Clinical signs and evoked response alterations associated with chronic experimental cord compression

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Cortical and spinal evoked potentials were used to monitor the effect of experimental chronic cord compression in cats. An implantable compression screw made it possible to maintain the animals unrestrained. The mean compression period was 10 weeks (maximum 16.5 weeks). Compression was increased by stepwise tightening of the screw at intervals of 4 to 7 days under ketamine anesthesia. Evoked potentials were monitored before and after each compression step with repeated recordings, and were analyzed in terms of alterations in amplitude, latency, and waveform. Amplitude response curves were plotted where the amount of compression at each recording was expressed as a percentage of total compression. Changes in spinal evoked potentials occurred rather early (mean 36% of total compression), while obvious cortical evoked potential changes appeared rather late (mean 91% of total compression). Neurological alterations appeared later than alterations in spinal evoked response but prior to alterations in cortical evoked response. Thus, alterations in cortical somatosensory evoked potentials in the presence of chronic spinal compression indicate a severe degree of compression and do not seem to be of diagnostic value in the early detection of chronic spinal cord compression. It is suggested that the monitoring of spinal rather than cortical evoked responses would be more useful in locating and detecting chronic compression spinal cord damage.

KEY WORDS - spinal cord compression • cortical evoked response • spinal evoked response • spinal cord injury

Following a series of very early reports on experimental cord lesions, Allen introduced a reproducible model of spinal cord injury in 1911. The first description of alterations in spinal cord potentials associated with cord injury was that of Gelfan and Tarlov. Since then, such alterations have been reported in a number of experimental studies. In 1970, Singer, et al., first reported changes in cortical evoked potentials (EP's) caused by experimental cord injury, and this finding has since similarly attracted attention.

Few models of truly chronic experimental cord compression have been described and these sometimes have required very long periods of compression. Only Bennett and McCallum have used EP's to monitor the effects of nonacute cord compression. In a previous study, we monitored the effects of slow subacute cord compression at the spinal and cortical level. Compression times, however, were too short to be clinically comparable. In the present experiment, we studied a model of truly chronic cord compression in cats and analyzed the relationship between clinical signs, cortical and spinal EP changes, and the extent of spinal cord compression.

Materials and Methods

Preparation

The experiments were performed on nine cats, each weighing 2.6 to 4.0 kg (mean 3.2 kg). Electrodes and compression screws were implanted under intramuscular hexobarbital anesthesia (40 mg/kg). For the subsequent recording sessions, animals were anesthetized with ketamine (40 mg/kg). In two control animals, screws and electrodes were implanted for 4 weeks without compression. In one of the control animals, a skin erosion was managed conservatively; in three experimental animals, infected implants ne-
Chronic experimental cord compression

![FIG. 1. X-ray film, lateral projection, showing a compression screw and connection sockets in situ.](image)

<table>
<thead>
<tr>
<th>Cat No.</th>
<th>Duration of Experiment (days)</th>
<th>Compression distance (mm)</th>
<th>Increments No.</th>
<th>Steps (× mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3</td>
<td>97</td>
<td>4.75</td>
<td>19</td>
<td>19 × 0.25</td>
</tr>
<tr>
<td>C4</td>
<td>131</td>
<td>4.5</td>
<td>18</td>
<td>18 × 0.25</td>
</tr>
<tr>
<td>C5</td>
<td>84</td>
<td>4.0</td>
<td>10</td>
<td>4 × 0.25</td>
</tr>
<tr>
<td>C6</td>
<td>74</td>
<td>4.25</td>
<td>11</td>
<td>6 × 0.5</td>
</tr>
<tr>
<td>C10</td>
<td>43</td>
<td>3.0</td>
<td>7</td>
<td>5 × 0.5</td>
</tr>
<tr>
<td>C12</td>
<td>74</td>
<td>4.75</td>
<td>12</td>
<td>7 × 0.5</td>
</tr>
<tr>
<td>C13</td>
<td>43</td>
<td>3.5</td>
<td>7</td>
<td>5 × 0.5</td>
</tr>
<tr>
<td>mean</td>
<td>78</td>
<td>4.1</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

* Compression is described by the number of stepwise plate descents and the total distance of plate descent.

The time intervals between tightening the compression screw varied from 4 to 7 days, and an attempt was made to maintain similar intervals in each animal (Table 1). In the first two animals, only 0.25-mm increments were used, resulting in compression periods much longer than the 6 to 10 weeks initially aimed at. The regimen of compression was then altered by using 0.5-mm steps in the first two-thirds of compression (as estimated from x-ray films of the spinal canal diameter and from body weight).

The neurological condition of the animals was constantly monitored using a modified Tarlov scale as follows: Grade 0 = complete paraplegia; Grade 1 = slight movements; Grade 2 = good movements of all extremities with reduced weight tolerance; Grade 3 = impaired walking and weight tolerance; Grade 4 = normal motor activity. The compression plate was screwed down in increments of 0.25 or 0.5 mm, as indicated in Table 1, until the animal was completely paraplegic. The animal was then anesthetized, a last recording session was performed, and Evans blue dye (20 mg/kg body weight) was injected intravenously. Two hours later, the animal was sacrificed with an overdose of hexobarbital and the injured segment of the spinal cord removed.

Intraoperative recordings were made during the implantation procedure to insure proper placement and function of the system. During the period of chronic compression, a protocol of EP measurements immediately before and after each increase in compression was established and could be followed with few exceptions. The skull electrodes and the connector sockets of the spinal electrodes were punctured percutaneously under sterile conditions with standard No. 12 and No. 1 needles connected to the recording apparatus. A subcutaneous needle electrode served as a ground. The sciatic nerve was stimulated via two percutaneous needle electrodes with a 10- to 20-V,
FIG. 2. Peak amplitude response curves of cortical evoked potentials in two animals (Cat C13, left, and Cat C5, right). The compression is indicated both in millimeters and in percent of total compression. Clinical grading is indicated by the dotted line. D marks the beginning of wave deformation; L marks the increase in latency. In Cat C5 (right), the total period of compression was 76 days. In this animal, the spinal evoked injury potential appeared at 2.5 mm of compression, equivalent to 59% of total compression. In Cat C13 (left), the total period of compression was 36 days. The spinal evoked injury potential appeared at 2.5 mm of compression, corresponding to 71% of total compression. AP1,2 = amplitudes of evoked potential positive waves 1 and 2.

Results

The duration of chronic implantation varied from 43 to 131 days in the animals subjected to spinal cord compression (mean 78 days). The period of compression ranged from 36 to 127 days (mean 71 days). Compression periods in the range of months were achieved by small compression steps and longer intervals, as in Cats C3 and C4. In the latter animal, the skin was allowed to close above the screw sleeve, further minimizing the risk of infection, thus demonstrating that even longer compression periods are feasible. The range of plate descent varied from 3.0 to 4.7 mm (mean 4.1 mm). On the average, 12 compression increments were used (Table 1). The number of compression steps varied because of variations in spinal canal diameter and compression step size (Table 1). The number of recordings was larger than that of compressions because of control recordings at implantation and before sacrifice.

Neurological Changes

In all animals except one, normal movement was retained until at least 50% of total compression had been reached. Average compression required for the onset of motor impairment was 66% of total compression (Fig. 3); thus, neurological Grade 3, with impaired walking, was reached at between 50% and 78% of total compression, with a mean of 66% (Table 2). Grade 2, with movement of all extremities and reduced weight-bearing capacity, was reached at between 67% and 95% of total compression, with a mean of 80%. Grade 1, with only minimal movement of the legs, was reached with an average of 94% of total compression, ranging from 82% of total compression at the earliest to 100% of total compression at the latest. In three animals, the motor grade changed abruptly from Grade 2 to Grade 0, and in two animals,
Chronic experimental cord compression

FIG. 3. Relationship between the degree of compression and clinical grading. The time course in the development of clinical grading for every single animal is shown in its relationship to the degree of total compression. The appearance of the first clinical signs (corresponding to clinical Grade 3) lies between 48% and 78% of total compression (mean 66%). Neurological grading is by a modified Tarlov scale (see text).

directly from Grade 4 to Grade 2. Marked motor deficit (corresponding to motor Grade 2) was seen on the average at 80% of total compression. No clinical abnormality was seen in the two control animals.

Changes in Cortical Evoked Potentials

The normal cortical evoked response in the cat has been described previously. In the chronic experiments, however, a marked variability in amplitude was found from recording session to recording session. Therefore, amplitude response curves appeared less regular than in subacute experiments (Fig. 2). As previously defined, amplitude response curves were abrupt in three cats, gradual in one, and mixed in three. The mixed pattern, where a slow amplitude decrease is followed by a quick reduction, was seen more often in these animals than in subacute compression. There was also a larger variability in latency values in cortical EP's. As demonstrated in Table 2, the amplitude loss occurred late in relation to the time course of total compression, and then it occurred rapidly (range 83% to 95%, mean 91% of

| TABLE 2 |
| Development of clinical signs and somatosensory evoked potential (SEP) alterations related to the degree of compression |

<table>
<thead>
<tr>
<th>Cat No.</th>
<th>Clinical Grade*</th>
<th>Spinal SEP Alteration at Compression†</th>
<th>Cortical SEP*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>C3</td>
<td>58</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>C4</td>
<td>50</td>
<td>83</td>
<td>(83)</td>
</tr>
<tr>
<td>C5</td>
<td>75</td>
<td>82</td>
<td>82</td>
</tr>
<tr>
<td>C6</td>
<td>77</td>
<td>83</td>
<td>(100)</td>
</tr>
<tr>
<td>C10</td>
<td>67</td>
<td>67</td>
<td>(100)</td>
</tr>
<tr>
<td>C12</td>
<td>(78)</td>
<td>78</td>
<td>94</td>
</tr>
<tr>
<td>C13</td>
<td>57</td>
<td>71</td>
<td>88</td>
</tr>
<tr>
<td>mean</td>
<td>66</td>
<td>80</td>
<td>94</td>
</tr>
</tbody>
</table>

* Values shown are percentage of total compression at which each event occurred. The neurological condition of the animals is described using a modified Tarlov scale (see text). Latency increase in cortical SEP's in Cats C5 and C10 occurred twice, with subsequent rapid return to normal values. Numbers in parenthesis indicate compression levels at which the animal suddenly deteriorated.
† Appearance of the evoked injury potential at amount (mm) of compression and percent of total compression.
FIG. 4. Development of evoked injury potential (Cat C13). Spinal evoked responses recorded 10 mm rostral to the site of compression. Note triphasic potential in top tracing (compression 0 mm) as compared to large positive potential at 71% of total compression (2.5 mm). Positivity is downward; vertical bar represents 10 μV in second tracing, 20 μV in all other tracings. Numerals give degree of compression (mm).

Changes in Spinal Evoked Responses

Spinal evoked responses in all animals showed the typical triphasic configuration for the thoracolumbar area, with some minor variability in phase and configuration of later components. The changes in spinal EPs were quite uniform. Very early in the course of compression, the polyphasic potential changed into a monophasic positive potential, the so-called "evoked injury potential" (Fig. 4). As indicated in Table 2, in five animals these changes were observed rather quickly, either shortly after a new stepwise increase in compression or at the time of the subsequent pre-compression recording. In only two cats (C6 and C13) did the transition from the normal spinal cord potential to the evoked injury potential occur somewhat more slowly, producing a transitory waveform, incorporating features of the normal and of the evoked injury potential. Here, a change occurred from a triphasic to a monophasic positive waveform, but several peaks were superimposed upon the monophasic wave. In these two cats with a definite transition period, the evoked injury potential appeared at 59% and 71% of total compression, respectively, and 2.5 mm of screw lowering was needed to achieve this result. In the remaining animals, around 1 mm compression was needed on the average to produce a typical evoked injury potential. In this latter group, the evoked injury potential appeared at between 10% and 33% of total compression. The mean compression required to produce the evoked injury potential in all seven animals was 36% of total compression. No consistent significant increases in latency were noted in spinal recordings. The most prominent finding in spinal evoked responses near the site of compression was that the compression invariably produced this particular monophasic potential rather early.

Neurological Condition Related to Evoked Potentials

The appearance of the first neurological sign, disturbance of gait, occurred at 66% of total compression as a mean for the total group (range 50% to 78% of total compression). Marked paraparesis, corresponding to clinical Grade 2, was seen on the average at 80% of total compression (range 67% to 95% of total compression). Both the appearance of the first neurological sign and the appearance of a marked neurological sign occurred, on the average, earlier than the alterations in cortical evoked responses. The cortical evoked response changes given as a mean for the total group (namely, wave deformity at 83%, latency delay at 88%, and amplitude loss at 91%) all appeared later. That means that, although the period of time during which clinical alterations appeared (50% to 78% of total compression) largely overlapped with the increase in peak latency and, finally, by a rapid loss in amplitude. These three changes occurred mainly around the last two compression steps.

total compression). Wave deformities occurred at from 57% to 100% of total compression (mean 83%). Latency delays of the first two positive peaks were found in all animals. They preceded conduction block but occurred relatively late, ranging between 71% and 100% of total compression (mean 88%). In two animals, an early transient latency increase was found at 37.5% and at 33% of total compression, with rapid return to control values. The total compression time in these two animals was 5 and 11 weeks, respectively.

These experiments showed that cortical EP changes associated with chronic compression mainly occur during the last 15% of total compression. Wave deformation, as the first change, is followed by a marked
Chronic experimental cord compression

period of time during which changes in cortical evoked responses appeared (51% to 100% of total compression), as a rule, neurological alterations preceded changes in cortical evoked responses.

Spinal evoked responses showed very early alterations during the course of spinal compression (mean 36% of total compression), and therefore occurred much earlier than clinical alterations (mean compression stage of earliest sign 66%). They also occurred much earlier than the cortical evoked response alterations, in which all three parameters given as mean for the total group did not change until at least 85% of total compression. The alterations in spinal evoked responses were not associated with any neurological alteration. Thus, from a diagnostic point of view, these alterations in spinal EP's might be interpreted as an early sign, even taking into account the wide range over which any of the alterations may appear.

Discussion

Before discussing the results, an introductory remark about the terminology of spinal evoked response changes seems appropriate. The term "final potential" previously used in our laboratory and the term "killed end potential" used by Deecke and Tator and by Woodbury have not been used in this paper because they imply irreversibility of these evoked response changes, which is not necessarily the case. We have called this positive potential the spinal cord "evoked injury potential" to avoid mistaking it for the common "injury potential." According to Woodbury and Lorente de Nó, a large positive potential may be recorded in volume if an ascending volley of action potentials does not reach and pass by the recording electrodes.

Mode of Compression

Theoretically, the principal disadvantage of our compression model seems to be the nonlinear type of compression. On one hand, changes in cortical EP's usually occurred after the turning of the compression screw, and changes in clinical grade were usually apparent after recovery from anesthesia after the last two or three compression steps. On the other hand, compression increments of either 0.25 or 0.5 mm never changed cortical somatosensory EP's or clinical grade during the first half of compression (Table 2). Therefore, one might conclude that the rate of compression in the early phase is better tolerated and does not impair conduction as immediately as the same rate of compression in the late phase. As long compression periods were required when we used 0.25-mm steps, while at the same time, no clinical changes appeared in the first half of the compression period, we thought it was justified to increase the rate of compression in the subsequent animals.

Our model of chronic compression achieved a mean compression period of 71 days with a maximum of 131 days. This is certainly long enough to simulate certain clinical conditions, as suggested by the results of Ikeda, et al., who produced paraplegia in rabbits 20 days after implantation of tumor cells. Ushio, et al., achieved paraplegia in rats between 20 and 30 days after inoculation with tumor cells. The chronic model used by Bennett and McCallum had two disadvantages. The mean compression time was only about 14 days, and the increase in compression could not be controlled after the implantation of the plastic rod. On the other hand, there is no doubt that compression periods like ours in the range of months cannot simulate the time spans needed by benign tumors to compress the spinal cord in man.

The interval between compression increments is another important factor in the rate of compression, as it describes the time available for demyelination and other mechanically induced factors that might cause conduction impairment. Using a model of experimental demyelination, McDonald and Sears demonstrated the influence of demyelination on conduction time in the central nervous system. They found that a reduction in mean conduction time in a compound action potential is to be expected because the proportion of slowly conducting fibers increases. Previous findings in subacute graded compression showed a latency increase in cortical EP's in 60% of experiments, whereas, in this chronic study, a noteworthy latency increase was found in all cases. Therefore, it might be hypothesized that the changes in cortical evoked potentials in slowly growing benign tumors in man differ from those found in our experiments. In fact, in a series of 48 spinal space-occupying lesions, including 28 slowly growing tumors, latency delays were found early as compared to the clinical grade, and were sometimes quite extensive (unpublished data).

One more factor possibly not linearly proportional to the rate of compression as expressed in millimeter steps is the effect on the vasculature and local blood flow. To our knowledge, data concerning spinal cord blood flow in chronic preparations have not been published, although alterations of the vascular bed in long-standing cord compression have been described. Apart from this vascular factor, the relationship of cord and spinal canal diameters and some variation in determining the starting point of compression may account for the variation in the compression needed as expressed in the amount the plate is lowered. The same could be assumed for variability in the onset of clinical changes. As might be expected, the plate pressure on the dorsal columns results in a rather early appearance of the evoked injury potential. More widespread effects of the descending plate require the build-up of a transmedullary pressure gradient. The degree of compression as expressed in millimeters of plate descent does not run parallel to the increase in the pressure acting on the spinal cord. In the early phase of compression, some of the energy is used up in compressing the epidural
veins and fat and deforming and displacing the cord. In the later stage of compression, a small increase in plate descent results in a more marked intramedullary pressure increase. These and the above-mentioned vascular factors may account for the variability in the development of neurological signs and cortical EP alterations.

**Slow versus Chronic Compression**

Comparing the amplitude response curves of animals subjected to chronic spinal compression (where there were days between individual recording sessions) to the amplitude response curves in animals subjected to slow subacute compression (where all recordings take place within a few hours), a greater variability in amplitude becomes evident. This variability in amplitude reduces significantly the chances of differentiating between spontaneous fluctuations and pathological losses in amplitude. This is unfortunate as the loss in amplitude usually occurs within the last 10% to 15% of total compression, and then rather quickly. Latency increase and wave deformation are no sure help in differentiating a spontaneous amplitude fluctuation from a pathological amplitude loss since increases in latency and wave deformation usually occur after loss in amplitude has begun, and are usually not apparent before the loss is significant.

As regards chronic cord compression, our findings indicate that an amplitude loss associated with latency increase and deformation of cortical somatosensory EP's suggests a very severe degree of cord compression and will be very quickly followed by a total block of conduction. The earliest changes in cortical EP's were those of waveform, which are difficult to quantify reproducibly and may therefore be of limited diagnostic value in clinical application. This means that cortical somatosensory EP's do not seem to be of much use in the early detection of chronic spinal cord compression. This is in contrast to the findings of Bennett and McCallum, who stated that cortical EP's consistently signaled the increase in compression and the postoperative loss of function.

Although the chronic animals in this study and in the study of subacute graded compression are not comparable in number, it may be noted that, in the chronic animals, the average plate descent (4.1 mm) was larger than in the subacute animals. A striking difference is found in the changes of spinal evoked responses. Changes in spinal responses occurred much earlier in chronic than in subacute compression. Abnormality of cortical responses occurred slightly earlier in chronic compression, while rapid loss in amplitude occurred at approximately the same amount of total compression in both groups. The mixed type of amplitude response curve, in which the abrupt cutoff is preceded by a slow decrease, was seen more frequently in the group subjected to chronic compression.

The different time course of changes in spinal and cortical EP's, with definite spinal EP alterations at a mean of 36% of total compression as compared to definite cortical EP changes at a mean of 91% of total compression, suggests that recording spinal EP's could be more useful in the detection of a chronic compressive spinal cord lesion than recording cortical EP's. The most remarkable finding remains that changes in spinal evoked responses recorded close to the site of compression preceded clinical signs.

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**References**

Chronic experimental cord compression


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