CORTICALLY EVOKED DEPOLARIZATION OF PRIMARY AFFERENT FIBERS IN THE SPINAL CORD

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INTRODUCTION

THE CORTICAL EXCITATORY action on interneurons of the spinal cord was first studied in detail by Lloyd (15), and has recently been investigated by means of intracellular recording (16). In the spinal cord, afferent volleys have a presynaptic inhibitory action by depolarizing primary afferent fibers, an action which is mediated by various types of interneurons (6, 8, 10, 11). Stimulation of the sensorimotor area of the cerebral cortex depresses the synaptic relay of impulses up several ascending tracts of the spinal cord (12, 13, 18) and also depresses the N wave produced by a testing cutaneous volley (14). It has been suggested (4, 18) that these effects may be examples of presynaptic inhibition, and this suggestion is confirmed by the investigation here reported. There have been preliminary publications of two independent studies which indeed showed that stimulation of the sensorimotor cortex depolarized several types of primary afferent fibers in the spinal cord and so effected presynaptic inhibition (1, 2).

METHODS

The experiments were performed on cats lightly anesthetized with pentobarbital sodium. The experimental techniques resembled those previously reported for comparable investigations on the presynaptic depolarization of primary afferent fibers (8, 9). The excitability of primary afferent fibers has been tested by the method of Wall (22) in which brief electrical pulses were applied from a Grass stimulator with isolation unit through a low-resistance microelectrode (1–1.5 megohms) filled with 4 M NaCl. Since the ventral roots were cut the number of primary afferent terminals thus stimulated can be assessed from the size of the antidromically conducted spike potential in various nerves.

The following muscle and skin nerves were prepared and mounted on electrodes for stimulation and recording, and their abbreviations are also given: (PBST) posterior biceps and semitendinosus, knee flexors; (SMAB) semimembranosus and anterior biceps, hip extensors; (GS) gastrocnemius and soleus, ankle extensors; (FDHLPL) flexor digitorum and hallucis longus and plantaris, physiological digital extensors; (PDP) the peronei, tibialis anterior and extensor digitorum longus, physiological ankle flexors; (SU) sural; (SP) superficial peroneal; (PT) posterior tibial nerve, the three latter being skin nerves.

The convexity of the cerebral cortex was exposed and covered in a pool with warm mineral oil.

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Dorsal rootlets were severed peripherally and mounted so as to record dorsal root potentials (DRP) in the cervical segments C_3 and T_1 and in the lumbar segments $L_{5,6,7}$ and S_1.

RESULTS

Dorsal root potentials and P waves evoked by cortical stimulation

Repetitive stimulation of the appropriate areas of the sensorimotor cortex evokes large dorsal root potentials and the corresponding P waves of the cord dorsum (Fig. 1, *A*, *B*). These potentials correspond closely to the potentials produced by afferent volleys from limb nerves (Fig. 1, *C*, *D*), particularly to those produced by cutaneous volleys and group III afferent volleys (6). From their summits onward the DRPs and P waves had an approximate mirror-image relationship, but earlier there was a large N wave of the cord dorsum (2, 14), just as was observed with cutaneous (Fig. 1*D*) and group III afferent volleys. The total duration of about 200 msec. is in good agreement with the DRPs produced by afferent volleys from the limb nerves (Fig. 1, *C*, *D* and ref. 6), but the summit is much later.

A single cortical stimulus evokes a negligible DRP (Fig. 1*E*) and repetitive stimulation is required for the production of large DRPs, as in *A* and *B*. This facilitation by repetitive stimulation (*F–M*) corresponds very closely to the observations on DRPs evoked by group I afferent volleys from the nerve to the knee flexor muscles (10). Comparison of Fig. 1, *J–M* with *F–I* shows that facilitation at 300 sec. was about twice that at 150 /sec. With the longest stimulations (Fig. 1, *I*, *M*) the DRP declined from an early summit.

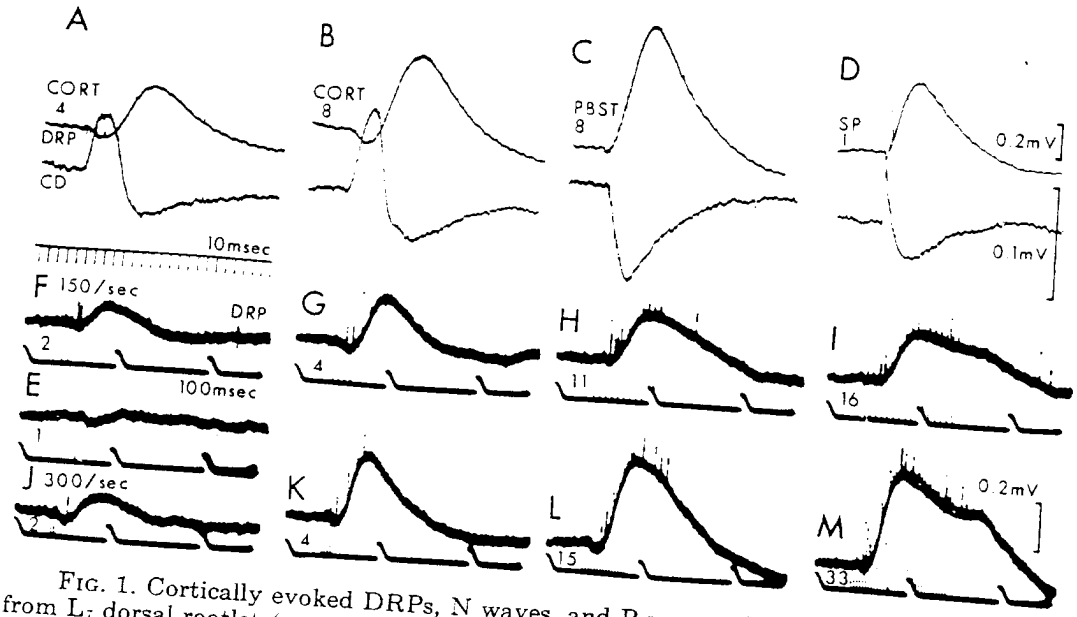

FIG. 1. Cortically evoked DRPs, N waves, and P waves of cord dorsum. *A*, *B*: DRP from L_7 dorsal rootlet (upper trace) and N and P waves (lower trace) evoked by 4 and 8 shocks at 300/sec. to the contralateral postcruciate cortex, respectively. *C*: corresponding potentials evoked by a train of 8 shocks at 300/sec. to PBST nerve and by a single shock to the SP nerve in *D*. *E–M*: DRP from L_7 dorsal rootlet evoked by indicated number of shocks to contralateral postcruciate cortex at 150/sec. (*F–I*) and 300/sec. (*J–M*).

but later reached a lower plateau just as with the DRPs evoked from limb nerves (10, 11).

Cortical areas evoking dorsal root potentials

Dorsal root potentials and P waves, as in Fig. 1, have been evoked only from quite circumscribed areas of the convexity of the cerebral cortex. In Fig. 2*A* the specimen records of DRPs in a T_1 dorsal rootlet were evoked from the indicated points on the convexity of the contralateral cortex. The diameters of the filled circles on the drawings are proportional to the sizes of the DRPs in the T_1 rootlet that were evoked by stimulation of the underlying cortical areas. It will be recognized that the only effective cortical areas are the somatosensory arm areas I and II. Similarly, in Fig. 2*B* the only effective areas for evoking DRPs in the L_7 dorsal root are from the somatosensory leg areas I and II. The somatotopical organization is thus quite definite in SI, but has not been demonstrated with SII.

The ipsilateral somatosensory cortex is much less effective than the contralateral. For example, in Fig. 3, *A*, *B* stimulation of the SI leg area of the cortex produced a much larger DRP in the contralateral than in the ipsilateral L_7 dorsal root. However, there was very little difference in the effec-

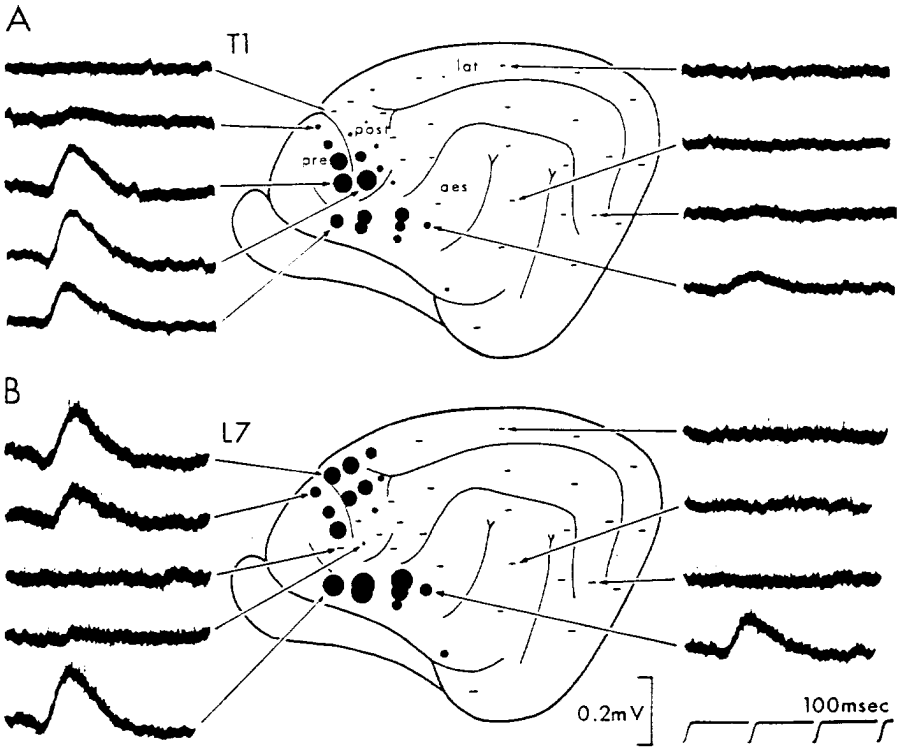

FIG. 2. Effective cortical areas for production of DRPs. *A*: DRPs recorded from T_1 dorsal rootlet, right side. *B*: DRPs recorded from L_7 rootlet, right side. Diameters of the filled circles in the diagrams of the left cerebral hemisphere are proportional to the size of the DRP evoked by stimulation of that point. – indicates negative points.

tiveness of somatosensory area II on the two sides (Fig. 3*C*). The DRPs evoked from the ipsilateral SI area have a longer latency and later summit than the contralateral. A possible pathway from the ipsilateral cortex is via the corpus callosum to the contralateral cortex, but section of the corpus callosum did not abolish the ipsilaterally evoked DRPs.

The series of observations (Fig. 3, *D–F*) suggests that the precruciate cortex evokes DRPs, not directly by a projection pathway, but indirectly through synaptic activation of cells in the postcruciate cortex. Removal of the precruciate cortex resulted in a slight diminution in the DRPs evoked by precruciate stimulation (*E*), but, after removal of the postcruciate cortex,

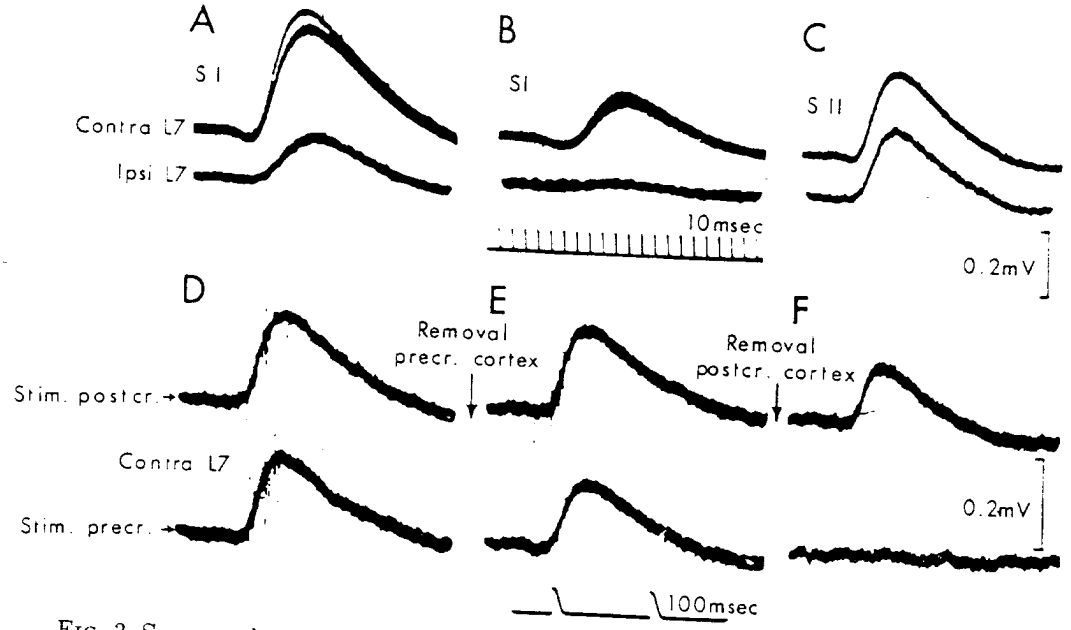

FIG. 3. Some pathways involved in the cortically evoked DRPs. *A*: DRPs evoked by stimulation in hind-leg part of SI area: *B*: stimulation 2 mm. caudal to *A*; *C*: stimulation in SII area. Upper traces show DRPs from contralateral, lower traces from ipsilateral L$_7$ dorsal rootlet. *D*: DRP recorded from a L$_7$ dorsal rootlet evoked by stimulation of the postcruciate (upper trace) and precruciate cortex (lower trace). *E*: as *D*, but after removal of the precruciate cortex, the electrode now stimulating the white matter. *F*: as *D* and *E*, after the additional removal of the postcruciate cortex. Both stimulating electrodes placed on the white matter.

precruciate stimulation was ineffective, though postcruciate stimulation was not greatly reduced (*F*). The projection fibers from the postcruciate cortex would of course be stimulated directly after removal of their cell bodies in the grey matter.

Identification of afferent fibers depolarized by cortical stimulation

Excitability tests. The excitability of primary afferent fibers in the lumbar cord has been investigated by the standard procedure of stimulating by brief pulses applied through a microelectrode in close proximity to the fiber terminals and recording the antidromic volley in the peripheral afferent

nerve (8, 9, 11, 22). The increase in excitability produced by a conditioning stimulation can be calculated as a percentage of the control level by reference to a calibration curve constructed from the responses evoked by a controlled series of stimuli.

The specimen records in Fig. 4*A* give traces of the control spike potentials evoked in the superficial peroneal nerve by application of stimuli of 60 V. and 100 V. through the microelectrode at a depth of 1.5 mm. in the L_7 segment of the spinal cord. Superimposed thereon are the increased spikes obtained when a conditioning tetanus (4 stimuli at 300 sec.) was delivered to the contralateral postcruciate cortex 78 msec. earlier than the test stimulus. The lower traces are the electrically integrated records. The calculated excitability increases are to 140% of the control. Each of the points in the curve of Fig. 4*A* was obtained in this way at a range of testing intervals from 30 to 455 msec. The curve of increased excitability so plotted (broken line) is seen to be in good agreement with the DRP evoked by this same cortical stimulus (full line). Figure 4*B* shows a similar series for conditioning by a single volley in the sural nerve, there being of course a much more rapid onset to an earlier summit with both the excitability curve and the DRP.

In Fig. 4, *C* and *D* are similar curves for the group I afferent fibers of the hip extensor muscles, semimembranosus plus anterior biceps. However, the cortical effect, *C*, was much less than that produced in *D* by conditioning volleys from the knee flexor. This smaller action of the cortical stimulus can be seen by comparing the specimen records in Fig. 4, *E* and *G*. When the microelectrode was much deeper (at 3.5 mm.), only group Ia afferent fibers to muscle could be excited; and the conditioning cortical stimulation had no effect whatsoever on the excitability, *F*, while in *H* the PBST conditioning caused a considerable increase in excitability of the group Ia fibers, as previously reported (8). In Fig. 4*I* the increase in excitability of group I fibers of the SMAB nerve is plotted against the depth of the applied test stimulus for the series partly illustrated in Fig. 4, *E–H*. In response to conditioning by PBST volleys the group I fibers display an increased excitability down to the furthest penetration of the group Ia fibers (9), but cortical conditioning was not clearly effective for depths beyond 2.1 mm., and only a trace of the effect could be observed at a depth of 3.0 mm. This failure of cortical stimulation to depolarize group Ia afferent fibers has been observed in all four experiments where it was tested, as in Fig. 4, and has been independently reported by Carpenter, Lundberg, and Norrsell (2).

The selective action of cortical stimulation in depolarizing the group Ib and not the group Ia afferent fibers can be demonstrated with stimulation of both groups when the microelectrode is in the intermediate nucleus (Fig. 5). The slower conduction velocity of group Ib fibers causes the antidromic spike to have two components. In Fig. 5*A* conditioning by cortical stimulation results in increase of only the second component of the spike recorded from the nerve to PBST, though Fig. 5*B* shows that the first could be greatly increased by strengthening the control current pulse through the micro-

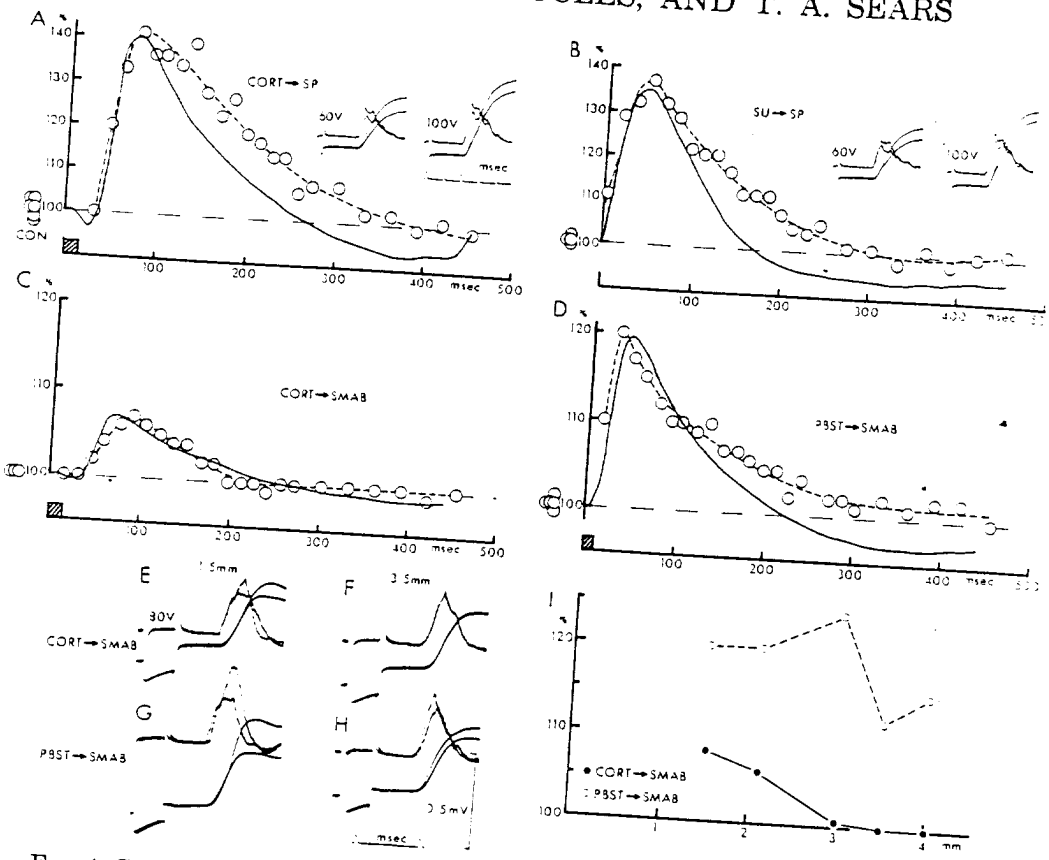

FIG. 4. Cortically evoked excitability increase of primary afferent fibers. *A:* excitability of SP nerve terminals plotted against time after first shock of 4 at 300/sec. delivered to the contralateral leg area of the postcruciate cortex (open circles), and DRP recorded from L_7 dorsal rootlet in response to the same cortical stimulation (full line). Insets show the antidromically conducted spike in the SP nerve in response to 60-V. (left) and 100-V. pulses through the microelectrode 1.5 mm. below the dorsal surface of the cord. The lower traces are the integrated records. The control response and the response preceded by a cortical train 78 msec. earlier, are superimposed. *B:* similar to *A*, but with a single SU volley as the conditioning stimulus. *C:* display as in *A*, but testing the excitability of SMAB fibers at a depth of 1.5 mm. produced by a cortical conditioning stimulation. *D:* similar to *C*, with 4 shocks at 300/sec. to PBST nerve as conditioning stimulus. *E–H:* antidromic spikes in SMAB nerve produced by an 80-V. pulse through a microelectrode at depth of 1.5 mm. (*E*, *G*) and 3.5 mm. (*F*, *H*). In *E* and *F* a conditioning cortical train preceded the test stimulus by 80 msec. In *G–H* the conditioning stimulus was delivered to the PBST nerve. Upper traces show control test responses and conditioned responses superimposed. Lower traces are the corresponding integrated records. Note complete disappearance of cortically evoked excitability increase at 3.5 mm. depth (*F*). *I:* excitability of SMAB fiber terminals as conditioned by a cortical train of 4 shocks at 300/sec. with conditioning-test interval 80 msec. (filled circles), or by a similar train to PBST nerve, conditioning-test interval 61 msec. (open circles).

electrode. The selective action of cortical stimulation in increasing the second component is also seen in Fig. 5*C*. When, by submaximal conditioning stimulation to the intact PBST nerve, almost all of its group Ia fibers were rendered refractory at the time of the test stimulation (cf. ref. 9, Fig. 7), cortical stimulation still caused the same increase in the response to the test

stimulation (Fig. 5*D*). It can be concluded that the increased excitability was exclusively in the Ib component of the group I fibers of the PBST nerve.

Intracellular recording from primary afferent fibers. The preceding investigations have shown by indirect means that cortical stimulation produces a depolarization of group Ib and cutaneous primary afferent fibers. Intracellular recording from these fibers provides a direct demonstration of this depolarization, named primary afferent depolarization (PAD) (Figs. 6 and 7; and the previous report by Carpenter, Lundberg, and Norrsell (2)).

In Fig. 6, *A–C*, the microelectrode was in a cutaneous afferent fiber of the SP nerve, as shown by the spike potential of 50 mV. in *A*, and in *B* the cortical stimulation produced a depolarization almost as large as that pro-

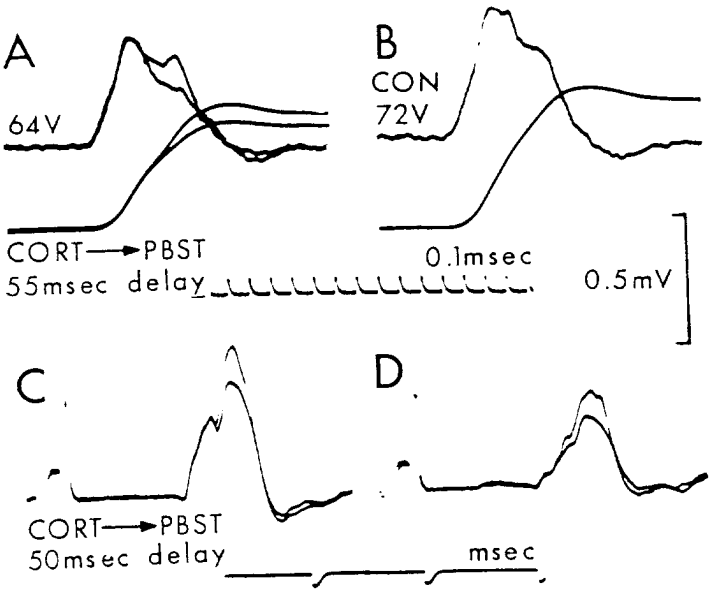

FIG. 5. Exclusive Ib excitability effect from cortex. Excitability of fiber terminals of PBST nerve. *A*: antidromic spike in PBST nerve with and without conditioning cortical train (4 shocks at 300/sec.) that precedes the test pulse of 64 V. by 55 msec. Superimposed records, lower traces are integrated records. *B*: control stimulus only, 72 V. *C*: as in *A*, but another experiment. Only the late component in *C* (Ib) shows excitability increase. In *D* the majority of Ia fibers were made refractory to the test pulse by a shock delivered to the hamstring nerve in continuity at the hip joint (9). The Ib component still shows the excitability increase.

duced by an afferent volley in the SP nerve, *C*. The depolarization is determined by subtracting the subjacent extracellular from the intracellular record, as previously described (8). It can be seen that the PAD, as so determined, corresponds closely to the primary afferent depolarization observed as a DRP after electrotonic propagation to the dorsal root (lowest records of Fig. 6, *B* and *C*). Figure 6, *D–G*, are records from a PT fiber. Increasing numbers of cortical shocks have the same facilitatory action on the PAD as with the DRPs in Fig. 1, *E–M*. Subtraction of the extracellular from the intracellular traces shows that two cortical stimuli produced a negligible de-

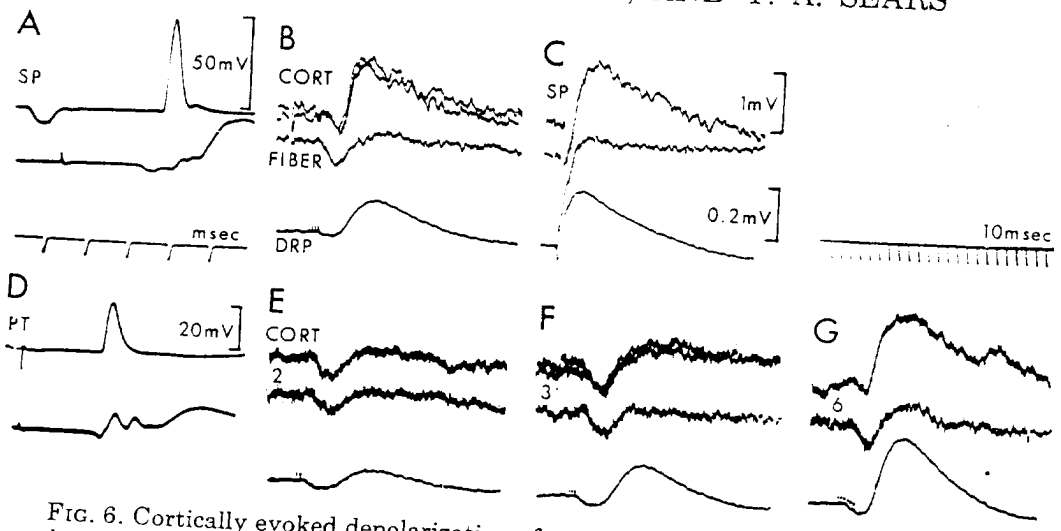

FIG. 6. Cortically evoked depolarization of cutaneous fibers. *A*: spike of a SP fiber. *B*: long-lasting depolarization produced by a short train (4 shocks at 300/sec.) delivered to leg area of contralateral postcruciate gyrus (upper trace). Middle trace shows extracellular record. True depolarization is found by subtraction of the extracellular from the intracellular record. Lower trace shows DRP of a L_7 dorsal rootlet. *C*: similar depolarization produced by single SP volley. *D*: spike of a PT fiber. Increasing depolarizations are produced by increasing number of shocks in the postcruciate tetanus: *E*, 2 shocks; *F*, 3 shocks; *G*, 6 shocks. Display as in *B* and *C*.

polarization (*E*), and with three it was still small (*F*), while with six it was quite large (*G*). Similarly, facilitation was also exhibited by the DRPs in the lowest traces of *E*–*G*.

The primary afferent fiber of Fig. 7 was in the mixed posterior tibial nerve. The small depolarizing actions of the cutaneous volleys SU and SP

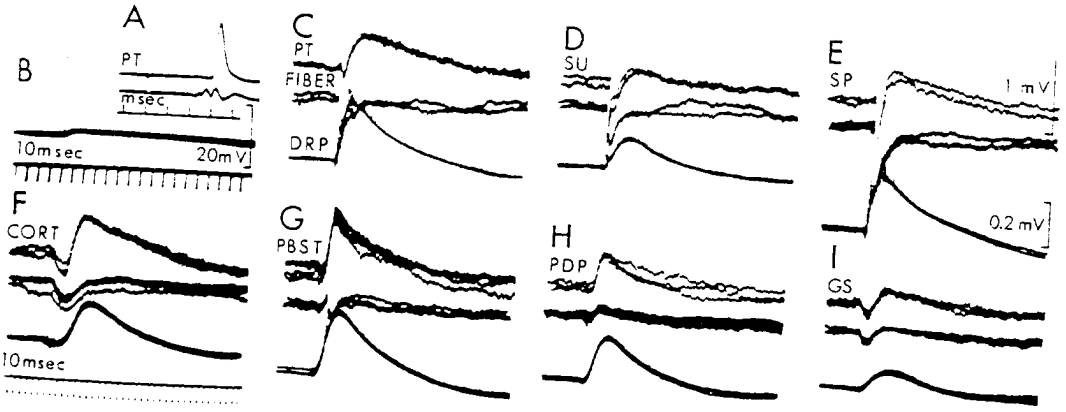

FIG. 7. Cortically evoked depolarization of a Ib muscle afferent fiber. *A*: spike potential of a PT fiber, the spike potential followed by a long-lasting depolarization (*B*). Long-lasting depolarizations at higher gain produced by single volleys in the cutaneous nerves indicated (*C*–*E*), or by short trains to the contralateral postcruciate cortex (*F*), and to the indicated muscle nerves in *G*–*I*. Each assemblage of records (*C*–*I*) shows from above downward: the intracellular record, the extracellular record, and the DRP recorded from a L_7 dorsal rootlet.

(*D*, *E*) relative to the muscle afferent volleys (*G*, *H*, *I*) establishes that it was not a cutaneous fiber (11). Since afferent volleys from ankle (*I*) and toe (not shown) extensor muscles had a depolarizing action, the fiber may be identified as a group Ib afferent fiber (9). Cortical stimulation had a large depolarizing action (*F*), which again had a time course comparable with the DRP.

Cortical activation of interneurons in the spinal cord

Repetitive cortical stimulation always exhibits a very effective facilitation in the depolarization of primary afferent fibers (Figs. 1 and 6), and this

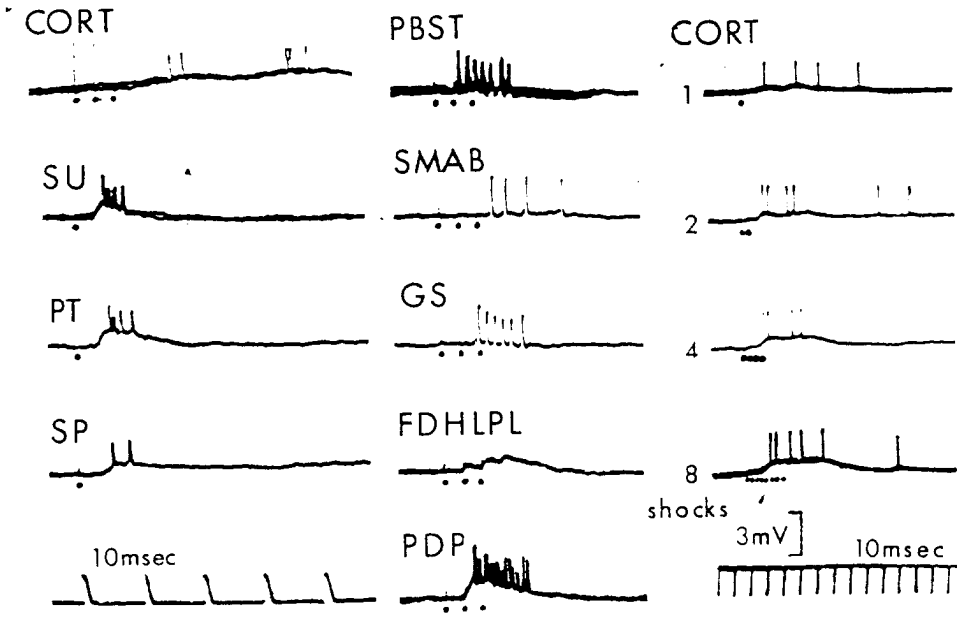

FIG. 8. Cortically activated spinal interneuron. Interneuron in dorsal horn activated by a short tetanus to the contralateral postcruciate cortex (CORT) and by single volleys in three cutaneous (SU, SP, PT) and four muscle nerves (PBST, SMAB, PDP, GS). Increasing number of shocks in the cortical tetanus increases the discharge frequency (column to the right).

facilitation is observed equally well when the stimulation is applied to the subjacent white matter after cortical ablation; hence it can be postulated that the descending impulses from the cortex act on primary afferent fibers via an interneuronal pathway in the spinal cord. It is well known that the pyramidal tract fibers are powerful excitants of interneurons in the dorsal horn of the spinal cord (15, 16, 17, 20). The present investigation represents merely a preliminary attempt to see if some of the excited interneurons have properties that would be expected for interneurons responsible for depolarization of primary afferent fibers.

In Fig. 8 the interneuron was caused to discharge repetitively by a wide range of afferent volleys from cutaneous nerves (SU, PT, SP) and from muscle (PBST, SMAB, GS, PDP), only one muscle nerve (FDHLPL) being

ineffective. In no case was the latency so brief that monosynaptic activation was indicated. It would appear that this interneuron resembles those that were postulated to be at a second or later position on an interneuronal pathway giving presynaptic inhibition of cutaneous or group Ib afferent fibers, the type D interneurons of Eccles, Kostyuk, and Schmidt (6). This interneuron was also activated by cortical stimulation (CORT) and in the series

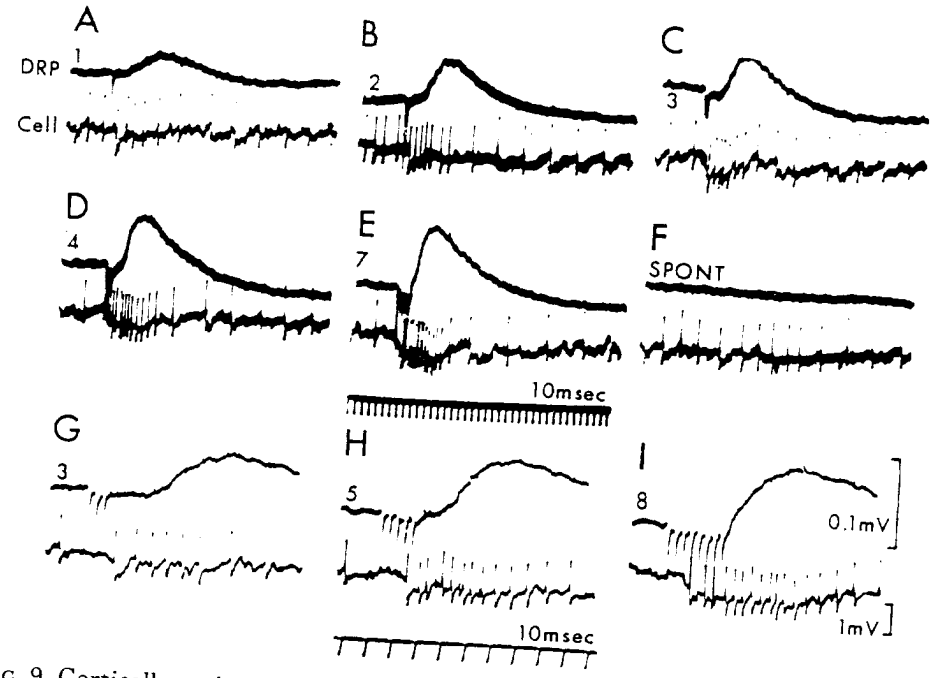

FIG. 9. Cortically activated interneuron in the dorsal horn. Upper trace: DRP recorded from a L_7 dorsal rootlet; lower trace: interneuron discharges. *A* – *E* and *G*–*I* show effect of increasing number of shocks in the cortical tetanus as indicated. Note parallelism between high discharge rate and steepness of DRP. *F*: spontaneous discharge.

in the right-hand column of Fig. 8 it exhibits facilitation in its responses to varying numbers of cortical stimuli. Since this interneuron appears to be one of the D-type interneurons, its activation by cortical stimulation shows that it might also participate in the cortically evoked depolarization of primary afferent fibers.

The facilitatory influence of repetitive cortical stimulation is illustrated by the interneuron of Fig. 9, which was spontaneously firing (*F*). The simultaneously recorded DRPs show a good correlation between the interneuronal frequency and the rising phase of the DRP, particularly in the faster series of Fig. 9, *G*–*I*.

Presynaptic inhibitory action of cortical stimulation

The action of presynaptic depolarization in depressing the synaptic excitation of primary afferent fibers has been so well established that no systematic study has been made of cortical inhibitory action, but the expected

presynaptic inhibition has been observed. For example, in Fig. 10 a conditioning cortical stimulation has lengthened the latency of a testing interneuronal discharge (*B*) and reduced the number of responses (*C*), exactly as has been observed with conditioning afferent volleys (7). The long duration of these depressant actions (about 150 msec.) corresponds with the duration of the cortically induced depolarization of afferent fibers, and suggests a presynaptic inhibitory action.

The synaptic excitatory action of a cutaneous volley generates a large

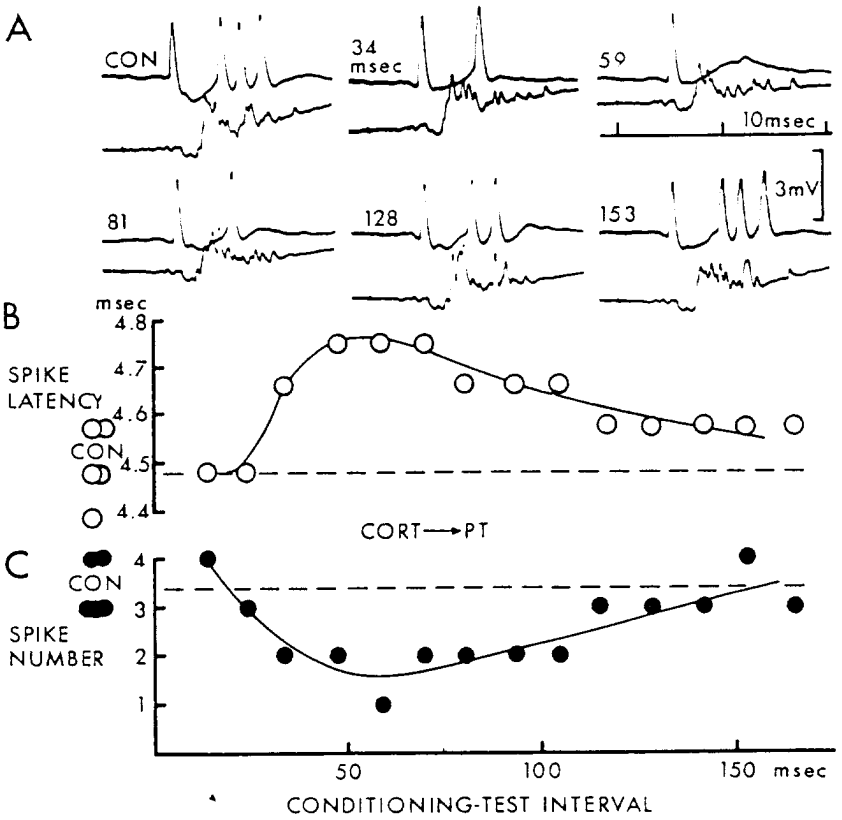

FIG. 10. Cortically evoked inhibition of synaptic effect on interneuron in dorsal horn. *A* (upper trace): effect of a short tetanus to postcruciate cortex on latency of first spike, and on the number of spikes evoked by a PT volley. *B*: graph where latency of first spike is plotted against conditioning test interval. *C*: plotting of number of spikes against conditioning-test interval.

negative potential, or N wave, at the region of its synaptic relay in the dorsal horn (5, 6), the size of which gives an approximate measure of the intensity of action. In Fig. 11*A* it is seen that the N wave due to a SP volley was depressed by a conditioning cortical stimulation. This depression had a time course characteristic of presynaptic inhibition with a summit at about 40 msec. after the onset of the conditioning stimulation, and a total duration of about 150 msec. Conditioning by a volley in another cutaneous nerve (SU) also depressed this N wave, but to a lesser extent beyond 20 msec. Lindblom and Ottosson (14) reported a depression of the surface N wave by a condi-

tioning cortical or pyramidal stimulation. However, the testing interval was so brief (25 msec.) that the testing N wave was superimposed on the N wave produced by the conditioning cortical stimulus, which makes it difficult to decide if this is a true inhibition or an example of occlusion.

Since cortical stimulation never depolarized group Ia fibers in our experiments, it would be expected that it would have no action on the monosynaptic EPSP of motoneurons (5). However, with one motoneuron a clear depression of the monosynaptic EPSP was observed that had a time course

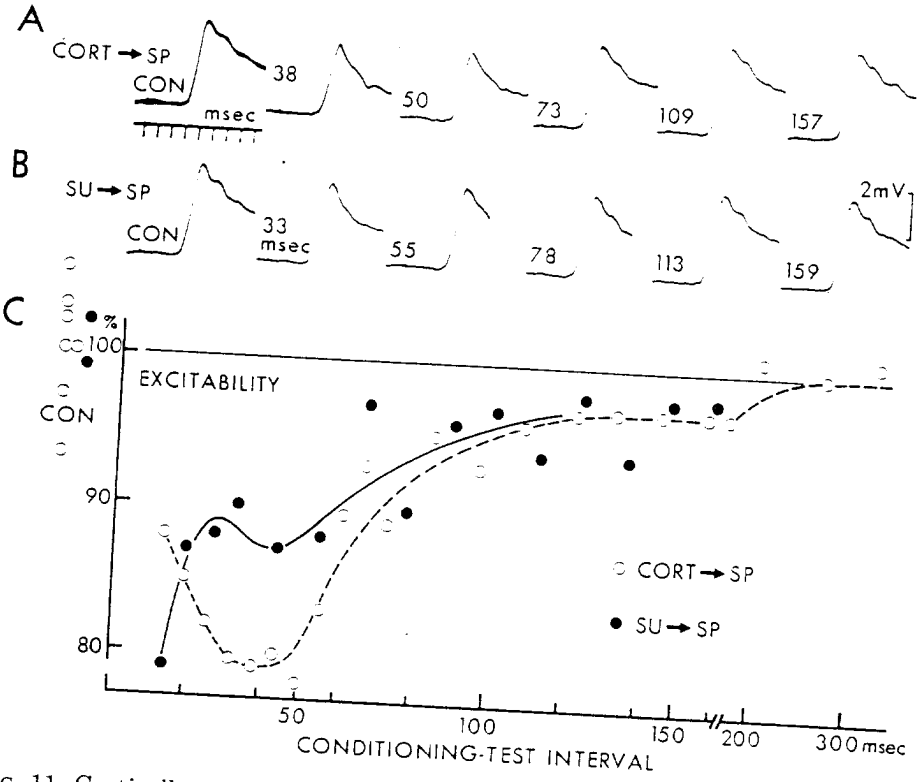

FIG. 11. Cortically evoked inhibition of synaptic effect of a cutaneous afferent volley. *A*: N wave recorded in L$_7$ dorsal horn on SP stimulation. Reduction in size produced by short cortical tetanus delivered at indicated times before the test nerve stimulus. *B*: comparable effect produced by a single SU volley as conditioning stimulus. *C*: graph in which N wave size is plotted in relation to conditioning-test interval. Open circles: conditioning stimulus to cortex: filled circles: conditioning stimulus to SU nerve.

sufficiently long (ca. 100 msec.) to suggest that it was due to presynaptic inhibition. Comparably, Lundberg and Voorhoeve (17) observed that cortical stimulation depressed the monosynaptic EPSP in one of the 22 motoneurons investigated, and yet caused no detectable postsynaptic response.

DISCUSSION

The experimental observations are in such close accord with the standard pattern of presynaptic inhibition that it will suffice merely to summarize them before raising special topics for discussion.

First, the only areas of the cortex which were effective were those broadly classified as sensorimotor, which is in agreement with the finding of Carpenter, Lundberg, and Norrsell (2) that the pathway mediating the presynaptic depolarizing effect is the pyramidal tract.

Second, the long latency, the slow rising time, and the necessity for facilitation by rapid repetitive stimulation of the corticospinal fibers all indicate that a complex interneuronal system mediates the transmission from the synaptic terminals of the corticospinal fibers to the presynaptic inhibitory endings on the synapses of primary afferent fibers. Interneurons with appropriate properties have been found and in all cases have also been activated from local afferent inputs into the spinal cord.

Third, except for the long latent period, usually 12–20 msec., and the slow rising time, the depolarization of the primary afferent fibers corresponds closely with that produced by local afferent inputs. It has been demonstrated by intracellular recording, by the increase in excitability, by the dorsal root potential, and by the P wave of the cord dorsum.

Fourth, the cortically induced depolarization is regularly observed both with the large cutaneous fibers and with the group Ib fibers from all types of muscle, but there has been no trace with group Ia fibers.

Finally, preliminary investigations have disclosed that there is an associated depression of the synaptic excitatory action of the primary afferent fibers.

This cortically induced presynaptic inhibition is most likely the mechanism responsible for the inhibitory effect reported by Hagbarth and Kerr (13).

In a very thorough histological study Nyberg-Hansen and Brodal (19) have found that corticospinal fibers from the sensorimotor cortex have numerous synapses on interneurons at the base of the dorsal horn. These corticospinal fibers most likely form the anatomical pathway for the cortically evoked presynaptic inhibition in the spinal cord. Fibers having a postcruciate origin tend to have a rather more dorsal termination, which would perhaps give significance to our evidence that the postcruciate area gives the primary projection from the cortex (Fig. 3). Very few corticospinal fibers were found ending in the ipsilateral dorsal horn; hence the ipsilateral dorsal root potentials (Fig. 3) possibly are produced by a commissural relay in the spinal cord. This explanation accords with the recent finding that cutaneous afferent volleys cause contralateral depolarization of cutaneous primary afferent fibers and possibly also of group Ib fibers (manuscript in preparation).

Towe and Zimmerman (21) have found that an ascending afferent volley from the spinal cord evoked a reflex discharge down the pyramidal tract to the cuneate nucleus. Presumably this pyramidal tract discharge would also continue down the spinal cord and have a presynaptic inhibitory action on the afferent input. There would thus be a long negative feedback loop, from spinal cord up to the sensorimotor cortex and down the pyramidal tract. This feedback loop would be of special significance physiologically for it would subserve cortical control of the afferent input into the spinal cord of both cutaneous and group Ib afferents.

SUMMARY

1. Repetitive stimulation of certain areas of the cerebral cortex causes a depolarization of primary afferent fibers in the spinal cord, which resembles the depolarization produced by afferent nerve volleys, that is responsible for presynaptic inhibition. With both there are associated electrotonically conducted depolarizations of dorsal root fibers (the dorsal root potentials), positive waves of the cord dorsum (P waves), and dorsal root reflexes.

2. The effective cortical areas are the somatosensory areas I and II. The effect is predominantly contralateral from SI, whereas the SII effect is bilateral. The SI arm and leg areas act specifically on the arm and leg afferent fibers, respectively.

3. Single cortical stimuli were relatively ineffective. Repetitive stimulation caused a large recruitment of the responses, particularly when at high frequency; this summation was independent of cortical action and was a property of the pathway in the spinal cord.

4. Excitability testing of the central terminals of primary afferent fibers showed that the cortically induced depolarizing action occurred in large cutaneous fibers, and in Ib afferent fibers from muscle, but not from the Ia fibers from muscle. Similar results were given by intrafiber recording from primary afferent fibers.

5. Interneurons were found in the dorsal horn and in the intermediate nucleus of Cajal that were fired by cortical stimulation and otherwise had properties making them possible candidates for the mediation of the cortically evoked presynaptic depolarization.

6. Cortically induced reduction of the synaptic action of primary afferent skin fibers was observed to have a time course typical of presynaptic inhibition. These effects were reduction of the N wave produced in the dorsal horn by an afferent volley in a skin nerve, reduction of number of spikes, and increase of latency of interneurons activated by cutaneous volleys.

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