Effect of sympathectomy on spinal blood flow autoregulation and posttraumatic ischemia

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✓ The hypothesis that the paravertebral sympathetic ganglia play a role in spinal blood flow regulation was tested in cats. Five cats were subjected to paravertebral sympathectomy, two to combined sympathectomy-adrenalectomy, three to adrenalectomy alone, and five controls received no treatment. Laminectomy was carried out to expose the T4-10 cord, and autoregulation was tested by measuring blood flow from the lateral columns with the hydrogen clearance technique during manipulation of systemic pressure with intravenous saline infusion and nitroprusside administration. The cord was then contused at T-7 with a 400 gm-cm impact injury. Posttraumatic blood flow was recorded, and neurophysiological function was assessed with somatosensory evoked potential (SEP) monitoring.

Before injury, blood flow in the untreated (control) group had no consistent relationship with mean systemic pressure over the range 80 to 160 mm Hg. In contrast, in all cats with paravertebral sympathectomy, whether accompanied by adrenalectomy or not, blood flows increased with systemic pressure (correlation coefficient 0.86, p < 0.01). After injury, the control and adrenalectomized cats showed blood flow decreases of > 60% to 4 to 6 ml/100 gm/min (p < 0.01) by 2 to 3 hours. However, cats with paravertebral sympathectomy maintained blood flow above 9 ml/100 gm/min for up to 3 hours after injury. All the sympathectomized cats recovered their SEP by the 3rd hour after injury, compared with none of the controls.

Thus, in the absence of the paravertebral sympathetic ganglia, spinal blood flow autoregulation was impaired and the typical posttraumatic loss in blood flow did not occur. The sympathectomy also protected the spinal cords from the neurophysiological loss usually seen in 400 gm-cm injury. The data suggest the need for caution in using acetylcholine blocking agents to paralyze animals in experimental spinal injury, since these agents alter sympathetic activity and may influence the injury process. The spinal cord is an excellent model in which to investigate sympathetic regulation of central nervous system blood flow.

Key Words • sympathectomy • spinal cord injury • blood flow • autoregulation • somatosensory evoked potential

Fibers from paravertebral sympathetic ganglia enter the spinal cord alongside blood vessels and synapse on the vessels. Fibers may regulate spinal cord blood flow. Control of central nervous system blood flow by peripheral sympathetic fibers is a controversial subject. In a comprehensive review of the subject, Edvinsson and MacKenzie found papers reporting a whole gamut of increased, unchanged, and decreased cerebral blood flow resulting from cervical sympathetic stimulation or ablation. Experimental study of sympathetic regulation of cerebral blood flow has been difficult due to the heterogeneity of supratentorial structures and the presence of vasoregulatory centers in the brain which may take precedence over peripheral sympathetic structures. In the spinal cord, these difficulties may be circumventable due to its simpler longitudinal structure which is segmentally innervated by peripheral sympathetic ganglia.

We investigated the effects of surgical sympathectomy on spinal blood flow, particularly the role of the paravertebral sympathetic ganglia in blood flow autoregulation and posttraumatic ischemia. To distinguish between local sympathetic and adrenal influences, we studied cats with paravertebral sympathectomy alone, combined sympathectomy and adrenalectomy, and adrenalectomy alone. Prior to injuring the cord, we tested autoregulation of spinal blood
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Flow in response to systemic pressure changes. The spinal cord was then contused with a 400 gm-cm impact and observed for blood flow changes. Spinal function was assessed with somatosensory evoked potential (SEP) monitoring.

Materials and Methods

Experimental Protocol

Fifteen healthy adult cats were tested in four experimental groups (Table 1). The control group consisted of cats that did not receive any sympathectomy procedure. The sympathectomy group underwent T1-T12 paravertebral sympathectomies. The third group received bilateral sympathectomies and adrenalectomies. The adrenalectomy group had only adrenal glands removed.

All the cats were lightly anesthetized with 25 mg/kg of pentobarbital, administered intravenously. This sufficed for the 6-hour experiments, of which the 1st hour was spent performing the sympathectomy and laminectomy procedures, the 2nd and 3rd hour was devoted to testing autoregulation, and the remainder for observing the effects of contusion injury on blood flow and neurophysiological function. No paralyzing agents were used because of previous observations that such agents influence sympathetic ganglionic activity.15,16,30,38 Blood pressure and end-tidal CO2 were measured continuously throughout the experiments. When necessary, we ventilated the animals to maintain end-tidal CO2 in the range of 30 to 34 mm Hg partial pressure. The SEP and blood flow measurements were obtained every half hour.

To test autoregulation of blood flow, the mean systemic pressure was first raised to between 160 and 180 mm Hg by intravenous infusion of 100 ml of saline. Nitroprusside was then judiciously administered to lower blood pressure, in steps of 20 to 40 mm Hg. In the 2 hours prior to contusion of the spinal cord, three to four correlations between systemic pressure and blood flow were obtained per cat. These data were pooled from cats in each group and tested for correlational tendencies, using linear regression analysis. The effect of the nitroprusside usually lasted only 20 to 30 minutes. By the time the cats were contused, their mean systemic pressures stabilized in the range of 20 to 30 minutes. By the time the cats were contused, their mean systemic pressures stabilized in the range 110 to 130 mm Hg, with the exception of cats with episode, with mean systemic pressure less than 80 mm Hg, before injury.

Surgical Procedures

The surgical procedures for these experiments have been described previously.38 Briefly, the sympathetic ganglia were resected via bilateral transthoracic incisions and were confirmed histologically to include both pre- and postganglionic fibers and the ganglia themselves. The adrenal glands were ablated through an abdominal incision. Laminectomy was performed to expose the cord at the T4-10 level. To allow insertion of the blood-flow monitoring electrode into the lateral columns, a 1-mm slit was cut in the dura overlying the cord.

The spinal cord was injured by dropping a 20-gm weight 20 cm onto the thoracic cord exposed by laminectomy, at T-7. We took care to injure each cat identically, in a manner found in this laboratory to produce permanent paraplegia in 90% of cats. All the cats had intact SEP's and blood flow in the normal range prior to injury. No cat suffered any hypotensive episode, with mean systemic pressure less than 80 mm Hg, before injury.

Blood Flow Measurement

Both the theoretical bases and technical aspects of the H2 clearance technique have been published.4,16,35,36 To saturate the spinal tissues with H2, the cats were respirated for 3 minutes with a 7% mixture of H2 and air. Tissue concentrations of H2 were measured polarographically with a Teflon-coated, platinum-iridium electrode (150 μ in outer diameter), inserted 1.5 mm into the lateral white matter column with a micromanipulator. Polarized to +350 mV, these electrodes oxidized H2, yielding approximately 100 to 200 nA of current/1 mm Hg of H2 partial pressure, linearly relating to H2 concentration over a wide range (0.01 to 500 mm Hg partial pressure). A virtual ground voltage clamp, with picoamperere resolution, amplified the current relative to a Ag-AgCl reference electrode placed in contact with the cerebrospinal fluid.36 Tissue H2 current typically rose to 10 μA saturation levels within 3 minutes and began falling within 30 seconds of stopping H2 administration. End-tidal H2, monitored with an electronic gas detector, usually fell below detection level of 20 parts per million within a minute of clearance.

Blood flow was calculated from the exponential clearance rate of tissue H2. A computer+ was used to

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* Electronic gas detector, Model BT-44, manufactured by Quantum Instruments, Garden City, New York.
+ MINC II computer manufactured by Digital Equipment Corp., Maynard, Massachusetts.
TABLE 2

Effect of sympathectomy on blood flow (mL/100 gm/min)*

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Cats</th>
<th>Preinjury</th>
<th>0.5 Hr</th>
<th>1 Hr</th>
<th>2 Hrs</th>
<th>3 Hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>5</td>
<td>13.1 ± 2.7</td>
<td>12.1 ± 4.3</td>
<td>9.5 ± 2.0</td>
<td>5.5 ± 1.3</td>
<td>4.7 ± 0.6</td>
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<tr>
<td>sympathectomy</td>
<td>5</td>
<td>9.4 ± 2.9</td>
<td>9.5 ± 2.7</td>
<td>9.5 ± 3.6</td>
<td>9.3 ± 1.7</td>
<td>9.4 ± 1.2</td>
</tr>
<tr>
<td>sympathectomy-adrenalectomy</td>
<td>2</td>
<td>11.6 ± 2.3</td>
<td>7.6 ± 1.6</td>
<td>9.8 ± 2.8</td>
<td>11.9 ± 2.8</td>
<td>13.8 ± 1.6</td>
</tr>
<tr>
<td>adrenalectomy</td>
<td>3</td>
<td>13.0 ± 1.4</td>
<td>7.0 ± 0.7</td>
<td>6.6 ± 1.6</td>
<td>6.0 ± 2.1</td>
<td>4.8 ± 0.4</td>
</tr>
</tbody>
</table>

* Mean blood flows ± standard deviations obtained from lateral column white matter before and after 400 gm-cm contusion injury.
† Significant deviation from preinjury levels (p < 0.01).

TABLE 3

Mean blood pressure at time of blood flow measurement (mm Hg)*

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Cats</th>
<th>Preinjury</th>
<th>0.5 Hr</th>
<th>1 Hr</th>
<th>2 Hrs</th>
<th>3 Hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>5</td>
<td>121 ± 9</td>
<td>104 ± 7</td>
<td>96 ± 11</td>
<td>100 ± 13</td>
<td>105 ± 15</td>
</tr>
<tr>
<td>sympathectomy</td>
<td>5</td>
<td>112 ± 21</td>
<td>82 ± 9</td>
<td>79 ± 11</td>
<td>85 ± 15</td>
<td>95 ± 5</td>
</tr>
<tr>
<td>sympathectomy-adrenalectomy</td>
<td>2</td>
<td>105 ± 29</td>
<td>72 ± 3</td>
<td>93 ± 17</td>
<td>106 ± 7</td>
<td>139 ± 29</td>
</tr>
<tr>
<td>adrenalectomy</td>
<td>3</td>
<td>141 ± 1</td>
<td>102 ± 1</td>
<td>104 ± 1</td>
<td>105 ± 7</td>
<td>103 ± 7</td>
</tr>
</tbody>
</table>

* Averaged blood pressure ± standard deviations.

The SEP's were elicited by stimulation of the sciatic nerve (2.3/sec, 2 × twitch threshold) and recorded epidurally from the contralateral somatosensory cortex. After × 10,000 amplification and filtering (bandpass 150 to 3000 Hz), 256 traces were averaged and then plotted on an x-y recorder. Each SEP test consisted of three SEP recordings. A cat was said to have an intact SEP when on three consecutive recordings the response showed a prominent positive peak at 17 to 20 msec latency.

Results

Blood flow fell significantly (p < 0.01) in the control group, from a preinjury mean of 13.1 mL/100 gm/min to between 5.5 and 4.7 mL/100 gm/min at the 2nd and 3rd hour after injury. Cats with paravertebral sympathectomy had apparently lower preinjury flow values compared with the controls (although not significant, p > 0.10); they did not show blood flow decreases for up to 3 hours after contusion. Cats with sympathectomy-adrenalectomy had blood flow changes similar to the sympathectomy group. Blood flow in the adrenalectomy group did not differ significantly from the controls. Table 2 summarizes the blood flow data, and Table 3 lists the mean blood pressures for each group.

All the cats that received paravertebral sympathectomy, combined with adrenalectomy or not, had impaired autoregulation of blood flow in response to systemic pressure changes. Figure 1 is a graph of blood flow versus systemic pressure, pooled from the control and sympathectomy groups. In the non-sympathectomized cats (control and adrenalectomized groups), there was no consistent relationship between spinal white matter blood flow and mean systemic pressure, within the range of 80 to 160 mm Hg. However, in cats with paravertebral sympathectomies (sympathectomy and sympathectomy-adrenalectomy groups), there was a significant linear relationship between pressure and flow (correlation coefficient r = 0.86, p < 0.01).

All the cats lost their SEP responses shortly after contusion injury; however, all the sympathectomized cats had regained their SEP by the 3rd hour after injury. This was true whether or not adrenalectomy was added to the sympathetic ablations. None of the control cats had return of SEP responses at 3 hours after injury; some, however, showed a transient recovery of SEP between the 1st and 2nd hour, only to lose the response by the 3rd hour.

Discussion

These findings implicate the role of the sympathetic ganglia in spinal blood flow autoregulation before injury and development of posttraumatic ischemia. Specifically, cats with paravertebral sympathectomies lost their ability to regulate spinal white matter blood flow.
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flow in response to systemic pressure changes. The sympathectomized cats did not exhibit the posttraumatic ischemia typically produced by contusion injury.1,11,17,20,31-34 The critical factor appears to be the presence of the paravertebral sympathetic ganglia and not the adrenal glands.

Our data do not necessarily imply a cause and effect relationship between sympathetic activity and changes in spinal blood flow. We have not ruled out the possibility that sympathectomy increased the threshold of spinal cord to injury and thereby indirectly ameliorated the posttraumatic blood flow decrease.33,34 Nevertheless, these results do represent the first evidence for peripheral sympathetic involvement in spinal blood flow autoregulation, and suggest an important role of the sympathetic ganglia in the pathogenesis of posttraumatic ischemia. This study also indicates a need for caution in using acetylcholine blockers to paralyze animals in spinal injury experiments; tubocurare, gallamine, and succinylcholine all produce varying degrees of sympathetic blockade.15,16,30 We observed recently38 that these agents can significantly alter the pressor response induced by spinal contusion. It is, therefore, of interest to note that published studies of spinal blood flow in pharmacologically paralyzed animals tend to report higher posttraumatic flows (that is, 6 to 8 ml/100 gm/min25,32-34 or greater17,20) than those measured in unparalyzed animals in this study.

The finding that all the sympathectomized cats recovered their SEP by 3 hours after injury suggests that the sympathectomy protected the spinal cord in some manner. Whether or not this is due to improvement of blood flow is not clear. An alternative possibility is that the sympathectomy ameliorated the injury by blunting the pressor response associated with contusion and consequently the extent of intra-cord hemorrhage.29 However, the adrenalectomized cats also had lessened pressor responses and yet developed posttraumatic ischemia. Note that some pressor response, albeit diminished,28 remains in the sympathectomized cats, suggesting the presence of residual sympathetic outflow.

There may be other effects of sympathectomy on spinal cord, such as an inadvertent disturbance of spinal blood flow due to surgical manipulation of the paravertebral space and alteration of neuronal transmitter release in the cord. The first possibility may account for the tendency for flow to be lower in the sympathectomized cats before injury, but does not readily explain either the loss of autoregulation or the protection of the cord against contusion injury. The latter possibility is of particular interest in view of our recent finding38 that naloxone, a specific opiate receptor antagonist, prevents posttraumatic ischemia. Since the sympathetic nervous system contains significant amounts of endogenous opiates,6,18,22,23,26,35 sympathectomy may influence blood flow by reducing neuropeptide release. Clearly, the subject of sympathetic regulation of spinal blood flow deserves further study.

Acknowledgments

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References


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