The authors report studies indicating that delayed local cooling is effective in minimizing the neurological deficits of experimental spinal cord injury in cats. Cortical evoked responses were useful in predicting the neurological outcome; untreated animals whose evoked response disappeared for 6 hours failed to recover whereas all treated animals in the same group recovered dramatically. Decompression by laminectomy alone proved ineffective. Possible explanations for the therapeutic effects of cooling and the significance of the delay are briefly discussed.

**Key Words** • spinal cord injury • cooling • evoked potential • paraplegia

Cooling of the spinal cord has been suggested as an effective means of lessening neurological deficits following acute spinal cord injury. However, there has not yet been a fully controlled study for the evaluation of this technique. In fact, it has recently been suggested that whatever benefits do result from spinal cord cooling may be related only to the perfusion and not to the decrease in temperature.

If animal studies are to provide a basis for the widespread clinical acceptance of this technique, certain factors must be considered. First, to evaluate fully any therapeutic approach, the experimental model used for creating the lesion must be carefully chosen. We have used the closed-injury model recently described by Martin and Bloedel. With this approach, the area of the spinal cord to be injured need not be exposed or “decompressed” prior to injury; this contrasts with other injury models that use a weight drop or circumferential balloon, both of which require a laminectomy at the site of injury. Furthermore, the cooling should be proven effective when administered some time after the trauma. Only if this is possible would it be realistic to employ this technique after a patient has been evaluated at a clinical center. Both of these considerations have been incorporated into the experiments presented below.

Since changes in cortical evoked responses in cats provide a reliable indication of the neurological deficit to be expected in the injured animal, this method was chosen to evaluate the extent of the injuries produced in this study. It has previously been shown that animals in which cortical responses disappeared and did not reappear within 6 hours are left with severe neurological deficits, while animals whose cortical evoked responses did...
Delayed local cooling for spinal cord injury

reappear within that time period recover significant neurological function. In the study presented below, the effect of cooling was evaluated in animals in both groups.

**Methods**

Experiments were performed on 28 adult cats weighing 2 to 5 kg. Each animal was anesthetized with halothane-oxygen mixture administered by mask.

Under aseptic conditions the left sciatic nerve was exposed down to its bifurcation into common peroneal and posterior tibial nerves. A small metal screw was then positioned through a small burr hole 4 mm anterior to the coronal suture and 2 mm from the sagittal suture on the right side overlying the primary sensory area of the cortex. The screw was inserted just deep enough to contact the dura. A reference electrode was placed in the neck muscle. Each animal was positioned in a small animal frame. The sciatic nerve was then placed on a bipolar electrode of silver wire. Stimulus pulses of 0.1 msec duration at amplitudes of 4 to 6 V and a rate of 1/sec were applied to the nerve. The nerve was protected from loss of moisture by cotton pledgets soaked in mineral oil. The responses recorded from the screw in the skull were amplified by a Tektronix series 122 preamplifier* and then fed into a Fabritek 1072 averager.† In all experiments, 128 successive responses were averaged.

After adequate control records had been taken, a small laminectomy was performed over the L-2 vertebra. A No. 3 French Fogarty catheter‡ was passed extradurally in the cephalad direction for 6 cm. The balloon was then inflated instantaneously with 0.6 to 0.9 cc of air injected by hand from a tuberculin syringe and then immediately deflated. After deflation the catheter was removed and the laminectomy site closed in layers. Averaged cortical evoked responses were then taken at 5 minutes, and 1, 3, and 6 hours after injury. After 6 hours, all animals that were not to be treated were allowed to recover from anesthesia, while those to be treated were prepared for one of the designated therapeutic procedures.

On each treated animal a three- to four-level decompressive laminectomy was then placed over the area of injury. When cooling was employed, the exposed cord (with dura intact) was perfused at a rate of 95 to 125 cc/min with normal saline solution cooled with a dry ice water bath to a temperature of 15° ± 2°C. The walls of the pool into which the solution was perfused were formed with paraspinal muscles and skin. Cooling was performed for 2 hours, after which the second laminectomy was closed in layers and the animals were allowed to recover from anesthesia.

Postoperatively, each animal was observed daily in the first postoperative week; the neurological status was carefully recorded and graded according to the scale in Table 1 at this time as well as at Days 10 and 14 and each week thereafter until the animal was sacrificed. The period of follow-up varied

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*Tektronix series 122 preamplifier manufactured by Tektronix Inc., Post Office Box 500, Beaverton, Oregon 97005.

†Fabritek 1072 averager manufactured by Fabri-Tek, Inc., 5901 South County Road 18, Minneapolis, Minnesota 55455.

‡No. 3 French Fogarty catheter manufactured by Edwards Laboratories, 17221 Red Hill Avenue, Santa Ana, California 92705.

**TABLE 1**

Criteria for clinical grading of neurological function

<table>
<thead>
<tr>
<th>Clinical Scale</th>
<th>Degree of Paraplegia</th>
<th>Symptoms</th>
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<tr>
<td>0</td>
<td>flaccid</td>
<td>minimal or no leg movements; variable tone; bowel/bladder out</td>
</tr>
<tr>
<td>1</td>
<td>spastic</td>
<td>moderate or vigorous but purposeless leg movements; legs spastic and extended; no sitting; bowel/bladder out</td>
</tr>
<tr>
<td>2</td>
<td>severe</td>
<td>only moderate spasticity in legs; vigorous, coordinated movements suggesting walking; can sit and stand; bowel-bladder out</td>
</tr>
<tr>
<td>3</td>
<td>moderate</td>
<td>sitting, standing, walking is present; legs and hips obviously unstable; leg lagging; bowel/bladder variable</td>
</tr>
<tr>
<td>4</td>
<td>mild</td>
<td>walking with some leg and hip instability; bowel/bladder functional</td>
</tr>
<tr>
<td>5</td>
<td>&quot;normal&quot;</td>
<td>hip instability seen only with jump or run</td>
</tr>
</tbody>
</table>
Results

The 28 animals were divided into two groups according to the changes in the cortical evoked responses. Group 1 included 13 animals whose cortical evoked responses disappeared after injury and had not reappeared 6 hours later; eight of these were subsequently treated with decompressive laminectomy and cooling, while the remaining five were treated with laminectomy alone. Group 2 consisted of the 15 animals in which the cortical evoked responses disappeared at the time of injury but reappeared within 1, 3, or 6 hours; seven of these were treated with laminectomy and cooling; eight were untreated. Representative examples of cortical evoked responses recorded from selected animals in both groups are shown in Fig. 1.

Group 1

Animals injured with the closed technique whose cortical evoked responses failed to reappear 6 hours after injury did very poorly without any form of treatment; none of them recovered the ability to walk (Fig. 2). The average time course of the recovery of the five animals whose evoked responses failed to reappear and who were treated only with decompressive laminectomy was not statistically different from that of the controls ($p = 0.4$). The outcome in the controls and in animals treated by decompression alone contrasts sharply with the outcome in eight animals that were treated with laminectomy and cooling. The average extent of recovery in the latter animals differed from that of the controls at a statistically significant level of $p < 0.01$. All of these animals recovered enough neurological function to walk within 2 weeks after injury and subsequently progressed to normal or near normal neurological function.
Delayed local cooling for spinal cord injury

**Group 2**

The outcome of neurological function in the remaining 15 animals in which cortical evoked response reappeared at various intervals is shown in Fig. 3. These animals experienced significant neurological recovery regardless of whether or not they were treated with decompressive laminectomy and cooling. All regained the ability to walk within 10 days or 2 weeks with no significant difference between treated and untreated groups (p = 0.4). These findings are very similar to those previously reported for untreated animals in which the evoked response was present 6 hours following injury.10

**Discussion**

Various reports have suggested cooling as an effective early therapeutic approach for spinal cord injury.2,4,7,9,17 There are at least two reasons why these reports have not proved to be an adequate basis for more widespread implementation of this potentially useful therapeutic tool. First, the clinical applicability of many of these studies may be challenged since an open method was used to produce the lesion, thus requiring that the spinal cord be pretreated with decompressive laminectomy even before the injury was produced. Second, most of the experimental reports were presented with few controls. In our experiments, we have taken both objections into account by using a closed injury model and by employing enough experimental and control animals so that the conclusions could be validated statistically.

One of the most striking findings of this study is that 100% of all animals with a severe injury recovered significant neurological function (including ambulation) following cooling. This contrasts markedly with the lack of recovery of the animals in the control group which had comparable changes in the cortical evoked response. Moreover, cooling was proven effective even when administered as long as 6 hours after injury. This suggests that cooling may indeed be valuable in a clinical setting where patients with spinal cord injury often arrive at a neurosurgical center 2 or 3 hours after the injury. We should emphasize however, that the duration of the critical period during which cooling is effective may be quite different in cats than in man. The finding that the time course of spinal shock following spinal injury is very different in cats and man underscores the possibility of such a difference.

Recent reports have argued that the perfusion rather than the cooling itself may be the most important factor in minimizing the neurological deficit;14 however, more recent studies refute this argument.5 Since cooling in our studies was done with the dura unopened, cooling is almost certainly the most important factor. Although compounds could possibly be dialyzed across the thin dura in the cat, the drop in temperature more probably caused a marked reduction in the chemical processes that may be necessary for development of severe pathophysiological changes.8,18 In most studies of this type, the duration of the cooling ranged from 2 to 4 hours. The fact that a duration of 2 hours was effective suggests that a retardation of the pathophysiological processes for a few hours soon after the injury may be sufficient to prevent the most severe deficits.

**Conclusions**

This study has shown delayed local cooling to be extremely useful in reducing the neurological deficits resulting from severe experimental spinal cord injury in cats. We believe these results provide ample basis to consider this treatment in selected patients with spinal cord injury. For this therapy to have maximal value, a better set of objective prognostic criteria, such as changes in reflexes and cortical evoked potentials, must be developed for evaluation of the patient with a spinal cord injury.

**References**


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