The value of decompression for acute experimental spinal cord compression injury

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A clip compression method was used to produce acute spinal cord compression injury in rats. The force and duration of the spinal cord compression were independently varied, and functional recovery of the cord was assessed using the inclined plane technique. Mathematical modeling produced a curve defining the relationship between force, duration, and functional recovery for each week after injury. The study clearly showed the beneficial effect of decompression and that increasing either the force or duration of compression, or both, caused a reduction in recovery.

KEY WORDS • spinal cord compression • decompression

Previous studies in this laboratory and elsewhere have shown the importance of the duration of spinal cord compression upon subsequent functional recovery. Increasing the duration of compression resulted in worsening of the functional recovery. The present work examines the relationships between the force of compression, the duration of compression, and subsequent functional recovery. Although Tarlov and colleagues examined some of these relationships in their studies in the 1950's, there have been no studies of the value of decompression for accurately defined compression forces and durations. Thus, with respect to acute spinal cord compression injury, the present study is the first systematic analysis of the effects on recovery of both the force and duration of compression, and the first to accurately document the value of decompression for defined forces of varying magnitude.

Materials and Methods

Operative Procedure
Female white Wistar rats, weighing between 280 and 300 gm, were used in this study. All animals operated on received pentobarbital, 4 mg/100 gm intraperitoneally, and then a laminectomy was performed at T-1 as described previously. Ten animals had a 5-mm long segment of the spinal cord totally removed (the myectomy group). The other animals received a spinal cord compression injury with a compression clip, as described by Rivlin and Tator. Ten rats served as control animals; they received no anesthetic and did not undergo the surgical procedure (normal group).

All animals were kept in a heated room (30°C) after the operation, or in the case of the unoperated control group, after their inclusion in the study. The bladders of the animals operated on were expressed manually four times daily during the initial week after the operation, and then twice daily for the duration of the study. Urinary tract infections were treated with intraperitoneal gentamicin sulphate, 0.4 mg twice daily. The animals were followed for a total of 8 weeks.

Protocol
A single modified Kerr-Lougheed clip was used to produce all the spinal cord injuries. Different springs were utilized so that different compression forces could be delivered to the spinal cord. The compression force of the clip was determined by the method described previously. The study analyzed forces of compression of 16, 71, or 178 gm and durations of compression of 3, 30, 60, 300, or 900 seconds.
The experiment was a factorial design, with three forces of compression (16, 71, and 178 gm) and four durations of compression (3, 30, 60, or 300 seconds). In addition, a 900-second compression with the 16-gm force was examined. Seven animals were studied for each combination of force and duration of compression (that is, for each force-time pair), making a total of 91 animals in the study.

Assessment

Spinal cord recovery was assessed weekly for 8 weeks by the inclined plane method, which measured the rats' ability to maintain themselves on an incline. The maximum angle at which an animal maintained itself on the incline was taken as a measure of its functional recovery.

Analysis

The mean and standard deviation of the angle of the inclined plane for each force-time pair were calculated and plotted for each week. The data were analyzed using nonlinear regression analysis and an IBM 3033 computer. Mathematical modeling produced an equation that best described the relationship between the force and duration of compression and subsequent functional recovery. Using a Gould plotter, the relationship between the three variables (force, duration, and recovery) was graphically displayed for each week following injury.

Results

The mean and standard deviation for the maximum angle on the inclined plane for each force-time pair are shown in Figs. 1, 2, and 3. Figure 1 shows the results for the normal and myelectomy groups. In each group, there was very little change in the angle achieved on the inclined plane from week to week. The overall mean value over the 8-week period for the normal group was 81.4 ± 1.8°, and for the myelectomy group it was 23.0 ± 2.5°. These latter values were used for the boundary values for the maximum and minimum recovery, and for determining the equation relating the force and duration of compression to the subsequent functional recovery of the animals.

Figure 2 shows the effect of increasing the duration of compression while keeping the force fixed. Functional recovery decreased as the duration of compression increased. Figure 3 shows the effect of increasing the force of compression while keeping the duration of compression fixed. Functional recovery decreased as the force of compression increased. Thus, Figs. 2 and 3 prove that both the force and duration of compression affected functional recovery.

The curves in Figs. 2 and 3 also show that in most cases recovery gradually increased for the first few weeks after injury and then reached a plateau. Thus, to define the exact relationship between force of compression, duration of compression, and recovery, one must take into account the length of time elapsed after injury. The two-dimensional graphs in Figs. 2 and 3 accurately show the relationship between any two of the variables with the third variable constant. To depict the relationship between all three variables, a three-dimensional graph is required. However, because recovery improved with elapsed time from the time of the injury, the relationship between force, duration, and recovery has to be studied at defined intervals from the time of injury. In a three-dimensional graph, the relationship between the three variables is a surface, and in the present context, the surface will not be constant after the injury but will undergo alterations over the first few weeks before achieving its final shape. The two equations that were derived, using nonlinear regression analysis to describe the surface of the three-dimensional graphs and thus to define the relationships between the three variables, are as follows:

\[ R = (Y_0 - Y_1) \exp \left( -\frac{a}{W} + \frac{b}{F} \right) + dT + Y_1 \]  
\[ R = (Y_0 - Y_1) \exp \left( -bF + cF^2 \right) + dT + Y_1 \]

where \( R \) = angle achieved on the inclined plane (functional recovery), \( W \) = weeks after injury, \( F \) = compression force (gm), \( T \) = compression duration (sec), \( Y_0 \) = inclined plane value for normal animals (81.4°), and \( Y_1 \) = inclined plane value for myelectomized animals (23.0°). Thus, if

\[ W < \frac{1}{k} \ln \left( \frac{a}{b} \right) \]
Decompression of spinal cord compression injury

![Graph showing the effect of increasing the duration of compression while keeping the force constant.](image)

**TABLE 1**  
*Coefficients of the equation for the surface*

<table>
<thead>
<tr>
<th></th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>k</th>
</tr>
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<tbody>
<tr>
<td>value</td>
<td>0.026430</td>
<td>0.013050</td>
<td>-0.000034</td>
<td>-0.015020</td>
<td>0.225710</td>
</tr>
<tr>
<td>SE*</td>
<td>$3.93 \times 10^{-3}$</td>
<td>$6.7 \times 10^{-4}$</td>
<td>$4.2 \times 10^{-6}$</td>
<td>$1.68 \times 10^{-3}$</td>
<td>$8.87 \times 10^{-2}$</td>
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*Standard error of the coefficients. Sums of squares = 1854.06; variance = 18.73; degrees of freedom = 99.*

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751
Fig. 3. The effect of increasing the force of compression while keeping the duration of compression constant. The graphs show the mean weekly recovery measured by the inclined plane technique, with standard deviations for each force-time pair. Upper left: 3-second duration of compression; upper right: 30-second duration of compression; center left: 60-second duration of compression; center right: 300-second duration of compression; lower: 900-second duration of compression.
Decompression of spinal cord compression injury

Figure 4 shows the surface at 1, 2, and 8 weeks after injury, and Table 2 shows the actual mean values for each force-time pair. The mean values in Table 2 are the points shown in Fig. 4. The area of the curve for Weeks 1 and 2, where the surface crosses the force-time plane, is marked with horizontal lines and represents an angle on the inclined plane, or functional recovery of 23.0°. Recovery values calculated from the equation are negative in this area. Since negative recovery values are not possible in reality, the equation breaks down in this area and has no meaning. It was found that the surface did not change shape between 4 and 8 weeks after injury (not shown).

Discussion
Pharmacologists have found the dose-response curve, a graph relating the effective response versus the drug dosage, to be invaluable in assessing new drugs. Such a curve allows easy comparison of the potencies of various drugs, and the efficiency of antagonism or agonism of a drug. With respect to spinal cord injury, a trauma dose-response curve would be valuable for many reasons. For example, it could define the trauma dose that would produce no recovery, and could provide a basis for comparison of various treatments. A shift of the curve, such that higher or lower trauma doses were required to produce the same recovery, could be used to assess the effectiveness or hazards of a particular treatment.

To date, only three studies of spinal cord injury have examined trauma dose-response curves. Tarlov, et al. attempted to define the upper limits for recovery after acute or chronic spinal cord compression in dogs. The acute experiments involved rapidly inflating a small (0.8 ml), medium (0.9 ml), or large (1.0 ml) extradural balloon in the area between T-5 and T-7, and maintaining compression for from 1 minute to 5 hours. The chronic experiments involved inflating the balloon over 75 minutes, 20 hours, or 48 hours. Animals were followed for 11 to 20 days. The number of animals at each time point was too small (usually one) to establish accurately a dose-response curve; however, the studies did establish a maximum
duration of compression compatible with full recovery. With the large balloon, full recovery occurred when compression was released within 1 minute; with the medium balloon, full recovery occurred with compression for less than 30 minutes; and with the small balloon, full recovery occurred with up to 2 hours of compression. In the chronic experiments, full recovery occurred if compression was relieved within 9 hours of the onset of total paralysis. Thus, Tarlov and Klinger attempted to define the maximum force and duration of compression the spinal cord could tolerate, although they did not measure the actual force on the cord.

Ducker, et al., studied the weight-dropping method of experimental spinal cord injury, and, by plotting the number of animals at each level of clinical recovery against the gram-centimeter dose, they obtained a dose-response curve. They then showed that immobilization of the spine after injury shifted the curve to the right, implying that more force was required to produce the same degree of injury, and that this treatment had a protective effect. However, the number of animals at each trauma dose point and the number of points on the curve were too small for accurate comparisons to be made. Also, recent work suggests that the use of gram-centimeters as a measure of the trauma dose for the weight-dropping technique of cord injury is inaccurate. With further work, it is possible that an accurate trauma dose-response curve can be obtained for the weight-dropping technique of cord injury.

Rivlin and Tator devised the clip compression model of experimental spinal cord injury in rats, and attempted to define a trauma dose-response curve. They found that recovery on the inclined plane was related to log compression time. For example, compression for longer than 8 minutes was shown to produce as severe an effect on spinal cord function as removal of an entire segment of the spinal cord (myelotomy). However, their experiments only examined a single compression force at three different durations of compression (3, 60, and 300 seconds). The present experiments extend this work, and take into account both variables in the clip model of acute spinal cord compression injury: the force of compression and the duration of compression.

The present results clearly show that increasing the force of compression or the duration of compression caused a reduction in functional recovery. There was a characteristic pattern of recovery in that the animals tended to improve during the first 4 weeks after injury, followed by a plateau in recovery. This pattern is similar to the recovery curves seen by Tator and Deecke in monkeys, and by Wells and Hansebout in dogs. Thus, any studies looking at the effects of treatment of spinal cord injuries, using functional recovery as an indicator of effectiveness, must follow the animals for several weeks. In the case of monkeys, the follow-up period must be at least 8 weeks, but in rats 4 weeks appears to be sufficient.

The mathematical model developed here is the first the authors are aware of that is able to predict functional recovery in terms of the initial injury parameters. Within the bounds of the force and duration values tested, the model predicts functional recovery at each week, except for the undefined areas in Fig. 4. Extrapolation outside the experimental limit is always hazardous, particularly in this case, as the curve becomes asymptotic to the force-duration plane. Thus, no definite value can be given for the maximum duration or force of compression that would produce no functional recovery. However, computer analysis suggests that a duration of at least 1 hour with a 300-gm force would be required.

Unfortunately, the present data cannot be extrapolated directly to human injuries, due to the

### TABLE 2

The relationship between force of compression, duration of compression, and recovery on the inclined plane*

<table>
<thead>
<tr>
<th>Force (gm)</th>
<th>Duration (secs)</th>
<th>3</th>
<th>30</th>
<th>60</th>
<th>300</th>
<th>900</th>
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<tbody>
<tr>
<td>1 week after injury</td>
<td>16</td>
<td>68.6 ± 7.5</td>
<td>69.3 ± 3.5</td>
<td>65.7 ± 7.9</td>
<td>58.6 ± 12.8</td>
<td>52.1 ± 15.0</td>
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<tr>
<td></td>
<td>71</td>
<td>38.6 ± 4.8</td>
<td>34.3 ± 5.3</td>
<td>30.0 ± 6.5</td>
<td>32.5 ± 4.2</td>
<td>—</td>
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<tr>
<td></td>
<td>178</td>
<td>28.6 ± 3.8</td>
<td>29.2 ± 6.6</td>
<td>29.3 ± 3.5</td>
<td>27.1 ± 2.7</td>
<td>—</td>
</tr>
<tr>
<td>2 weeks after injury</td>
<td>16</td>
<td>71.4 ± 3.8</td>
<td>68.6 ± 3.8</td>
<td>70.7 ± 4.5</td>
<td>66.4 ± 10.7</td>
<td>58.6 ± 12.5</td>
</tr>
<tr>
<td></td>
<td>71</td>
<td>45.0 ± 2.9</td>
<td>43.6 ± 5.6</td>
<td>35.7 ± 7.3</td>
<td>35.8 ± 2.0</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>178</td>
<td>31.4 ± 4.8</td>
<td>33.3 ± 7.6</td>
<td>31.4 ± 7.5</td>
<td>30.0 ± 5.0</td>
<td>—</td>
</tr>
<tr>
<td>8 weeks after injury</td>
<td>16</td>
<td>72.1 ± 7.6</td>
<td>67.9 ± 4.9</td>
<td>70.0 ± 6.5</td>
<td>67.1 ± 7.6</td>
<td>55.7 ± 12.4</td>
</tr>
<tr>
<td></td>
<td>71</td>
<td>58.6 ± 3.8</td>
<td>50.0 ± 5.8</td>
<td>45.0 ± 4.1</td>
<td>43.0 ± 5.7</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>178</td>
<td>52.9 ± 7.0</td>
<td>41.7 ± 5.2</td>
<td>31.4 ± 5.6</td>
<td>35.0 ± 4.47</td>
<td>—</td>
</tr>
</tbody>
</table>

*Recovery is measured by the angle achieved on the inclined plane in degrees (mean ± SD).
Decompression of spinal cord compression injury

species difference, and the probable biomechanical differences related to the different spinal cord sizes. The study can, however, be applied indirectly to clinical situations, especially with respect to the therapeutic value of decompression for acute spinal cord injury in the presence of persisting spinal cord compression. As shown, the subsequent functional recovery that can be achieved by acute cord decompression is related to the duration of compression, regardless of the actual force. The study also shows that the earlier the persisting compression is removed, the better the functional recovery. Unfortunately, in clinical practice, the actual force of compression is usually unknown. It is likely that in many injuries the force of compression is so great that it is impossible to achieve decompression early enough to yield any recovery. However, based on clinical experience in which some patients have recovered following decompression, it is likely that many more patients would recover if decompression were performed earlier.

The present study documents the deleterious effect of continuing cord compression and emphasizes the need for a careful search for, and removal of, any continued compression of the spinal cord. This is probably true for patients with incomplete cord injuries with retention of some motor or sensory function below the level of the injury. Whether or not patients with complete cord injuries with low enough compression forces could be decompressed soon enough to produce some functional recovery is unknown, although the present results suggest that they too might recover some function after decompression.

Conclusions

1. Trauma dose-response curves have been established for the clip compression model of acute cord compression injury in rats.
2. The relationships between force of compression, duration of compression, and functional recovery after acute spinal compression injury in the rat can be described by two equations, one for the first 4 weeks and the other for the 5th to 8th week, during which there was a plateau in recovery.
3. The study demonstrates the importance of early decompression for the relief of persisting compression of the spinal cord after acute cord compression injury.

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References


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