Cardiovascular response to experimental spinal cord compression

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Anesthetized, and unanesthetized decerebrate, cats were used to study the arterial pressor response to spinal cord compression. To produce a cervical compression it was necessary that the cervical cord be functionally connected to the thoracic cord, pressor response by the reverse was not true. A pressor response above 200 mm Hg systolic was associated with electrocardiographic (EKG) signs of left ventricular overload and ventricular ectopic beats. These changes were not prevented by atropine, hexamethonium, or propanolol. Both the pressor response and the EKG abnormalities were prevented by an alpha-adrenergic blocking agent. The authors conclude that alpha-adrenergically mediated arterial vasoconstriction is the effector mechanism in the pressor response to increased intracranial pressure or cord compression.

KEY WORDS · spinal cord compression · Cushing reflex · arterial hypertension · electrocardiogram · alpha adrenergic blockade

IT has been known for a long time that increased intracranial pressure is often accompanied by systemic arterial hypertension. After craniocerebral surgery or trauma arterial hypertension may contribute to brain swelling by increasing the filtration pressure of plasma. Cushing was one of the first to recognize the clinical significance of the pressor response and the associated bradycardia, and this phenomenon has since been usually referred to as the “Cushing reflex” or the “Cushing phenomenon.” The mechanisms by which this sequence of events develops are still not entirely understood. The work of Naunyn and Schreiber, Cushing, and others has established that comparable pressor responses can be obtained by mechanically compressing the exposed spinal cord, but do not develop in animals with cervical cord transections. Their data also indicate that intracranial hypertension produces vasoconstriction in the limbs and abdominal viscera.

In the course of a series of studies on the pathophysiology of spinal cord injury in cats we encountered the pressor response and restudied it as a possible contributing factor to the local bleeding into the cord which almost always follows spinal trauma. Recording of the electrocardiogram (EKG) concurrently with arterial pressure showed some striking changes which, to our knowledge, had not been reported previously; a series of pharmacological experiments gave us some clues as to the identity of the intermediary adrenergic events in the process. We felt it worthwhile to report these findings as being perhaps of potential value in the clinical management of patients exhibiting the “Cushing reflex.”

Methods

We used adult mongrel cats. All preliminary surgical procedures were carried out under general anesthesia by methoxyflurane (Penthrane) and oxygen. These included
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tracheotomy and arterial (carotid or femoral) and venous (cephalic) cannulation. This was followed in most animals by intravenous injection of 60 to 80 mg/kg of alphaglucochloralose, dissolved in polyethylene glycol 200, as the long-term anesthetic agent. In some of the control preparations either pentobarbitone anesthesia or supracollicular decerebration was used instead of chloralose, with no differences in the results. In all cases a laminectomy of two to three vertebrae served to expose the appropriate segments of the cord, without opening the dura. The vertebral column was rigidly supported by spinous process clamps above and below the laminectomy. The animals received a slow continuous infusion of glucose (5%) in Ringer's solution, and their temperature was kept stable (36–38°C) by infrared lamps. They were immobilized by Flaxedil and maintained under artificial respiration with room air, at 20 strokes/min and 30 to 40 ml/stroke.

Damage to the cord was produced by compressing one to two segments by means of a weighted cylindrical pressor foot so positioned that its long axis was parallel to that of the cord. The total weight applied was 500 gm/cm². After completion of the experiments the animals were perfused with Ringer's solution and then 10% formalin, the exposed cord was removed and post-fixed in formalin, blocked, sectioned (in paraffin) and stained with a gallocyanin-methyl green stain.

Continuous recordings of the electrocardiogram (standard I-II-III leads) and the femoral or carotid arterial pressure (Statham P23 transducer) were made on a four-channel heated stylus recorder (Sanborn).

Results

We found, as had others,1,3,10,11 that compression of the cervical, thoracic, and upper lumbar cord of neuraxially intact animals, either under chloralose or pentobarbitone anesthesia, produced a marked arterial pressor response with a latency of 2 to 6 seconds. Even slightly touching or bruising the dorsal surface of the cord elicited a transient pressor response. When a full compression of 500 gm for 15 min was used, the pressor response lasted up to 4 to 5 minutes and then slowly faded away; this degree of compression invariably resulted in complete and irreversible paraplegia.

The pressor response consisted of a rapid rise in both systolic and diastolic pressures, although the pulse pressure was also increased. The systolic pressure often exceeded 300 mm Hg. The pressor response was usually accompanied by some degree of bradycardia. More interesting, however, was the fact that as soon as the systolic pressure exceeded 200 to 220 mm Hg the EKG showed gross alterations consisting of rotation of the heart electrical axis and the appearance of prominent ventricular ectopic beats (Fig. 1). As the pressor response began to wane so did these EKG abnormalities and the bradycardia. Decerebration prior to thoracic cord compression did not prevent any of these changes. Figure 2 illustrates the fact that pressor responses were elicited by compressing the cervical, thoracic, and lumbar cord. Although the number of experiments (three in each group) is too small to derive any firm conclusions we are left with the impression that the response, in amplitude and duration, was greatest when the cervical cord was compressed, and minimal when the pressure was applied to the lumbar cord. Transection of the cord at T-1 completely eliminated the pressor and EKG response to compression at C3–4 but did not affect responses to compression at T3–4.

A number of drugs were used in an attempt to block the pressor response to T3–4 compression, using neuraxially intact cats under chloralose anesthesia. Hexamethonium bromide (5.0 mg/kg) (Fig. 3) injected 15 to 30 min before compression, and propanolol (Inderal, 0.5 mg/kg) injected 15 min before compression failed to prevent the pressor response or the concurrent EKG changes. In contrast to these negative results, phenoxybenzamine (Dibenzyline 5.0 mg/kg) injected 60 min before compression completely prevented the pressor response and the concurrent EKG changes. In contrast to these negative results, phenoxybenzamine (Dibenzyline 5.0 mg/kg) injected 60 min before compression completely prevented the pressor response in all but one of our preparations (Fig. 3), and that one showed only a mild pressor response (systolic 200 mm Hg) and no EKG changes. Each drug was tested in at least three animals. Figures 3 and 4 show the mean and range values recorded.

Discussion

The work of many others before us has
established three fundamental points. First, the pressor response to cord damage is a real phenomenon\textsuperscript{1,10} due to direct injury of the cord and not to anoxia,\textsuperscript{6} damage to extraneural structures, or to activation of extraneural baroceptors. Second, the pressor response elicited from the cord does not depend on the integrity of the supraspinal structures, but the elicitation of a pressor response to intracranial increased pressure or mechanical deformation of the brain stem requires the integrity of the connections between the brain stem and the cord.\textsuperscript{1,10} This clearly suggests that the cord is an essential efferent link in the so-called "Cushing reflex."\textsuperscript{3,12,14} Third, cord segments essential to the production of the pressor response appear to be between the upper thoracic and upper lumbar segments.\textsuperscript{1,7,10,13} Our data are in full agreement with these findings by others.

Some of our findings extend beyond those previously reported, however. The first of these new observations is the fact that floss electrocardiographic alterations accompanied the peak of the pressor response and appeared to be linked to the concurrently slowed arterial pulse rate. The EKG changes, because of their temporal relationship to the pressor effect, were interpreted as reflecting the cardiac response to the sudden overload imposed upon the left ventricle; this interpretation was reinforced by the fact that both diastolic and systolic pressures...
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were elevated, indicating an increase in peripheral vascular resistance accompanied by increased left ventricular pumping. It is interesting that propanolol, which is reported to be effective in blocking ventricular arrhythmias due to other causes did not prevent the EKG changes in our experiments. The fact that atropine did not prevent the slowing of arterial pulse rate suggests that vagal reflex inhibition was not a critical factor in the bradycardia.

The failure of ganglionic (hexamethonium)\(^{13}\) \(\beta\)-adrenergic (propanolol) blocking agents contrasted with the effectiveness of an \(\alpha\)-adrenergic blocking agent (phenoxybenzamine) in preventing the pressor and EKG responses suggests that the pressor response is mediated through alpha adrenergic mechanisms acting upon arteries and possibly also veins.\(^4,8,9\)

The fact that only thoracolumbar cord compression elicits the pressor response in the absence of cranially or caudally directed cord pathways suggests that the thoracolumbar sympathetic efferents, which innervate thoracic and abdominal vessels, are fundamentally involved in the production of the pressor response.\(^7,10\) We believe that response can be best interpreted at this time as due to thoracoabdominal vasoconstriction, as was originally proposed by Cushing.\(^6\) Alexander and Kerr\(^4\) and Hoff and Reis\(^10\) have given abundant reasons to support the concept that the primary event is the activation of sympathetic preganglionic cells in the cord by mechanical deformation, rather than

![Graphs showing mean arterial pressure changes with cord compression](image-url)

Fig 2. Records of mean arterial pressure from at least three experiments for each record to show the results of compressing the cord (600 gm for 15 min) at the levels indicated. Range of variation indicated by vertical bars.

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Fig. 3. Records taken from cats during cord compression at T3-4 by 600 gm for 15 min initiated at 0 time. Animals were pretreated as indicated with atropine sulf, hexamethonium bromide, propanolol, and phenoxybenzamine.

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...anoxia or adrenal catecholamine release (the latency of the pressor response is far too brief for this possible alternative to hold) or to activation of specific baroceptors in the spinal canal.

Whether or not alpha-adrenergic blockade can be of therapeutic value in patients exhibiting the Cushing phenomenon remains to be determined experimentally. We will report separately our histopathological observations in material from these and other experimental groups, which essentially show that the pressor response does not appear to contribute substantially to the local cord damage produced by compression. It would be interesting to learn to what extent the pressor response is a contributor to early death after spinal cord injury in man.

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References

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