CENTRAL INFLUENCES ON SPINAL AFFERENT CONDUCTION

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(Received for publication October 9, 1953)

It has been shown that in mammals the small efferent gamma fibers of the ventral root are capable of influencing the activity of muscle spindle afferents (11, 12, 14, 15). More recently, Granit and Kaada (8) demonstrated that the efferent gamma system is tonically activated from central regions and that stimulation of various central nervous structures influences the afferent discharge from the muscle spindles. These results indicate the existence of descending nervous pathways, the specific task of which is to regulate and modify the character and intensity of afferent messages. The question arose as to whether such sensory regulating pathways are unique for muscle spindle afferents or whether they are more widespread and common in the nervous system. As far as the gamma system is concerned, it is the initiation of afferent impulses from the highly specialized end-organ itself that is regulated. It seemed reasonable to assume, however, that not only the initiation but also the synaptic transmission of afferent messages in the central nervous system might be under the influence of specific regulating mechanisms. This possibility has earlier been suggested (5, 9, 18, 27), but the problem undoubtedly deserves further experimental study.

The present experiments were undertaken in order to determine whether it is feasible to influence a conducted afferent volley in the spinal cord by repetitive stimulation of various structures in the brain. This, indeed, proved to be possible. Furthermore, the results indicate that spinal afferent pathways can be tonically influenced from higher levels of the nervous system.

METHODS

Animal preparation. Twenty-five cats were used and most of them were curarized and maintained with artificial respiration. Operative work was performed under ether. The spinal cord was exposed from sacrum to the middle of the thoracic region. The dorsal and ventral roots, Lₕ-S₁, were cut and the central stump of the right dorsal root L₇ was routinely dissected free for stimulation. In the middle thoracic region, a few roots were cut to enable slight rotation of the cord and make the ventral columns accessible to the recording electrode. Before discontinuing the ether anesthesia, necessary craniotomies were performed and all exposure margins were infiltrated with procaine. During the experiment...
the animal's head was fixed in a Horsley-Clarke stereotaxic instrument and the body was held by clamps gripping spinal processes. Exposed tissues were covered with liquid paraffin and kept warm by radiant heat.

Stimulation and recording. Dorsal root L7 was stimulated with rectangular pulses at regular intervals by synchronization with the sweep. Unless otherwise stated, the strength of this test-stimulus was supramaximal. Recordings from the ventral or dorsal columns of the spinal cord were obtained by means of a thin steel needle insulated down to the tip and an indifferent electrode attached to the neighboring muscle. Subcortical structures in the brain were explored with bipolar concentric electrodes oriented stereotaxically. For the exposed surface of the brain silver ball cortical electrodes were used. Condenser discharges, with a falling phase of 1–2 msec. and a usual frequency of 100/sec. were delivered for repetitive conditioning stimulation. A condenser coupled amplifier and a two-beam cathode-ray tube were used for recording. The brains were checked histologically for localization of deep electrode placements.

RESULTS

Central nervous structures influencing afferent conduction

Afferent conduction in the dorsal columns. The afferent response in the dorsal columns following single shock stimulation of a dorsal root has been thoroughly described by Hursh (13). The action potential starts with a sharp spike-like elevation and is continued a few msec. later by a more prolonged relayed discharge. These responses have repeatedly been obtained also in the present experiments. According to Hursh, the spike is the record of impulses passing directly upwards along the central branches of dorsal root fibers while the relayed response is the centrally directed counterpart of the dorsal root reflex (26). Whatever the nature of this reflex may be (4), its centrally directed counterpart can be followed up to the dorsal column

![Graph](image-url)
nuclei in the medulla where it influences the relay into the medial lemniscus (25).

In the present experiments it was found that repetitive stimulation of various structures in the brain can influence the size of the dorsal column relayed response as well as the size of the dorsal root reflex. The primary afferent spike in the dorsal column, however, was never affected by such stimulation. In the experiment illustrated in Fig. 1, the tip of the recording needle was placed in the right dorsal column a few tenths of a millimeter below the surface and about 9 cm. above the zone of entrance of the stimulated ipsilateral dorsal root (L1). This root had been split into two branches, one of which was stimulated. The other branch was used for recording the dorsal root reflex. The dorsal column response was recorded on the lower beam and the dorsal root reflex on the upper (Fig. 1, A1). Repetitive stimulation in the bulbar reticular formation caused an almost complete disappearance both of the dorsal root reflex and the relayed response in the dorsal columns (A2). The primary spike in the dorsal columns, however, remained unchanged during stimulation.

The dorsal column relayed response and the dorsal root reflex could be depressed by stimulating the bulbar and midbrain reticular formation, the ventromedial part of the anterior vermis, the precentral motor cortex, the primary sensory cortex and the second somatic sensory area (22). In one experiment the effect was obtained also from the anterior part of the cingulate gyrus. The various central regions stimulated will be discussed further in connection with their effect upon afferent responses in the ventral columns (p. 298). The most pronounced effects were usually evoked with a stimulus frequency of about 100/sec. and the effective stimulus strength varied between 2-8 V. Variations of the frequency or the intensity of the stimulus never caused any qualitative changes of the results.

It is striking that the only effect upon the test responses was a depression. In all instances the relayed dorsal column response and the dorsal root reflex were depressed in parallel and to about the same degree. Sometimes the effect was most pronounced within the first seconds and gradually died away during the stimulation. More often, however,
the depression remained constant even during prolonged stimulations (10–15 sec.). Sometimes the effect remained even a few seconds after the end of the stimulation, but in a few cases a fast rebound phenomenon was obtained. Figure 2 shows the complete run of an experiment where such a rebound of the dorsal root reflex was evoked following stimulation of the contralateral sensory cortex.

It is of special interest to note that the primary afferent spike in the dorsal column is not influenced by central stimulation. This indicates that the simple presynaptic conduction of afferent impulses along the dorsal column fibers is not interfered with and that the effect is produced in the internuncial pool around the root entry zone. This conclusion is further supported by the fact that the local negative intermediary potential (10) recorded from the dorsum of the spinal cord at L7 is depressed in parallel with the relayed dorsal column response and the dorsal root reflex (Fig. 1B).

Backfiring into the dorsal columns causing refractoriness of the afferent fibers was frequently seen when stimulating the region of the ipsilateral dorsal column nuclei in the medulla (Fig. 3). In this case there was a depression not only of the dorsal root reflex and the dorsal column relayed response but also of the primary afferent spike in the dorsal columns (Fig. 3A). Meanwhile, there was a marked activity of antidromic impulses passing through the dorsal column out into the dorsal root (Fig. 3B). It is obvious that this effect is quite different from the depression described above (cf. Fig. 1A).

**Afferent conduction in ventral columns.** In order to record the afferent volley in the ventral columns, the cord in the middle thoracic region was slightly rotated and the tip of the recording needle was placed 1–2 mm. lateral to the anterior medial fissure, and just penetrated the surface of the cord. When a single afferent volley was initiated by a shock applied to the dorsal root L7 it was usually possible to record a response in the ventral column. The response was most easily found in the ventral column on the
side opposite to the dorsal root stimulated. Both the latency and the shape of the response were somewhat variable. Usually, however, after a latency of about 2-4 msec. there was an initial negative potential followed about 10 msec. later by a second elevation. After these two negative waves there was often a prolonged positivity. Cutting the dorsal columns 7 cm. below the point of recording did not change the appearance of the response. Furthermore, the response was usually quite localized to a restricted area along the ventral column which indicates that the activity was not picked up from a distance. The response, however, cannot be referred to activity in any particular afferent pathway in the ventral column. The second negative wave is probably not even an afferent response but is derived from impulses in descending pathways reflexly activated by the afferent volley (cf. p. 303).

The ventral column response was easily depressed by stimulating various structures in the brain. These structures proved to be essentially the same as those which have already been shown to cause depression of the relayed dorsal column response.

Figure 4 shows simultaneous recording of the afferent response in the ventral column (upper beam) and in the leg area of the sensory cortex (lower beam). Repetitive stimulation in the ventral part of the anterior vermis causes a marked depression of both responses (2). Naturally, a decrease of the cortical response should be predicted as a result of a decreased afferent volley in the ventral columns.
However, it cannot be definitely stated that the depression of the cortical response results solely from the decrease in the ventral column response. The records show that immediately after the stimulation there remains a depression of both responses (3). A few seconds later, however, the ventral column response has recovered while the cortical response still remains depressed (4). This is typical and it might indicate that the conducted afferent volley has been interfered with, not only in the spinal cord but also in higher centers.

During the stimulation there is an increased background activity in the ventral column, which can be attributed to impulses in descending pathways activated by the central stimulation. It is worth pointing out that the intensity of this evoked background activity has no direct relation to the amount of depression evoked upon the afferent volley. From many regions in the brain, a pronounced background activity was obtained without any effect upon the afferent response, while on the other hand this response was sometimes completely blocked during a hardly visible change in background activity in the ventral columns. This seems to indicate that some specific descending paths have to be activated in order to evoke an effect upon the afferent volley.

No attempts have been made to get detailed information concerning the complete extent of the cerebellar region from which the effects can be obtained. Cortical electrodes were used to stimulate that part of the cerebellar cortex that could easily be reached by a simple dorsal approach (posterior vermis, ansiform and paramedian lobe). Stimulation of these areas never evoked any effect upon the afferent ventral column response. Other parts of the cerebellum were explored by the coaxial needle electrode angled down through the dorsal exposure. With this technique it was found that stimulation in the ventral part of the anterior vermis frequently caused depression of the test responses. Usually the effect was produced from both sides of the midline. Occasionally stimulation in the region of the dentate nucleus also proved to be effective.

In a series of experiments the afferent volley in the ventral column was influenced by repetitive stimulation in the bulbar or midbrain reticular formation. The latter area is known to possess marked excitatory effects on the motor and gamma efferent system (8, 21, 24). In no experiments, however, could an increase of the afferent response be evoked from these structures. The only effect obtained was a depression. Variations of the frequency (30–300/sec.) and the intensity (2–8 V.) of the stimulation never caused any qualitative changes in the results. The effect remained unchanged even if the dorsal root stimulus was reduced to submaximal strength. It is worth pointing out, however, that in the present investigation the total extent of the brainstem reticular formation has by no means been completely explored. Usually the stimulating electrodes were inserted into the midbrain reticular formation at about the level of the red nucleus. The bulbar reticular formation was usually stimulated at about the level of the vagal nuclei. At
these levels stimulation in quite widespread areas on both sides of the mid-
line caused depression of the afferent test response.

Several points in the basal ganglia and in the thalamus have been explored by the stimulating electrode. Usually negative results were obtained from these areas, but in one experiment the afferent test volley was depressed by stimulation in the posterior part of the thalamus.

In the experiment presented in Fig. 5, the postcentral sensory cortex was stimulated. The afferent test volley evoked from the right dorsal root L7 was recorded simultaneously from the left ventral column and from the lateral part of the left midbrain (Fig. 5, A1). During stimulation of the left sensory cortex the afferent responses were completely abolished (Fig. 5, A2).

Similar results could usually be obtained from the sensory cortex of both hemispheres but the most potent effects were always evoked from the sensory cortex on the side opposite to the stimulated dorsal root. Furthermore, different areas of the sensory cortex were not equivalently effective, the medial portion being more potent than the lateral. Since the medial portion involves the leg area of the sensory cortex, the results might indicate a somatotopic organization.

In some experiments an afferent response was recorded from the medial part of the midbrain reticular formation (6). This response, which had a latency of about 18 msec., was almost completely abolished during stimulation. In a similar way an afferent response recorded from the anterior vermis could easily be depressed by stimulating the postcentral sensory cortex (Fig. 5B).

In one experiment the afferent volley in the spinal cord was depressed by stimulating the second somatic sensory area (22). The effect obtained from
this cortical region, however, was less pronounced than the effect evoked
from the postcentral sensory cortex.

Results similar to those obtained by stimulating the sensory cortex were
regularly seen also during stimulation of the precentral motor cortex. Again,
the effects were most pronounced from the hemisphere on the side opposite
to the dorsal root stimulated. The question arose as to what degree the
pyramidal tracts might be responsible for the effect evoked upon the afferent
volley in the spinal cord. With this problem in mind, the stimulating elec-
trodes were placed in the pyramidal tract at the middle level of the medulla
oblongata. Stimulation of this point caused a slight depression of the afferent
test response in the spinal cord, but since the effect was more pronounced
from the adjacent bulbar reticular formation, the possibility cannot be ex-
cluded that the result was due to a spread of the stimulus into this region.

We cannot claim to have done more than a preliminary exploration of
the total extent of the cerebral cortex. Besides most areas on the dorsolateral
surface of the hemisphere, however, the medial surface has also been stimu-
lated. Here, stimulation of the anterior part of the cingulate gyrus caused
depression of the afferent test response.

Afferent conduction modified by removing tonic descending influences

In the previous section a number of central nervous structures have
been described which, upon stimulation, influence the afferent conduction
in the spinal cord. The effect of such central stimulation upon the afferent

![Afferent conduction modified by removing tonic descending influences](image)

system is completely abolished by a moderate dose of anesthesia (Nembutal,
Chloralose). Thus, after injection of 15 mg. Nembutal/kg., it was no longer
possible to influence the size of afferent volleys in the spinal cord by stimu-
lating various structures in the brain. At the same time, as this effect upon
the afferent response was abolished, the evoked background activity in the
ventral column was definitely decreased.

The most striking effect of the anesthesia, however, was to increase
greatly the control size of the afferent response. In a few curarized animals
it was quite difficult to record any afferent response in the ventral column
following stimulation of the dorsal root. The record presented in Fig. 6A
was obtained from such an animal. The ventral column response is hardly
visible. After injection of about 45 mg. Chloralose/kg., there was a remark-
able increase of the afferent response (Fig. 6B) and similar augmentation occurred in the instances after Nembutal.

Considering the facts presented above, it seems reasonable to conclude that the increase of the afferent response during anesthesia is due to a removal of tonic, descending influences, capable of depressing afferent conduction in the cord. If this conclusion is correct it is logical to assume that a high transection of the spinal cord should influence the size of the afferent response in a way similar to anesthesia. In Fig. 7 is shown the ventral column response in a curarized animal before (A) and after (B) a high transection of the spinal cord. In most experiments of this kind the size of the afferent response was decreased immediately after the transection. After about 10–20 minutes it had recovered. Then it continued to grow for a variable period of time. Usually the maximum size was reached within about one hour.

**Fig. 7.** Effect of high cord section on left ventral column response. A before and B one hour after transection. Dorsal columns transected at L1.

It should be noted (Fig. 7) that not only the amplitude but also the appearance of the response has been changed by the transection. The late hump appearing in the first record (A) is no longer present in the second (B). This typical result would indicate that the late negative deflection, present in most of our ventral column records, is due to activity in descending pathways, reflexly activated by the afferent volley. This conclusion was further supported by an experiment in which the animal was not curarized but lightly anesthetized with a combination of Chloralose and Nembutal. The ventral column response in this cat showed a very pronounced late negative wave. Repetitive stimulation in the midbrain reticular formation had no effect upon the first afferent volley in the ventral column but the late negative wave was greatly increased. The different nature of the first and second hump is indicated by their different behavior during central stimulation. Furthermore, the large size of the late negative hump in this animal falls well in line with Moruzzi’s observation (17) that in animals under Chloralose an afferent stimulus regularly evokes a muscle twitch representing a reflex mediated by certain structures in the brain.

**DISCUSSION**

The synaptic transmission of motor impulses conducted from the brain to the effector organ is known to be under the influence of nervous mecha-
nisms capable of varying the excitability of the motor pathways. The synaptic transmission of sensory messages, on the other hand, has usually been looked upon as a more independent phenomenon supporting a direct relation between the peripheral and end-organ discharge and the afferent message arriving at sensory receiving areas.

In the present paper we have presented evidence that the transmission of an afferent volley in the spinal cord can be influenced by repetitive stimulation of various structures in the brain. The question arises as to how this effect upon the afferent volley is produced. It is conceivable that a central stimulation might cause backfiring of antidromic impulses into sensory pathways which thus are made refractory to orthodromic, afferent impulses. The existence of sensory synaptic relays between the spinal level and the central structures stimulated, however, excludes the possibility of backfiring into spinal afferent neurons. Furthermore, the nonsusceptibility of the presynaptic afferent volley in the dorsal columns indicates that the nonsynaptic conduction in spinal afferent neurons is not interfered with and that instead it is the sensory synaptic relays at the root entry zone that are influenced by the central stimulation. How, then, can these spinal sensory relays be affected by the central stimulation? It might be argued that marked induced activity in descending paths during stimulation of central structures could lead to an electrotonic field phenomenon which, by interacting with synaptic relays at the root entry, could depress the recorded afferent response. Because of the evidence, however, that descending pathways can exhibit a tonic influence upon afferent transmission, this interpretation seems highly improbable. A more reasonable conclusion is that the synaptic transmission from the first to the second sensory neuron is under a true physiological influence of specific descending pathways.

According to this interpretation, depression of the afferent response during central stimulation is due to an inhibition of sensory relays in the spinal cord. It might be objected that descending influences might converge on sensory synapses in the cord and occlude the passage of the afferent volley. This could result in depression of the afferent response during repetitive brain stimulation. If this were so, however, one ought to expect that a weaker stimulation of the effective central structures should facilitate rather than depress the afferent volley. Altering the parameters of stimulation did not cause any reversal in effect and therefore this possibility may probably be excluded. We have no information concerning the ultimate nature of the inhibitory process involved but there seems to be no major objection to the assumption that sensory interneurons can be inhibited by mechanisms similar to those underlying inhibitory processes in the motor system.

In the present experiments it has never been possible to cause an increase of the afferent response by central stimulation. This fact might be attributed simply to an incomplete exploration of the brain but it might also indicate that there are no descending pathways capable of evoking actual excitation of sensory relays. This does not necessarily mean that sensory relays cannot
be sensitized to incoming afferent impulses. It merely signifies that increased excitability of sensory relays can be looked upon as a release of tonic inhibition rather than as an active facilitatory process.

According to histological evidence (19) the long ascending afferent paths in the spinal cord are made up by branches of the same neurons that also form a link in the segmental reflex arcs. Thus, it is obvious that the present results have a certain significance also for the central regulation of spinal reflexes. As early as 1926 it was suggested by Fulton (7) that internuncial neurons participating in spinal polysynaptic reflexes may be under an inhibitory influence of descending pathways. According to Fulton, these descending influences might serve to regulate the distribution of incoming afferent impulses at a spinal level, suppressing some and deflecting others rostrally for higher integration. Recent experiments support the view that central effects can be evoked not only on the motoneurons but also on the interneurons of spinal polysynaptic reflex arcs (2, 3). The only spinal reflex whose afferents cannot possibly be influenced at an interneuronal junction is the monosynaptic one. In this case, however, modification of afferent discharge is known to take place peripherally at the end-organ itself (8, 14, 15).

Several unanswered questions are raised by the present observations. One is whether relays further centrally than those here experienced are similarly regulated by higher neural levels. Study should obviously be made of central influences acting upon afferent relays in the posterior columns and in thalamus. The present results indicate that the old interpretation of corticothalamic fibers as a regulatory mechanism for thalamic transmission (9, 18) deserves serious consideration and experimental study.

Another question is whether all spinal afferents can be influenced at their synaptic junction in the cord or whether certain modalities are excluded from central interference. It must be emphasized that a dorsal root stimulus evokes a quite unphysiological sensory response including a variety of afferent modalities. In order to get more detailed information concerning this problem it is therefore necessary to use more physiological afferent test stimuli.

It should also be determined whether or not central influences can be exerted upon the first and later relays in afferent paths from cranial receptor endings. It might be presumed that the cranial afferent system for common sensibility could be influenced in a manner similar to those in the cord. It would be of great interest to know additionally whether afferent conduction from the organs of special sense might similarly be modified at the first and later relays (cf. 18, 27). Histological evidence favors this possibility, for centrifugal fibers to the olfactory bulb and to the retina have been described by Cajal (20, cf. also 1).

The present results indicate that the reticular formation plays an important role in the central regulation of sensory relays in the spinal cord. Most other central structures which have been found capable, upon stimulation, of influencing the afferent response, are known to be functionally
connected with the reticular formation (16, 23). It is well known that the activity of the reticular formation is easily depressed by anesthesia. Therefore, it is not surprising that the inhibitory effect on the sensory system obtained from this area is eliminated by moderate doses of Nembutal or Chloralose. That anesthesia can increase the afferent response in sensory cortex has earlier been observed by French et al. (6) and others. The results obtained from motor cortex and the pyramids might indicate that to a certain degree the pyramidal tract also acts as a regulating mechanism on afferent relays (18). This possibility, however, deserves further investigation.

We have no information concerning the specific physiological circumstances under which the sensory regulating mechanisms are normally activated. Neither do we know to what degree the pronounced tonic inhibition of the afferent spinal relays that is obviously present in curarized cats is a specific phenomenon for this particular preparation. Clinically it is well recognized that variation in psychological states can modify the appreciation of various modalities of sensation. This is particularly true for pain. It is interesting to imagine the significance of a sensory regulating mechanism under such circumstances.

**Summary**

1. In curarized cats it has been shown that stimulation of various central structures influences the size of an afferent volley evoked by a dorsal root stimulus and recorded from dorsal and ventral columns, midbrain, cerebellum and sensory cortex.

2. The relayed response in the dorsal column and the dorsal root reflex were invariably depressed by stimulating certain central structures. The afferent volley in the ventral column as well as the afferent response in the midbrain, cerebellum and sensory cortex was depressed by similar stimulation. The primary afferent spike in the dorsal column was unchanged, however.

3. Depression of the test responses has been obtained by stimulating the bulbar and midbrain reticular formation, the ventral part of the anterior vermis, the postcentral sensory cortex, the second somatic sensory area, the precentral motor cortex and the anterior part of the cingulate gyrus. So far, no increase in the afferent response, except as a rebound, has been seen on stimulating these structures.

4. The effect of the central stimulation upon the afferent responses was completely abolished by a moderate dose of anesthesia. Anesthesia also caused a marked increase in the control size of the afferent ventral column response. A similar effect was produced by a high transection of the spinal cord in curarized animals.

5. It is concluded that synaptic afferent transmission in the spinal cord can be influenced in a physiological manner by descending pathways from certain structures in the brain. Furthermore, this sensory-regulating mechanism can evidently act in a tonic fashion.
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REFERENCES


