The effects of lumbar sympathectomy on regional spinal cord blood flow in rats during acute hemorrhagic hypotension

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It has not previously been determined whether the sympathetic nervous system has a role in the regulation of regional blood flow in the spinal cord. The authors used 14C-butanol distribution to measure regional spinal cord blood flow at seven cord levels, in the sciatic nerve, and in the biceps femoris muscle in 36 rats, 18 of which had undergone excision of both lumbar sympathetic chains at least 6 days previously. Blood flows were measured during pentobarbital anesthesia. Mean arterial blood pressure (MAP) was monitored and arterial pO2, pCO2, and pH were determined prior to flow measurement. Anesthetic dose and duration were controlled. Measurements were made in normotensive rats and in rats with MAP maintained at either 69 ± 3 mm Hg or 48 ± 3 mm Hg for 1 hour by the withdrawal of arterial blood. One-half of the rats in each group had undergone sympathectomy. The resting cord blood flow was lower than control values following sympathectomy only at the S1-4 cord level (p < 0.01) and caudal equina (p < 0.01), and was marginally lower at the L1-2 and L3-6 levels (p < 0.1). Cord blood flow was unaffected by sympathectomy during moderate hypotension. During severe hypotension, cord blood flow was less than control at the C3-5 level (p < 0.05), but did not differ from control at the other six levels. Flows in nerve and muscle were consistent with known effects of sympathectomy on peripheral tissues. It is concluded that, at most, sympathectomy may moderately decrease resting blood flow in the cord levels caudal to L1-1. Sympathectomy has no major effect on regional spinal cord blood flow in rats stressed by either moderate or severe arterial hemorrhage.

KEY WORDS • spinal cord blood flow • lumbar sympathectomy • graded hemorrhage • sciatic nerve • hypotension • rat

There is considerable anatomical evidence that sympathetic fibers from the paravertebral ganglia synapse on pial and parenchymal blood vessels of the spinal cord. Although the effect of sympathetic stimulation or ablation on regional blood flow in the brain has been extensively studied, it remains largely unknown whether the sympathetic nervous system has a role in the regulation of regional spinal cord blood flow (rSCBF) under either physiological or pathological conditions.

Previous investigations from this laboratory suggested that the rise in rSCBF associated with systemic hypothermia in rats was mediated to an important extent by sympathetic neural and neurohumoral mechanisms. The present experiments were performed to determine whether the rSCBF response to acute arterial hypotension induced by graded hemorrhage is altered in rats previously subjected to excision of both lumbar sympathetic chains.

Materials and Methods

Thirty-six male Sprague-Dawley rats, each weighing between 300 and 430 gm, were used for this study. Bilateral abdominal sympathectomy was aseptically performed in rats using 1.5% Fluothane (halothane) inhalation anesthesia induced after 0.004 mg/kg of atropine had been administered subcutaneously. After the fur had been clipped from the belly wall, a midline laparotomy was performed. With an operating microscope, both sympathetic trunks were readily identified within the paraspinal musculature. The trunks were excised from the level of vertebral body T-13 to that of L-2. The abdominal incision was sutured, the anesthetic discontinued, and the rats permitted to recover for an interval of at least 6 days prior to further study. The remaining 18 rats served as normal controls.

Animal Preparation

Both the normal and the previously sympathectomized rats were anesthetized with 50 mg/kg pentobarbital intraperitoneally after pretreatment with 0.004 mg/kg atropine subcutaneously and 10 ml/kg of lactated Ringer's solution intraperitoneally. Plastic catheters were inserted through cervical and axillary incisions into the right jugular vein and into the right axillary artery and the right common carotid artery (CCA). The
tip of the jugular catheter was positioned in the superior vena cava, and those of the axillary and the carotid catheters in the ascending aorta. In rats subjected to hemorrhage, an additional catheter was inserted into the left axillary artery so that its tip was in the descending aorta. All catheter tip placements were confirmed at the conclusion of the experiments by postmortem dissection.

Arterial Hemorrhage

The rats were positioned prone and heparinized with 1000 IU/kg of bovine heparin sulfate. In 12 rats constituting the “severe hypotension” group, blood was withdrawn by syringe from the left axillary catheter until the mean arterial blood pressure (MABP) was in the range of 40 to 60 mm Hg; in another 12-rat “moderate hypotension” group, blood was withdrawn until MABP was in the range of 60 to 80 mm Hg. Six rats in each group had undergone sympathectomy. The MABP was measured via the right axillary catheter using a transducer* positioned at heart level and connected to a pressure monitor. Blood was withdrawn or injected in increments as necessary during the next 60 minutes to maintain the MABP at the desired level. Rectal temperature was maintained near 37°C using an electric blanket or an external infrared heat source. Six normal and six sympathectomized rats served as unbled controls. Arterial blood pH, pO2, and pCO2 were measured immediately prior to the blood flow determinations described below using a blood gas analyzer.† The time between the induction of anesthesia and the determination of regional blood flow was controlled in all experiments.

Blood Flow Measurements

Regional blood flow measurements were performed using the 14C-butanol “indicator-fractionation” technique described in detail previously.6,13 Briefly, 25 μCi of 14C-butanol was rapidly injected (in less than 1 second) through the right jugular catheter 5 seconds after a constant rate of arterial hemorrhage had been visually verified from the previously unclamped right axillary catheter. Fifteen seconds after the injection had been injected, 1.0 ml cyanoacrylate glue was injected into the right carotid catheter. This resulted in the formation of a dense intraluminal coagulum which extended from the aortic valve to beyond the aortoiliac bifurcation and the near-instantaneous arrest of blood flow, as confirmed previously.14 Simultaneously, the right axillary catheter was clamped and the rat was sacrificed with an intravenous injection of concentrated KCl solution.

The following tissues were then obtained rapidly by postmortem dissection: seven cross-sectional spinal cord samples weighing at least 20 mg, at vertebral levels C3–5, T3–5, T7–9, T12, L1–3, L2–3, and L4–6; these vertebral levels of the spinal cord correspond to spinal cord levels C3–5, T3–5, T7–9, L1–2, L3–6, S1–4, and cauda equina, respectively. The samples from the C-3 to the L-6 cord levels, inclusive, contained no visible spinal nerve remnants from more rostral cord segments. The S1–4 sample, however, was composed largely of rostral spinal nerve segments, the caudal end of the spinal cord being very small in the rat. Samples of the sciatic nerve trunks and biceps femoris muscles were also obtained. After they were weighed, the arterial blood sample and the other tissue samples were solubilized for 48 to 72 hours and their radioactivity was determined by scintillation spectrophotometry. Regional blood flows were calculated using the equation: 

\[ F_i = (Q_{i} \cdot F_o)/(Q_{o} \cdot M_i) \cdot 100, \]

where: \( F_i \) is regional blood flow (ml · min\(^{-1} \) · 100 gm\(^{-1} \)); \( F_o \) is rate of external hemorrhage (ml · min\(^{-1} \)); \( Q_{i} \) is indicator content in the tissue (cpm · gm\(^{-1} \)); \( Q_{o} \) is indicator content in the arterial blood (cpm · gm\(^{-1} \)); and M is sample weight (gm). The theoretical basis for this methodology (derived from the Fick principle) and its validity in the tissues studied are given in detail in previous publications.10,13 Tissue vascular resistance (R) was calculated using the formula: 

\[ R = \frac{MABP}{F_i} \] (expressed in mm Hg · ml\(^{-1} \) · min\(^{-1} \) · 100 gm).

Statistical Analysis

Results are given as the mean ± standard error of the mean. An unpaired t-test was used to compare values measured in rats within unbled, moderate hypotension, or severe hypotension groups with or without sympathectomy. The null hypothesis was rejected at p < 0.05.

Results

Regional Blood Flow

All results are illustrated in Fig. 1. Compared to the unbled control group with intact lumbar sympathetic chains, rSCBF in the unbled sympathectomized rats was lower in the sacral and cauda equina segments by 25% and 26%, respectively. Although there were no other verified differences in cord blood flow, the values in sympathectomized rats were in all cases numerically less than those in the corresponding cord levels of the control group. The largest differences were at the L-1–2 (~19%, p < 0.1) and L-3–6 (~18%, p < 0.1) cord levels. In sciatic nerves, rSCBF was increased following sympathectomy from 9.5 ± 1.0 to 12.9 ± 1.0 ml · min\(^{-1} \) · 100 gm\(^{-1} \). There was a numerical flow increase in the muscle of sympathectomized rats (p < 0.1).

Except in the C-3–5 segment of the severely hypotensive rats, where blood flow was depressed by 33%, prior lumbar sympathectomy had no discernible effect on cord blood flow in either group of hypotensive rats compared to the flows in the corresponding cord levels of rats with intact lumbar sympathetic chains. There were no differences in regional blood flow in the sciatic

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![Graphs depicting regional blood flows in three groups of rats at all seven spinal cord levels, in the sciatic nerve, and in the biceps femoris muscle. Although in the unsympathectomized rats (NT), regional spinal cord blood flow was in all cases numerically less than in the controls, there was a significant difference only at caudal to S-1 levels. Prior sympathectomy had little effect on cord blood flow during either moderate or severe hemorrhage. MH = moderate hypotension group; SH = severe hypotension group. All groups consisted of six rats.](image)

Discussed

The spinal cord vasculature is innervated by adrenergic sympathetic neurons of extraspinal origin. But there has been little investigation as to whether, to what extent, or under which conditions sympathetic vaso-motor signals contribute to the regulation of rSCBF. This contrasts with the numerous reports of the effects of stimulation or ablation of the cervical sympathetic chains on regional blood flow in the brain; although conflicting results have been reported, sympathetic modulation appears to have a role in blood flow autoregulation in the brain. There is consensus that hemodynamic autoregulation of flow is also present in the spinal cord. But the only investigations of the role of the sympathetic nervous system in the regulation of rSCBF of which we are aware (apart from ours as described below) have been those of Young, et al., who used the hydrogen clearance technique to measure flow in the white matter of the thoracic spinal cord in cats that had been subjected to bilateral thoracic para-

**Physiological Variables**

Physiological variables in all groups are presented in Table 1. There were no differences between control and sympathectomized rats that were judged to be physiologically significant. The moderately hypotensive control rats weighed more than the sympathectomized rats in that subgroup.

**Discussion**

**Literature Review**

The spinal cord vasculature is innervated by adrenergic sympathetic neurons of extraspinal origin. But there has been little investigation as to whether, to what extent, or under which conditions sympathetic vaso motor signals contribute to the regulation of rSCBF. This contrasts with the numerous reports of the effects of stimulation or ablation of the cervical sympathetic chains on regional blood flow in the brain; although conflicting results have been reported, sympathetic modulation appears to have a role in blood flow autoregulation in the brain. There is consensus that hemodynamic autoregulation of flow is also present in the spinal cord. But the only investigations of the role of the sympathetic nervous system in the regulation of rSCBF of which we are aware (apart from ours as described below) have been those of Young, et al., who used the hydrogen clearance technique to measure flow in the white matter of the thoracic spinal cord in cats that had been subjected to bilateral thoracic para-
vertebral ganglionectomy. They found that sympathectomized cats lost their ability to regulate regional blood flow in the white matter independently of changes in MABP. Flow was also marginally (but not significantly) lower in sympathectomized cats prior to the commencement of perturbations of the MABP. Finally, they also found that the sympathetic ablated the early fall in flow that occurred following cord contusion.

Study Objectives

The present experiments were prompted by previous observations in this laboratory which strongly suggested that sympathetic modulation of rSCBF, which increased by 25% or more, was important in anesthetized rats in which acute corporal hypothermia had been induced by surface cooling.\(^5\)\(^6\)\(^9\) Specifically, the elevation of cord blood flow attendant hypothermia was ablated by prior lumbar sympathectomy, which was performed as in the present experiments. It therefore seemed useful to assess whether lumbar sympathectomy affects cord blood flow under conditions other than hypothermia. To this end, cord blood flow was again measured at rest and was also measured following hemorrhage, a stress known to induce sympathetic activation. We reasoned that this might bring out otherwise unapparent differences in the cord flow response following sympathectomy. Anatomically, sympathetic preganglionic neurons in the cord project to the paravertebral and major visceral sympathetic ganglia in a segmental manner, as demonstrated by the elegant morphological studies of Strack and coworkers.\(^1\)\(^1\)\(^2\) Although there are also sympathetic interneurons traversing the cord longitudinally (and higher sympathetic centers in the brain as well) that contribute to regulating outflow of the sympathetic preganglionic neurons, it would seem reasonable that, if lumbar sympathectomy influences cord blood flow, its effects should be most apparent in the more caudal regions of the spinal cord.

Role of the Sympathetic Nervous System

The present data provide little support for a major role of the lumbar sympathetic ganglia in the regulation of rSCBF. In unbled rats, flow in the S1–4 and cauda equina segments was depressed by about 25% following sympathectomy. But the cauda equina consists entirely of spinal nerves and, as already noted, the S1–4 cord segments were composed largely of spinal nerve segments. As these segments contain little or no gray matter, they likely are not well representative of more rostral cord levels. The flows at the L1–3 and L3–6 segments were numerically less than control after sympathectomy (p < 0.1 for both levels). However, in our previous experiments conducted under the same conditions and using the same methodology as in the present ones, lumbar sympathectomy had no apparent effect on resting cord blood flow in unbled rats at any of the same seven cord levels.\(^3\) Considering both the present and previous data, it therefore seems reasonable to conclude that lumbar sympathectomy does not have a pronounced or consistent effect on rSCBF in resting, pentobarbital-anesthetized rats. Whether ganglionectomy ablated all or most of the sympathetic outflow to portions of the spinal cord in these experiments is unknown, so it should be emphasized that our results apply only to the effects of excision of the lumbar sympathetic ganglia.

There were no consistent differences in the regulation of rSCBF attributable to sympathectomy in rats hypotensive from arterial hemorrhage. With a single exception, cord blood flow at all levels was similar to control levels in both groups of hypotensive rats; the exception was at C3–5, where flow was depressed following sympathectomy during severe hypotension (Fig. 1). We have no ready explanation for this isolated finding.

Our experimental design did not permit assessment of whether sympathectomy interferes with hemodynamic flow autoregulation in the cord, as the reductions in MABP in the bled rats were relatively drastic.

### TABLE 1

<table>
<thead>
<tr>
<th>Group</th>
<th>MABP (mm Hg)</th>
<th>Body Temperature (°C)</th>
<th>pH</th>
<th>pCO(_2) (mm Hg)</th>
<th>pO(_2) (mm Hg)</th>
<th>Body Weight (gm)</th>
<th>Anesthesia Time (min)</th>
<th>Volume Blood Withdrawn (ml)</th>
</tr>
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<tbody>
<tr>
<td>unbled control</td>
<td>125.3 ± 7.2</td>
<td>37.4 ± 0.2</td>
<td>7.38 ± 0.01</td>
<td>37.4 ± 1.3</td>
<td>92.2 ± 4.0</td>
<td>373.5 ± 15.2</td>
<td>117.8 ± 0.9</td>
<td>—</td>
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<tr>
<td>sympathectomy</td>
<td>111.3 ± 5.0</td>
<td>37.0 ± 0.4</td>
<td>7.41 ± 0.01</td>
<td>35.3 ± 0.9</td>
<td>86.6 ± 2.3</td>
<td>368.0 ± 8.2</td>
<td>118.0 ± 0.6</td>
<td>—</td>
</tr>
<tr>
<td>moderate hypotension control</td>
<td>65.0 ± 2.6</td>
<td>37.4 ± 0.1</td>
<td>7.43 ± 0.01</td>
<td>31.6 ± 1.8</td>
<td>104.6 ± 4.6</td>
<td>395.5 ± 12.0</td>
<td>120.0 ± 2.0</td>
<td>— 3.9 ± 0.3</td>
</tr>
<tr>
<td>sympathectomy</td>
<td>68.3 ± 1.8</td>
<td>37.4 ± 0.2</td>
<td>7.42 ± 0.01</td>
<td>32.5 ± 0.4</td>
<td>97.6 ± 2.8</td>
<td>35.0 ± 6.9</td>
<td>119.5 ± 0.7</td>
<td>— 1.7 ± 1.3</td>
</tr>
<tr>
<td>severe hypotension control</td>
<td>48.5 ± 2.9</td>
<td>37.4 ± 0.3</td>
<td>7.42 ± 0.02</td>
<td>30.0 ± 0.9</td>
<td>103.2 ± 3.4</td>
<td>375.8 ± 5.8</td>
<td>119.5 ± 1.0</td>
<td>— 5.6 ± 0.8</td>
</tr>
<tr>
<td>sympathectomy</td>
<td>48.2 ± 3.2</td>
<td>37.4 ± 0.3</td>
<td>7.44 ± 0.01</td>
<td>30.4 ± 1.0</td>
<td>102.5 ± 3.9</td>
<td>361.2 ± 10.1</td>
<td>119.0 ± 0.8</td>
<td>— 7.3 ± 0.5</td>
</tr>
</tbody>
</table>

* Each group consisted of six animals. Values are mean ± standard error of the mean. MABP = mean arterial blood pressure. — = not applicable.

† Statistical significance; p < 0.02 within subgroup.
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and so were near or below the levels at which autoregulation is normally operative. For example, we have previously found that autoregulation was present in rats with MABP in the range of approximately 60 to 160 mm Hg.10

The elevated regional blood flow and the fall in vascular resistance in sciatic nerve and biceps femoris muscle in rats with sympathectomy are consistent with the known effects of sympathectomy on peripheral tissues and so indirectly attest that denervation had been accomplished.

Conclusions

We conclude that lumbar sympathectomy has no major effect on the regulation of rSCBF in pentobarbital-anesthetized rats, either at rest or during hypotension induced by arterial hemorrhage.

References

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