AN INHIBITORY MECHANISM IN THE BULBAR RETICULAR FORMATION

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ACCORDING to the doctrine that the nervous system is organized as a series of levels, that portion of the brain stem lying immediately above the spinal cord, and described as bulbar, has traditionally been regarded as a level contributing excitatory influences to motor outflows. The basis for this view is the observation, first made by Sherrington (11), that decerebration leaving only the bulbar part of the brain connected with the cord, is followed by a state of over-activity or rigidity of the anti-gravity muscles.

It has not been widely recognized that this bulbar part of the brain stem, in addition, contains a mechanism capable of exerting a general inhibitory influence on motor activity. In the experiments to be reported, this inhibitory influence has been demonstrated by observing the effect of bulbar stimulation upon reflexes, upon decerebrate rigidity and upon responses evoked from the motor cortex.2

METHODS

In cats under chloroalose anesthesia, the blink, flexor and patellar reflexes were evoked respectively by a signal magnet, an inductorium and a solenoid, operating recurrently on a timing circuit, and the excursions of the lid and legs were recorded on a kymograph. Other animals, observed visually, were decerebrated under ether by the anemic method, but using a single parapharyngeal approach to ligate the "internal carotid" and basilar arteries. In other cats under chloroalose, the motor cortex or internal capsule were excited and the leg movements were recorded.

In each animal, the lower brain stem was stimulated, the fine "bipolar" electrodes being oriented with the Horsley-Clarke technique. Sixty cycle, sine wave current, at 3 to 5 r.m.s. volts, was employed routinely, the threshold for evoking responses comparing favorably with that determined with a Goodwin stimulator at higher frequencies. Microscopic examination of frozen sections of the explored area in each case permitted identification of the sites stimulated.

RESULTS

Bulbar inhibition of reflex activity. Bulbar stimulation during reflex activity was found to inhibit the reflexes. In the record shown in Fig. 1A, the flexor reflex of the foreleg (a), the patellar reflex of the hindleg (b) and the blink reflex of the eyelids (c) were reduced or abolished by bulbar stimulation during the period marked by the signal (d). These reflexes, initiated respectively by nociceptive, proprioceptive and tactile stimuli, involve muscles—flexor, extensor, and posturally indifferent—distributed over the length of the body. The bulbar inhibitory influence thus appears to be a

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2 Preliminary accounts have been published (7 and 8).
general one, not limited in its action to functionally specific or to topographically circumscribed reflex acts.

These reflexes were not invariably inhibited together, however, and Fig. 1B records an instance in which the flexor reflex was not susceptible to bulbar inhibition effective against the patellar and blink reflexes. The bulbar inhibitory effect was frequently followed at the cessation of the stimulus by a subsequent augmentation of whatever activity was proceeding, an example

Fig. 1A and B. Kymograph records of the effect of bulbar stimulation (d) on the flexor (a) patellar (b) and blink (c) reflexes evoked at 2 sec. intervals.

Fig. 2. Midsagittal reconstruction of the cat's brain stem upon which are projected in black circles the bulbar sites whose stimulation inhibited the patellar reflex. Abbreviations for Figs. 2 and 3 are as follows: A—aqueduct, AC—anterior commissure, BP—basis pedunculi, C—cerebellum, CG—periaqueductal grey, F—facial nucleus and nerve, H—hypoglossal nucleus and nerve, MI—massa intermedia, MLF—median longitudinal fasciculus, OC—optic chiasma, P—pons, PC—posterior commissure, PN—posterior column nuclei, PY—pyramidal tract, R—inferior reticular nucleus, SC—superior colliculus, T—nucleus of the spinal fifth tract, TS—tractus solitarius V—vestibular nucleus, 3V—third ventricle, 4V—fourth ventricle.
of which is seen in Fig. 1B, b in the case of the patellar reflex, and in Fig. 1A, c in the case of the blink reflex.

In the instances shown in Fig. 1, stimulation of the left side of the medulla was observed against reflexes of the left lid and legs. Whenever it was tested, however, bulbar stimulation was found to inhibit reflexes on both sides of the body.

The general location of the bulbar area inhibiting reflex activity is shown in Fig. 2, projected upon a mid-sagittal reconstruction of the cat’s brain stem. Points whose stimulation inhibited the patellar reflex, indicated by black circles, are seen to be distributed in the central portion of the lower brain stem, in what is called the bulbar reticular formation.

The precise locations of the effective points are illustrated in Fig. 3, on four transverse sections at the levels indicated in Fig. 2. Inhibition of the patellar reflex is seen to have been elicited by exciting a rather long antero-posterior extent of the bulbar reticular formation, chiefly its ventromedial part.

The dots and plus symbols in Fig. 3 indicate points whose stimulation did not inhibit the patellar reflex, and if their distribution is examined, most of the lateral reticular formation and the sensory systems bordering it—the trigeminal, vestibular, vagal and posterior column nuclei—can be ruled out as contributing to the effect. The inferior olive which lies immediately ventral to the excitatable area also appears without relation to the inhibitory responses for they have been elicited without impairment after olivectomy (14).

This bulbar inhibition of reflex activity has been obtained after decerebellation and transection through the front end of the medulla and so does not result from the activation of ascending connections to the cerebellum or higher parts of the brain. That it does not result from stimulating connec-
tions from rostral regions simply descending through this area has not been so certainly determined, but no such general inhibitory influence has yet been obtained by the stimulation of more rostral brain stem levels.

From points in the lateral portion of the medulla and others on the periphery of the inhibitory field, increase of the excursion of the patellar reflex resulted from bulbar stimulation (Fig. 3, plus symbols). At least some of these latter responses appear to have resulted from activating facilitatory pathways descending from higher levels (10). If such facilitatory connections in addition pass through the inhibitory field, the frequent appearance of subsequent augmentation after inhibition (Fig. 1) might be attributed to the activation of intermixed inhibitory and facilitatory elements. Such subsequent augmentation might, on the other hand, represent a release from inhibition temporarily depressed after activity.

**Bulbar inhibition of decerebrate rigidity.** It is evident from the above that bulbar stimulation can inhibit phasic reflex activity; it is equally effective in inhibiting tonic reflexes. Decerebrate animals were observed in the supine position with their rigidly extended legs in the air. During bulbar stimulation in the area indicated in Figs. 2 and 3, extensor tone was lost, the legs became flaccid and collapsed, were flail-like to manipulation, and reflexes could not be elicited. At the conclusion of stimulation, extensor hypertonus and other reflex activity promptly returned, the former sometimes with a snap and gain resembling rebound. On stimulating one side of the medulla, the loss of tone and reflexes was complete in all legs except the contralateral fore in which it was but partial.

**Bulbar inhibition of cortical motor response.** One further type of motor activity against which bulbar stimulation has been tested is the response evoked from the motor cortex. In Fig. 4A, flexion of the fore (a) and hind (b) legs, induced by exciting the motor cortex at 2 sec. intervals, was inhibited by bulbar stimulation during the period marked by the signal (c). The site of inhibition here is evidently spinal rather than cortical, for in Fig. 4B flexion of the hindleg (a) induced by activating descending fibers from the motor cortex in the internal capsule (c) was also abolished during the period of bulbar stimulation (b). A similar record, shown in Fig. 4C, illustrates the subsequent augmentation of cortical motor response which may follow its inhibition by bulbar stimulation.

Inhibition of cortical motor response was elicited by stimulating the same bulbar reticular area (Figs. 2 and 3) effective against reflex activity and decerebrate rigidity. In the records shown in Fig. 4, bulbar stimulation inhibited leg responses on the same side of the body, evoked in turn from the opposite motor cortex. In instances in which it was tested, however, inhibition from stimulating one side of the medulla was effective against cortical motor responses on both sides of the body.

**Descending inhibitory pathway in the spinal cord.** Inhibition of reflexes, decerebrate rigidity and cortical motor response was, then, bilateral from stimulation of each side of the medulla. Ipsilateral inhibition could, how-
ever, sometimes be obtained at a lower threshold, or with a given current strength was more complete. This does not necessarily mean that the responsible reticulo-spinal connections are predominantly uncrossed; they might, on the contrary, decussate at the bulbar level, the crossed fibers possibly being more readily excited than the ipsilateral cell groups.

The distribution of points yielding inhibition of the patellar reflex at the lower end of the medulla (Fig. 3D) suggests that efferent inhibitory connections descend in the ventral portion of the spinal cord. This is supported by instances in which bulbar inhibition of the knee jerk was tested after thoracic cord lesions. Interruption of the posterior column or dorsal part of the lateral column was without effect, but the response was impaired greatly by section of the antero-lateral portion of the cord.

**Coincidental responses.** Depending upon the sites from which they were elicited, the bulbar inhibitory responses were frequently accompanied by respiratory changes (9), vasomotor alterations (13), pupillodilation (3) and hypoglossal nerve reactions. It was evident in the course of the experiments that these bore a coincidental and not a causal relation to inhibition.

**DISCUSSION**

The results described above indicate that the bulbar segment of the brain stem contains neural elements capable of exerting an inhibitory influence on a wide variety of motor performances. While this bulbar function has, to say the least, long remained in obscurity, collateral support for its existence can be found in both old and recent investigations. Deductions drawn from cervical fracture cases led Hughlings Jackson (4) to attribute an inhibitory function to the bulbar region, to which he so aptly referred as "the highest center of the lowest level."

In a study of the early development of behavior in the frog embryo,
Wang and Lu (12) found initially repetitive spinal motor activity to become suppressed by the maturation of a higher inhibitory mechanism, which by transection experiments was localized in the hindbrain. It is not yet clear, however, that this localization can be applied to the mammalian brain, for Barcroft and Barron (1) described an analogous series of events in the maturation of behavior of the sheep embryo, but located the developing inhibitory mechanism in the forebrain. It has long been known that stimulation of the cerebellum is capable of inhibiting motor activity, and Hare, Magoun and Ranson (2) showed this inhibitory influence to be mediated by cerebello-bulbar connections.

Of the greatest relevance are the observations of Keller (5), that animals maintained into the chronic state after pontile transection of the brain stem exhibit an enduring generalized atonia and absence of some of the more complicated spinal reflexes. It is difficult to explain these symptoms as resulting simply from a loss of excitatory innervation, and, as Keller suggests, they would appear best accounted for by the existence of an active inhibition proceeding from some site below the transection. Since decerebellation did not alter the result, it is not illogical to assume that the bulbar inhibitory mechanism, outlined above, had by appropriate isolation been released and was maintaining the neuraxis below it in a state of reduced activity.

The role which the bulbar inhibitory mechanism plays in the management of motor activity in the intact animal awaits further study. It is likely that it is involved in cerebellar function (2), and its relation to the regulation of motor activity by the cerebral cortex has already been indicated by McCulloch, Graf and Magoun (6), who have reported the reception by the bulbar reticular formation of a descending projection from cortical area 4-S, and suggest that this reticular area constitutes the brain stem relay in an inhibitory extrapyramidal system.

SUMMARY

Electrical stimulation of the lower brain stem of the cat has revealed a bulbar area capable of inhibiting motor activity whether initiated reflexly, in decerebrate rigidity or from the motor cortex. The excitable region is distributed in the bulbar reticular formation, chiefly its ventromedial part, and efferent connections descend from it in the ventral part of the cord.

REFERENCES

BULBAR INHIBITION OF MOTOR ACTIVITY