Localization and Function of the Medullary Vasomotor Center in Infracollicularly Decerebrated Cats

By Percy Lindgren, M.D.

The medulla oblongata occupies a key position with respect to the central vasomotor control. If the nervous pathways between it and the preganglionic outflow are interrupted, for example by section of the brain stem at the level of the obex, vasoconstrictor tone will be lost, followed by substantial diminution of the peripheral resistance and greatly reduced blood pressure. On the other hand, an apparently normal control of the blood pressure will be retained if the communications are interrupted between the medulla oblongata and parts of the brain located higher. These fundamental conditions were originally elucidated by Dittmar and Owssjannikow and have been confirmed by several modern investigators.

According to current views, this vasomotor center in the reticular formation of the medulla oblongata not only exerts a tonic influence upon the sympathetic vasoconstrictor nerves, but is also an important vasoreflex center. Chen et al. and Alexander demonstrated that pressor reflexes elicited by electrical stimulation of a mixed peripheral nerve (brachial or sciatic) were probably relayed via the medulla oblongata. The blood pressure rise could be blocked by section of the afferent pathways in the two dorsal quadrants at the level of C2. Whether afferent impulses from the baroceptors inhibit the tonic activity of the vasoconstrictor center directly or at spinal level via a medullary inhibiting center ("depressor center") does not seem to be entirely clear. That the latter mechanism at least occurs was shown by Lim et al., Yi, and Alexander.

The anatomical and functional relationship

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MEDULLARY VASOMOTOR CENTER

lary vasomotor center in chronically decerebrated cats. An important advantage in using chronically operated animals rather than animals decerebrating during the acute experiment is that separate study of the location of true medullary neurons belonging to the vasomotor center is possible, since hypothalamo-fugal and mesencephalo-fugal neurons have degenerated. Furthermore, the animals have recovered from the decerebration shock; otherwise, it is possible that the acute release of central facilitory and inhibitory impulses might have some significant effect on the function of medullary and spinal neurons and centers. The operation itself might also excite, for a brief period, regions capable of influencing medullary structures in both directions.

Methods

Successful experiments were performed on three cats (weights 2.1, 2.6, and 2.8 Kg.), decerebrated infracollicularly 4, 6, and 9 days previously.

Bilateral Infracollicular Decerebration

In order to exclude not only hypothalamo-fugal fibers, but also mesencephalo-fugal fibers, the decerebration section was done infracollicularly, although the operation was more complicated than in supracollicular decerebration. The operative technique will be described in principle only, because it corresponds to a method of unilateral infracollicular decerebration published a few years ago.13

The animals were anesthetized with ether. The operation was performed caudal to the tentorium cerebelli and under aseptic conditions. After removal of parts of the occipital bone and the ventral portion of the cerebellum, the fossa rhomboidea and the caudal surface of the tectum mesencephali could be inspected. A thin silver plate with its lower edge fitted to the contours of the base of the brain was then inserted just behind the inferior colliculus and approximately in the middle of the pons so that the entire brain stem was cut. At this stage of the operation the anesthesia was discontinued. The silver plate was then left undisturbed in the brain. After careful hemostasis as possible, the dura was sutured, as were the muscles and the skin.

The postoperative management of the cats was very exacting. Since their heat regulation had been lost, they were placed in heated cabinets regulated by thermostats. The cats were observed, weighed, their rectal temperature was checked and annotated every two hours, day and night. During the first three days, the animals received fluid only parenterally, 100 to 200 ml. saline/Kg. Therefore, they were tube-fed three times daily with a mixture of 40 to 50 ml. milk and finely chopped fish. Fluid was administered parenterally also when required. Penicillin, 100,000 I. U. daily, was injected intramuscularly.

The mortality was very high; 11 cats were decerebrated, only three survived long enough to permit performance of the acute experiment. Some cats died during the operation, others from intracerebral bleeding, others from infection of the respiratory system during the postoperative period.

Performance of the Acute Experiment

Although not necessary, it was found to be advantageous in the acute experiments to give the cats light anesthesia (diallyl barbituric acid [Dial], 10 to 20 mg./Kg. intravenously), as a result of which the motor activity was diminished because of weakened reflexes.

A Y-shaped tracheal cannula was inserted, and the carotid arteries and vagal nerves were dissected free. The carotid sinus nerve on the right side was exposed for electrical stimulation. The previous incision in the skin of the back of the neck was reopened and the dorsal surface of the medulla oblongata was dissected free in order to permit introduction of the electrode. This was oriented by means of the Horsley-Clarke technique. The electrical stimulation consisted of square wave impulses. The generator had an output resistance of 1,000 ohms; each impulse had a duration of 2 milliseconds; the frequency was 70 impulses per second.

The blood pressure was measured in a brachial artery communicating with an ordinary mercury manometer. In two of the animals, the blood flow in one femoral vein was recorded by the method of Lindgren and Uvnäs;14 in the third experiment, the vascular areas of both hind legs were studied. In principle, the method consisted of directing the blood flow from the cannulated vein, via a plastic tube, to a phototube drop counter operating an ordinate recorder. From the drop chamber the blood stream was returned to the animal, entering the cannulated proximal stump of the same vein. The animals were heparinized; 25 mg. heparin/Kg. in a 5 per cent solution was given intravenously.

Histological Examination

When the experiment was concluded, the cat was killed and the brain was fixed by perfusion with a 10 per cent formalin solution. Frozen sections 40 microns thick were taken from the medulla oblongata and stained with hematoxylin by the method of Weil.15 The different electrode channels were identified at microscopic examination.
Results

Localization of the Medullary Vasomotor Center

The vasomotor active regions in the few animals studied seemed to have the same extension as in intact animals as shown, for example, by Chen et al.\textsuperscript{16} The investigations of these authors showed that the maximal responses were obtained on stimulation of the dorsal part of the medulla oblongata in the neighborhood of the fovea inferior. Wang and Ranson\textsuperscript{17} and Alexander\textsuperscript{7} also found the pressor center to be dominantly in the dorsolateral reticular formation, although points giving minor pressor reactions were scattered over most parts of the medulla oblongata, even in the ventral regions. The limited number of the experiments in the present investigation made it impossible to explore the whole medulla oblongata; therefore, most stimulations were applied in the dorsal region.

In two experiments, systematic exploration of the dorsal portion of the medulla oblongata located caudal to the section was undertaken. A consistent finding was the almost complete absence of vasomotor responses to stimulation in the zone just behind the section in the anterior part of the medulla oblongata. This zone had an extension of 3 to 5 mm. Caudal thereto it was possible to elicit pressor as well as depressor responses. Although the pressor structures appeared to be rather scattered, the maximal responses were generally obtained on stimulation in the vicinity of the fovea inferior. In this region, concomitant respiratory events were very small. Stimulation 1 to 2 mm. below the dorsal surface in the classic depressor area around the obex elicited typical depressor responses.

Figure 1 shows the results obtained in one of the experiments. The left part of the actual structures of the medulla oblongata was explored. Different points situated 1 to 2 mm. below the dorsal surface at intervals of 1 mm. along three longitudinal lines were stimulated. The most marked pressor responses were found along the middle longitudinal line, 3 mm. lateral to the midline and passing through the fovea inferior. Lateral as well as medial to this line, the pressor responses were smaller. The section level and the locations of the stimulation points are illustrated in figure 2.

Vascular Response to Central Electrical Stimulation

The peripheral responses did not differ from those observed in intact animals. As mentioned before, stimulation in the fossa rhomboidea as a rule caused a rise in blood pressure. The latency of the rise was very

\begin{figure}
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\caption{Cat 2.1 Kg., infracollicularly decerebrated nine days before the experiment. Pressor and depressor responses to systematic stimulation of different points in the left part of the medulla oblongata (intensity 2 volts, frequency 70/sec.). (1 to 8) = stimulation 1 to 2 mm. below the dorsal surface. The different points are situated along a longitudinal line 2.5 mm. to the left of the midline (see fig. 2). (9 to 13) = stimulation points 3.5 mm. to the left of the midline. (14 to 23) = stimulation points 1 mm. to the left of the midline. The maximal pressor response is obtained from the fovea inferior (6), and the maximal depressor response from points just to the left of the obex (20) and (21).}
\end{figure}
short, one or two seconds, indicating that it was effected by a nervous mechanism, in all probability via the sympathetic vasoconstric-
tor nerves. When light or moderate stimuli were applied, the blood pressure fell rapidly to its original level when the stimulation was discon-
tinued; but strong stimulation sometimes caused a biphasic reaction so that a second slow rise occurred after about 20 sec-
onds, lasting for one to two minutes, although the stimulation period was only 10 seconds. It is probable that the second phase was due to activation of the adrenal medulla.

Concomitant with the rise in blood pressure on stimulation in the fossa rhomboidea, the blood flow in the hind legs diminished or re-
mained unchanged, indicating a vasoconstriction. It is of special interest that unilateral stimulation in the medulla oblongata caused bilateral peripheral responses (fig. 3).

**Pressor and Depressor Reflexes**

Pressor reflexes were elicited by electrical stimulation of the central end of the cut brachial nerve. As seen in figure 4, this procedure caused a prompt rise in the blood pressure. In the same experiment, a sinus nerve was stimulated electrically and produced the ordinary depressor responses. The changes in the blood flow accompanying the blood pressure fluctuations are not very pronounced. Although there must be an increased or decreased vasoconstrictor tone, the influence of these changes on the blood flow is compensated by the blood pressure rise or fall, respectively.

**Discussion**

The difficulties in localizing the center to any anatomically distinct nucleus or cell
structure have made the conception "medullary vasomotor center" somewhat vague, and it has been differently interpreted. Some investigators have considered this medullary structure to be an extension of the syncytium, consisting probably of short neurons that are situated in the reticular formation from the hypothalamus to the medulla oblongata, and from which it is possible to elicit vasomotor responses. Others have emphasized its significance as a reflex and tonic center with an integrating character receiving afferent impulses from higher centers and from the periphery. A quality that definitely distinguishes this medullary region from higher parts of the reticular formation is its importance for normal sympathetic vasoconstrictor tone, which is nicely demonstrated by means of transection experiments.5

One essential qualification for a brain structure to have the nature of such a \"center\" is its consisting of cell bodies and synapses and not only of afferent or efferent tracts from centers located elsewhere. The aforementioned earlier investigations of normal vasomotor tone suggested that the medullary vasoconstrictor center may have such a nuclear character. This assumption seems to be fully proved by the present investigation, since the actual structures in the medulla oblongata did not degenerate after the decerebration, but retained their physiological properties and could still be activated by electrical stimulation. It was also interesting that the efferent pathways that mediate the stimulation responses seemed to be quite intact. As in normal animals, unilateral stimulation caused bilateral vasoconstriction, indicating a partial decussation of the pathways.

The hypothalamo-bulbar vasoconstrictor pathways facilitating the medullary vasoconstrictor center described by Thompson and Bach seem to have little importance for known functions of this center. Pressor as well as depressor reflexes could be elicited in a normal way in the chronically decerebrated cat. This observation corresponds well to what has been found in acutely decerebrated animals. As regards pressor reflexes elicited by stimulation of an afferent peripheral nerve, there has been discussion as to whether such reflexes are relayed via medullary regions or only via spinal synapses. Alexander postulated that they \"are dependent upon the integrity of the bulbar center.\" It has been shown, however, that they can be provoked even in spinal animals, but it is probable that spinal centers do not play any appreciable role under normal conditions.

Together with previous results, the present observations imply that the medullary vasomotor center is, to a great extent, an independent center. The significance of hypothalamo-fugal pathways projecting on it is uncertain. The bulbar vasomotor functions seem to function normally, even if those fibers have degenerated. It is possible to activate the bulbar \"vasoconstrictor center\" by means of electrical stimulation and to elicit bulbar-vasomotor reflexes. Yet, the number of present experiments is quite small; the positive results are clear and allow these conclusions. It is worth noting, however, that in the lateral and ventral parts of the medulla oblongata, hypothalamospinal and mesencephalospinal vasoconstrictor pathways pass which have neither anatomical nor functional rela-
MEDULLARY VASOMOTOR CENTER

tionship to the medullary vasomotor center.11,13 The latter pathways have no influence on normal vasomotor tone or medullary vasomotor reflexes.

Summary

The medullary vasomotor centers were studied in three cats, decerebrated below the mesencephalon four to nine days before the acute experiment. Exploration of the dorsal regions of the medulla oblongata revealed that the vasomotor active regions had about the same extension as in intact animals. Medullary pressor and depressor reflexes, elicited by electrical stimulation of a peripheral nerve and a sinus nerve, were also of a normal type in the decerebrated cats. The results indicate that the medullary vasomotor center constitutes a region of nuclear character with cell bodies and synapses functioning as a tonic and reflex center. In this respect, it seems to function normally even after the degeneration of vasomotor pathways from higher centers.

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