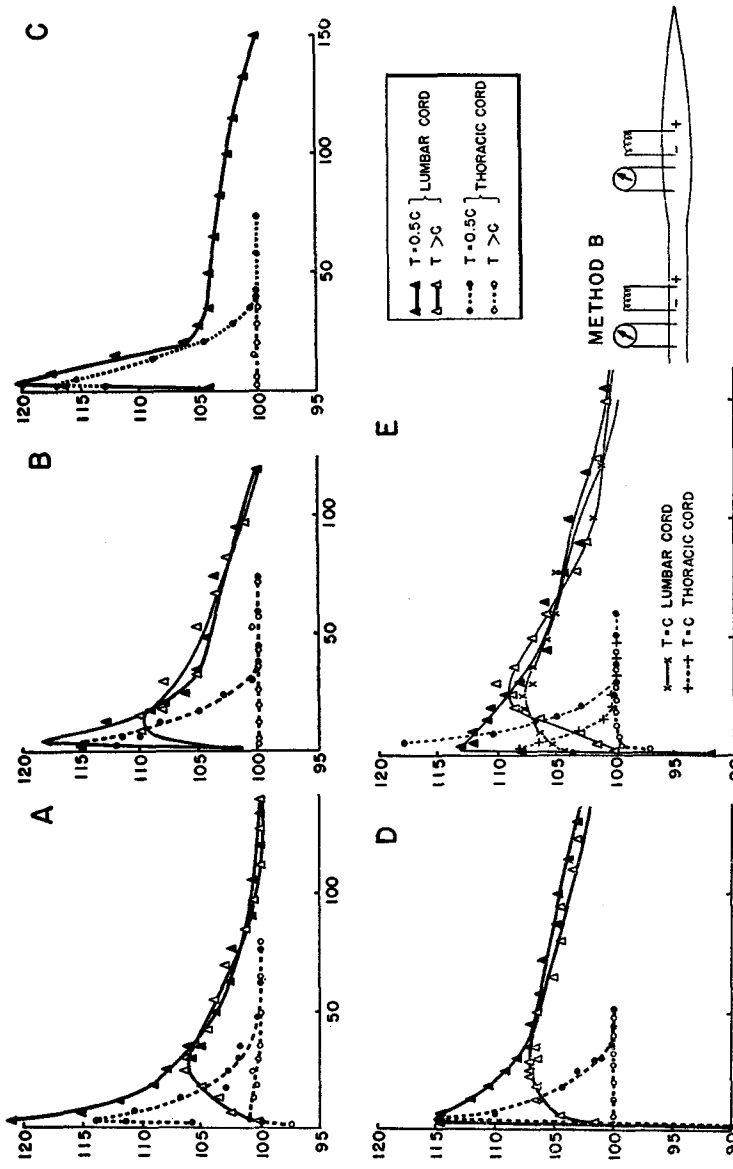

FIG. 3. Method B. Conditioning and testing volleys delivered through the same pair of electrodes on cord dorsum while recording the amplitude of response a few centimeters away. Lower right shows the electrode placement on thoracic (left) and lumbar (right) cord dorsum with plus and minus signs indicating polarity of stimulating electrodes. Solid triangles and solid circles, testing volley half the amplitude of the conditioning volley in lumbar and thoracic cord respectively. Open triangles and open circles, testing volley slightly larger than conditioning volley (*ca.* 1.3 times its amplitude) in lumbar and thoracic cord respectively.

Experiment E shows intermediate curves in addition to the routine curves. These were obtained by making the testing volley equal in size to the conditioning volley.

RESULTS

1. Recovery of Excitability in Passive and Active Dorsal Column Fibers Determined by Method A

Method A yielded four different combinations for initiating and recording the testing volley as shown in Fig. 2A. In Fig. 2 are presented all experiments in which a complete set of curves was derived (except for E, H, and L in which cases, the curves for unconditioned thoracic fibers were not obtained). A correction amounting to a few milliseconds has been introduced in each thoracic curve to account for the conduction time of the conditioning volley. While it is apparent that excitability change varied from cat to cat, the variation is seen to be consistent for all curves. Thus the relations between curves are constant from one preparation to another.

The curve of excitability change of passive fibers[5] in the lumbar cord (Fig. 2, open triangles) begins at a few milliseconds, reaches peak at 24 msecs., lasts 120 to 200 msecs., and in general form is identical with the electrotonic potential (or its excitability equivalent (7)) of a passive dorsal root (DRV in the terminology of Lloyd and McIntyre (10)) the two being superposable in a given cat.[6] Since the passive fibers have not conducted a volley of impulses, their altered excitability can only be the result of effects induced in them by action in surrounding cells.

The excitability change in active lumbar fibers (Fig. 2, solid triangles) on the other hand, shows for the first 30 to 40 msecs. far more supernormality than passive fibers, while later the two curves can be seen to run approximately the same time course.

The excitability changes of thoracic dorsal column axons have two characteristics. First is the absence of the prolonged DRV-like changes in excitability in either active (solid circles, Fig. 2) or passive (open circles, Fig. 2) fibers, the curve for passive fibers being flat throughout except for small and brief changes. Second, the active fibers of thoracic column maintain during the first 30 to 40 msecs. great supernormality which is approximately equal to the difference in supernormality between the active and passive systems in the lumbar region. Since, as already discussed, the data are expressed as per cent deviation from

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ments the responses to testing shocks slightly larger than conditioning were not altered (after the brief period of refractoriness) when testing to thoracic dorsal columns (Fig. 3 open circles), this assumption is justified.

[5] Passive in that they have not carried the conditioning volley.

[6] The first few milliseconds in the passive system were not studied in detail. Evidence of a depression of excitability corresponding to DRIV of Lloyd and McIntyre (10) can be seen in some of the plotted curves. The excitability changes in dorsal column fibers, the central counterparts of root electrotonus, will henceforth be referred to as DCIV and DCV, where DC stands for dorsal column.

control excitability, thoracic supernormality is in reality larger, by a small value relative to lumbar excitability, than the curves of Fig. 2 indicate.[7]

It is therefore apparent: first, that there is a component of prolonged excitability change occurring in passive as well as in active fibers (DCV) which is restricted spatially to the lumbar cord (region of heavy collateralization) and second, that there is a component of supernormality unique to active fibers which exists in essentially unaltered form throughout the longitudinal extent of the spinal tracts.[8]

The fact that a component of excitability change is maintained in a region of cord where no post-spike current flows are detectable and collaterals are poorly developed permits but one conclusion: namely, that this component is the fluctuation in excitability corresponding to the membrane after-potential sequence intrinsic to the myelinated longitudinal dorsal column fibers which are being tested.

2. Recovery of Excitability in Passive and Active Dorsal Column Fibers Determined by Method B

In Fig. 3 are presented the results of those experiments in which method B was carried out in both lumbar and thoracic cord. The solid curves plot excitability in lumbar cord, the dotted curves in thoracic cord. In lumbar cord when testing volley height is set greater than conditioning (open triangles), the the excitability change is similar to that observed in unconditioned lumbar fibers using method A (DCV, Fig. 2, open triangles). This is to be expected since excitability change determined in this manner with method B is solely a function of changes in unstimulated (passive) fibers. When testing volley height is set smaller than conditioning (Fig. 3, solid triangles), there appears in addition to the DCV excitability change a large excess of supernormality during the first 40 msecs. The curves thus resemble those seen in active lumbar fibers with method A (Fig. 2, solid triangles). Similarly, the curves obtained in thoracic cord by method B (Fig. 3, open and solid circles) resemble those obtained there by method A (Fig. 2, open and solid circles). In Fig. 3E (+'s and ×'s) results are plotted for an intermediate value in the ratio of conditioning and testing volley heights (testing height equal to conditioning height, $T = C$). The

[7] No *a priori* reasoning precludes the possibility that thoracic supernormality may exceed lumbar dorsal column excitability. In fact a following paper discusses some factors which might act to attenuate supernormality in the lumbar region in which the fibers are exposed to externally applied currents of diverse origin (17).

[8] Since the value of thoracic supernormality constitutes in first approximation the difference in the excitability curves of active and passive fibers in the lumbar cord, this may be taken as experimental confirmation of Lloyd's and McIntyre's conclusion from studies with asphyxia that DRV exists equally developed in both active and passive rootlets (10). However, differences between active and passive systems of small magnitude cannot be excluded.

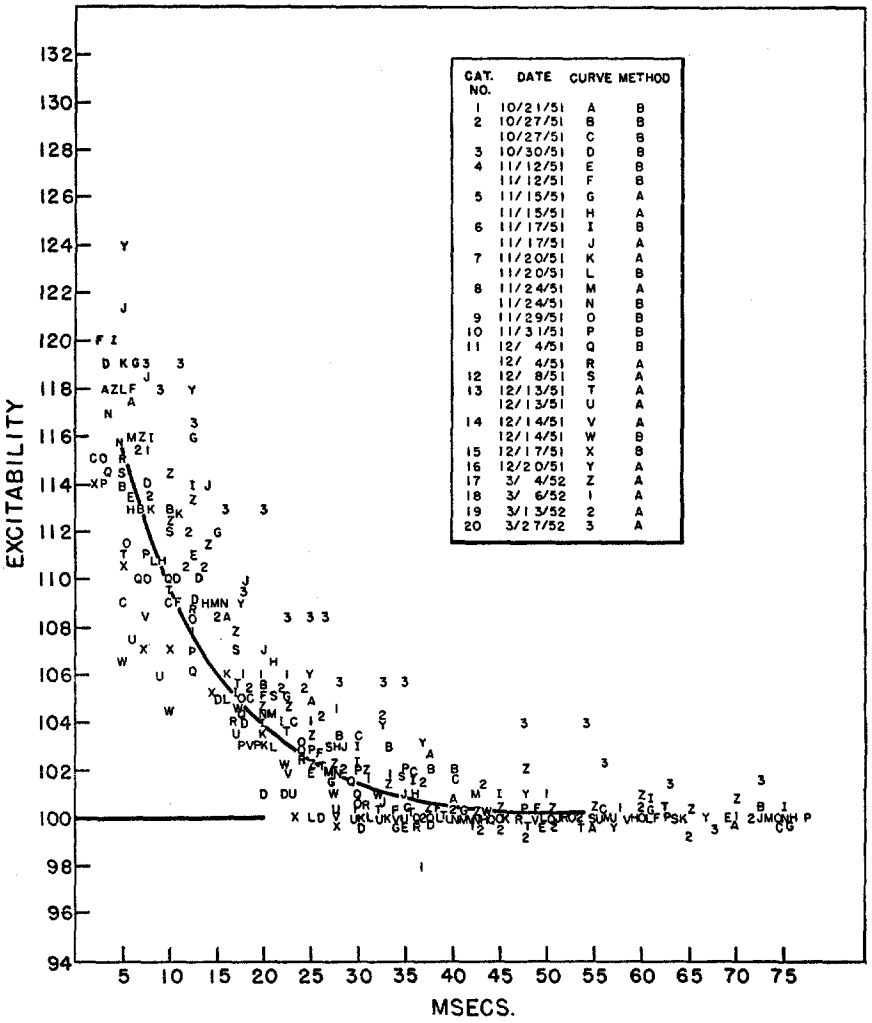

FIG. 4. Thoracic dorsal column excitability curves following conditioning by a single volley. Data compiled from Figs. 2 and 3 plus an additional thirteen experiments. Coordinates as before. The line is an exponential curve (7.5 msec. half-time) whose peak coincides with the average value of peak supernormality.

excitability change is seen to be a mixture of the active and passive extremes in the lumbar cord.

Although showing somewhat greater variability, the results of method B thus permit the same conclusions as those of Method A. Any objection to the use of method A because of possible interference with the height of the testing volley by junctional regions interposed between the site of the testing electrodes

and the recording station at the root (*e. g.* root-cord junction) seems answered by the similarity of the results obtained with the two methods.[9]

3. Additional Characterization of the Dorsal Column Recovery Sequence

Compiled in Fig. 4 are the results of 29 experiments in which determination of recovery curves of excitability in the thoracic cord has been made by both of the two methods presented. Some of these include the results already presented in Figs. 2 and 3. The ordinate is again scaled in percentage of resting excitability. Peak supernormality averages 15.7 per cent ± 4 (one standard

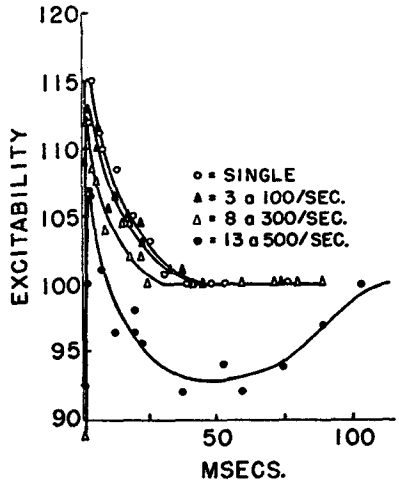

FIG. 5. Recovery curves of excitability in thoracic dorsal columns following conditioning trains of varying number and frequency. Data derived by method B, but representative of fifteen experiments with either method A or B.

deviation) at 5 msecs. Half-time of decay is approximately 7.5 msecs. On the chart is drawn an exponential curve regressing from the average value of peak supernormality with a half-time of 7.5 msecs. It describes a reasonable average for the data.[10] Cats 2, 3, 15, and 16 were unanesthetized preparations previously

[9] It may be noted that in regions of the central nervous system not conveniently supplied with root-like structures for leads, method B would appear to offer in principle an indirect means for determining the changes in membrane potential of conditioned as well as adjacent unconditioned fibers. With subsidiary assumptions the membrane potential changes intrinsic to the active cell could then be ascertained from these data.

[10] Consideration of calibration curves shows that variations in control volley size used in this study (20 per cent to 50 per cent of maximal) contributed to the scatter of the excitability plots by less than one-half a standard deviation. Since the same fractions of the fiber populations were tested in lumbar and thoracic regions, this is

rendered decerebrate or decapitate under ether. The results of these few experiments are seen to be no different from the general mass of data obtained under barbiturate anesthesia.

Supernormality in dorsal column axons is never followed by subnormality unless conditioning is by trains of volleys. Even then, more than three volleys at frequencies exceeding 100/sec., are required to produce subnormality. Presented in Fig. 5 are results typical of those obtained in 15 cats with either method A or B in thoracic cord when multiple conditioning volleys were used. Compared with peripheral nerve, dorsal column shows greater resistance to altering its recovery sequence when tetanized. In peripheral nerve subnormality is well developed following a single volley (5, 6), and after 3 volleys at 90/sec. the magnitude of subnormality is 140 per cent of the supernormality present following a single volley (Fig. 18 of 5).

DISCUSSION AND CONCLUSIONS

It is concluded that these experiments have revealed the form of the recovery of excitability intrinsic to active dorsal column fibers. In addition, since it was found that excitability changes in general correspond to potential in dorsal column fibers this excitability change describes what would be called the after-potential sequence were it recordable in the intact spinal cord.[11] The amount of supernormality in intact dorsal column is approximately four to five times that observed in mammalian peripheral nerve A fibers *in situ* when recovery is similarly calibrated (6),[12] and its average duration is longer (40 msecs. in dorsal column compared with 15 msecs. in peripheral nerve (5, 6)). The dorsal column recovery sequence following a single volley is unique among those of mammalian axons in that following supernormality it shows no subsequent subnormality. In mammalian peripheral nerve by way of contrast subnormality is about 40 per cent of supernormality (5, 6). Furthermore, dorsal column axons are far more resistant than peripheral axons to the development of subnormality following repetitive stimulation.

Neither the excitability change (DCV) restricted to the region of heavy collateralization nor the prolonged post-spike current flows (intermediary

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a random rather than a systematic error with respect to the comparison drawn between thoracic and lumbar columns.

[11] In principle this after-potential could be recorded as a variation in demarcation current if a crush were made in the thoracic cord. However, it is more feasible to determine the dorsal root after-potential and to record the electrotonic sign of the currents flowing between dorsal column and dorsal root as a result of differences in their after-potentials. In this way a direct confirmation of the form of the dorsal column after-potential has been obtained using potential recording rather than excitability measurement (17).

[12] For justification of the validity of this comparison see the third paper of this series (3).

potentials) can be attributed to activity intrinsic to myelinated longitudinal dorsal column axons according to the evidence of this paper. They are therefore the result of activity extrinsic to the dorsal column. Since the extrinsic depolarization of dorsal column axons arises neither from dorsal root nor from root-cord junction (it is still well developed 1.5 to 2.5 cm. above the level of root entry) it must arise as a consequence of activity located either transynaptically or in the collaterals of the dorsal column axons. This conclusion long held by most workers (1, 10) is thus supported by the experimental evidence of this paper.

Allocation of an impressively large negative after-potential to intramedullary portions of the primary afferent cell raises the question of the role it might play in generating intramedullary and root currents of classical description (4). Preliminary considerations basic to this type of analysis follow.

The primary afferent cell is justifiably regarded as composed of three dissimilar segments: a myelinated dorsal root segment, a myelinated segment confined mainly to the dorsal column parent fibers, and a non-myelinated segment consisting of the presynaptic collaterals in the gray matter. Electrical action in this system following conduction of an afferent volley may be discribed in terms of four parameters: the intrinsic membrane potential variation of the two myelinated segments, the intrinsic membrane potential variation of the unmyelinated segment, and the currents that flow between them. One of the parameters, the intrinsic potential variation of one myelinated segment, has been determined by experimental isolation of the dorsal column negative after-potential. Since only three of the parameters are independent the problem remains, ideally, to define experimentally two of the others and to calculate the fourth. An analysis based on these considerations forms a section of a subsequent paper (17).

SUMMARY

A method is evolved whereby the after-potential sequence intrinsic to longitudinal dorsal column myelinated fibers may be studied in isolation from those events occurring in intact spinal cord subjected to an afferent volley.

The recovery sequence intrinsic to dorsal column fibers, after refractoriness is over, is characterized by supernormality approximately four to five times greater than that seen in peripheral nerve. This supernormality averages 15.7 $\pm$ 4 per cent (current calibration) at peak and decays exponentially with a half-time of 7.5 msecs. It is not followed by subnormality unless conditioning is repeated more than three times at frequencies greater than 100/sec.

Characterization of the recovery curve of dorsal column fibers permits by exclusion, the allocation of the origin of DRV to structures more centrally located.

DCV (the dorsal column counterpart of DRV) is seen to exist equally developed in active and passive dorsal column fibers.

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BIBLIOGRAPHY

1. Barron, D. H., and Matthews, B. H. C., The interpretation of potential changes in the spinal cord, *J. Physiol.*, 1938, **92,** 276.
2. Cajal, S. Ramón y, Histologie du système nerveux de l'homme et des vertêbrés, Paris, A. Maloine, 1909, **1.**
3. Eisenman, G., and Rudin, D. O., Action potential of spinal axons *in vitro*, manuscript in preparation.
4. Gasser, H. S., and Graham, H. T., Potentials produced in the spinal cord by stimulation of dorsal roots, *Am. J. Physiol.*, 1933, **103,** 303.
5. Gasser, H. S., and Grundfest, H., Action and excitability in mammalian A fibers, *Am. J. Physiol.*, 1936, **117,** 113.
6. Graham, H. T., and Lorente de Nó, R., Recovery of blood-perfused mammalian nerves, *Am. J. Physiol.*, 1938, **123,** 326.
7. Grundfest H., and Magnes, J., Excitability changes in dorsal roots produced by electrotonic effects from adjacent afferent activity, *Am. J. Physiol.*, 1951, **164,** 502.
8. Hughes, J. and Gasser, H. S., Some properties of the cord potentials evoked by a single afferent volley, *Am. J. Physiol.*, 1934, **108,** 295.
9. Hursh, J. B., Relayed impulses in ascending branches of dorsal root fibers, *J. Neurophysiol.*, 1940, **3,** 166.
10. Lloyd, D. P. C., and McIntyre, A. K., On the origins of dorsal root potentials, *J. Gen. Physiol.*, 1949, **32,** 409.
11. Lloyd, D. P. C., and McIntyre, A. K., Dorsal column conduction of group I muscle afferent impulses and their relay through Clarke's column, *J. Neurophysiol.*, 1950, **13,** 39.
12. Lorente de Nó, R. A Study of Nerve Physiology, *Studies from The Rockefeller Institute for Medical Research*, 1947, **131** and **132.**
13. Lorente de Nó, R., Transmission of impulses through cranial motor nuclei, *J. Neurophysiol.*, 1939, **2,** 402.
14. Lorente de Nó, R., Action potential of motoneurons of the hypoglossus nucleus, *J. Cell. and Comp. Physiol.*, 1947, **29,** 207.
15. Lorente de Nó, R., personal communication.
16. Rudin, D. O., and Eisenman, G., A method for dissection and electrical study *in vitro* of mammalian central nervous tissue, *Science*, 1951, **114,** 300.
17. Rudin, D. O., and Eisenman, G., manuscripts in preparation.
18. Rushton, W. A. H., Effect upon the threshold for nervous excitation of the length of nerve exposed and the angle between current and nerve, *J. Physiol.*, 1927, **63,** 357.