Evaluation of experimental spinal cord injury using cortical evoked potentials

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Experiments were performed to determine if changes in cortical evoked responses could be used to predict the extent of the neurological deficits following spinal cord injury by sudden inflation of a Fogarty balloon in the epidural space cephalad to a laminectomy. The cortical responses to stimulation of the posterior tibial nerve were recorded over the sigmoid gyrus at various times following the lesion and compared with the control response. Severe, irreversible neurological deficits occurred in cats in which the cortical response either could not be evoked immediately after injury or disappeared rapidly during this period. At the end of at least 6 weeks following injury, all of these animals were paraplegic and showed severe cystic degeneration of the spinal cord. In animals in which the post-injury cortical response did not completely disappear, only mild changes were observed in a spinal cord 6 weeks following injury. This technique may be helpful in ascertaining the severity and irreversibility of a traumatic spinal cord lesion; because the technique is simple, the method may prove helpful in the clinical management of patients with spinal cord injury.

Key Words: spinal cord injury • cortical evoked response • motor function • dorsal and lateral fasciculi

It is important to determine the prognosis of patients with acute injuries of the spinal cord. The purpose of the experiments we are reporting was to determine whether the changes in cerebrocortical responses occurring after a spinal injury may be used for this purpose since changes in the amplitude of this response may reflect damage in ascending spinal pathways. In many reported studies, however, the injury model used was similar to that originally proposed by Allen and later adapted by Freeman and Wright in which the trauma is produced over a segment of the spinal cord that has been exposed by previous laminectomy. Results from these experiments, therefore, reflect changes in the evoked potential resulting from pathophysiological changes in an injured but decompressed region of the spinal cord. It is likely that the extent and duration of these pathophysiological changes would be more directly reflected by a model in which the injury was produced in a region of the spinal cord enclosed in the bony canal. For this reason, our experiments were performed using a "closed" injury model in which the spinal cord was intact over the traumatized segments. Although "closed" injury models have been described previously, they have not been used in a study of this type.
Methods

The experiments were performed in 25 adult cats weighing between 2 and 6 kg. All animals were anesthetized with fluothane delivered by mask. The left sciatic nerve was then aseptically exposed from the hip to its bifurcation to form the common peroneal and posterior tibial nerves. In addition, a short segment of the left radial nerve was exposed just above the elbow. A small burr hole was placed in the skull, 4 mm anterior to the coronal suture and 1 mm to the right of the sagittal suture. Preliminary studies indicated that this arrangement permitted the recording of evoked responses from the sensorimotor area (SM1) of the cerebral cortex. A stainless steel screw electrode was placed in the burr hole just in contact with the dura. A needle reference electrode was placed in the neck muscles. Each animal was then positioned on its right side for recording. A rectal thermister was inserted, and the body temperature was maintained within the normal range by an infrared lamp. The radial and posterior tibial nerves were placed on bipolar stimulating electrodes. The sciatic trunk was then positioned on a silver-wire recording electrode. Nerve desiccation was prevented by applying cotton soaked in mineral oil around the exposed nerve.

The cortical potentials were evoked by peripheral stimulation of the contralateral posterior tibial nerve at a frequency of 1 Hz. Evoked cortical responses were recorded before and at selected intervals after the spinal cord was injured. Signals were amplified by a WPI DAM-6 differential preamplifier and a Tetronix 3A3 differential amplifier. The 128 successive responses were averaged by a Fabritek 1072. Responses to stimulation of the radial nerve were also recorded to provide a method for determining whether changes in the response evoked by stimulation of the hindlimb nerves were due to pathophysiological changes in the spinal cord or to changes in the relation of the electrode and the cerebral surface that would be produced, for example, by accumulation of blood in the subdural space. The compound action potential evoked in the tibial nerve was monitored proximal to the site of stimulation to ensure that the stimulating electrode was adequately positioned. The stimuli had an amplitude ranging up to 100 V and a duration of 0.1 msec.

Spinal cord trauma was produced in all animals by passing a No. 4 French Fogarty catheter cephalad in the epidural space, 6 cm above a small midline laminectomy carried out at the L1-2 level. The balloon was instantaneously inflated with water with volumes ranging from 0.2 to 0.6 cc. Following deflation, the catheter was immediately removed. It should be emphasized that the inflation of the balloon was not used to produce lesions of quantitatively reproducible graded severity. Rather, this technique was used to produce a lesion severe enough so that the clinical prognosis of the animal was questionable, thus providing a means of testing the prognostic significance of the changes in the cortical evoked responses described below.

Recordings were made periodically after injury in the majority of the animals for as long as 3 or 4 days. When the time between the post-injury recording sessions exceeded 2 or 3 hours, the animals were allowed to awaken after the closure of the incision, and their motor performance was closely observed at regular intervals for at least 6 weeks and in most animals for a period greater than 10 weeks. At each examination, motor performance was graded according to the scale detailed in Figure 2.

Finally, animals were sacrificed under Nembutal anesthesia and the injured segment of spinal cord removed and placed in 10% formalin in preparation for histological study. After fixation, sections were taken through the midpoint of the damaged segment. The sections were stained with hematoxylin and eosin and studied under the light microscope. Special axon and myelin stain preparations were also made.

Results

Evoked Responses

On the basis of post-injury evoked responses, the 25 cats in this study fell into four very distinct groups. Group A consisted of 12 animals, two injured with 0.2 cc of water, three with 0.3 cc, six with 0.4 cc, and one with 0.5 cc. The responses in Fig. 1A
Evaluation of spinal cord injury by cortical evoked potentials

Fig. 1. Evoked cortical responses from animals in Groups A—D. Each record is averaged from 128 consecutive responses to stimuli applied at 1/sec. The time at which the stimulus was applied is indicated with arrows in this and all subsequent figures. Groups A and B = reversible injury. Groups C and D = irreversible injury.

The three animals in Group B were all injured with 0.4 cc of water. The responses recorded in one of these cats are shown in Fig. 1B. In all of these animals the evoked response was absent immediately post-injury; however, it returned after 3 hours and persisted until sacrifice. As shown in Fig. 2 (open circles), all animals became able to walk. However, in contrast to those of Group A, the evoked response was present immediately after injury and persisted throughout the post-injury period.

The clinical course of the changes in motor behavior is shown in Fig. 2. It is clear from these graphs that all of the animals in Group A either maintained or recovered their ability to walk.

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The clinical grades of 1 to 5 are: Grade 0 = flaccid paraplegia (minimal or no leg movements, variable tone, no bowel and bladder function). 1 = spastic paraplegia (leg movements moderate or vigorous, leg spastic and extended, no sitting, no bowel and bladder function). 2 = severe paraparesis (only moderate spasticity in legs, vigorous coordinated movements suggesting walking, ability to sit and stand, no bowel and bladder function). 3 = moderate paraparesis (able to stand and walk, legs and hips obviously unstable, leg lagging, bowel and bladder variable). 4 = mild paraparesis (walking with some leg and hip instability, bowel and bladder functional). 5 = (hip instability seen only with jump or run). Inability to walk is represented by broken line, while the circle followed by a solid line represents the onset and time course of walking. Note that the shortest follow-up was 8 weeks and that over half of the animals were followed for greater than 14 weeks. In Groups C and D, spastic paraplegia persisted and none of the animal recovered.
Evaluation of spinal cord injury by cortical evoked potentials

A, the recovery was quite slow and each had a significant neurological deficit at the time of sacrifice.

Group C included four animals, two injured with 0.4 cc of water, one with 0.5 cc, and one with 0.6 cc. A cortical response was observed in two immediately after injury, but the amplitude of the response then decreased rapidly with time and was absent at 6 hours. In the third and fourth animals of this group, the cortical response was absent immediately following injury (Fig. 1C). However, it returned within the subsequent 3-hour period. Unlike the changes in the responses observed in Group B (Fig. 1B), the amplitude of this response then became progressively smaller, and by the second day it was absent. In contrast to Groups A and B, all animals in this group remained paraplegic (Fig. 2).

Group D consisted of six animals, one injured with 0.2 cc of water, four with 0.4 cc, and one with 0.5 cc. In all of these cats, the cortical response was absent immediately following injury and never returned (Fig. 1D). Their clinical course (Fig. 2) was similar to that of the animals in Group C, namely, they all remained paraplegic.

Morphological Changes

Morphological studies also revealed a correlation between the changes in evoked responses and the chronic appearance of the spinal cord in Groups A–D. However, this was much less specific than was the correlation with the clinical neurological deficits. Pathologically, there tended to be a continuum in the severity of the lesion from Groups A through D. This was somewhat

![Fig. 3. Representative micrographs of cross sections taken from the injured spinal cord segments of animals in Groups A—D. All sections were stained with Chowsky silver technique.](image-url)
apparent by gross examination. Microscopically (Fig. 3), vacuolization, glial reaction, and cystic degeneration were only moderate in animals with preserved cortical responses and reversible injuries (Groups A and B). These histological changes were most commonly observed in the central region of the cord, and the posterior columns were usually preserved. Several animals in Group A had essentially normal cords. These findings are all quite consistent with the chronic changes previously reported in animals with reversible lesions. Assenmacher and Ducker found variably-sized central hemorrhages at 5 days after injury and 10 of their animals had normal histology.

In animals in which the evoked responses irreversibly disappeared (Groups C and D), the gliosis and central cystic degeneration was severe. Very little of the normal cord was preserved (Fig. 3). Similar lesions were found by Assenmacher and Ducker in all of their chronic animals with irreversible lesions.

Discussion

These results imply that changes in the cortical responses evoked by peripheral stimulation may indeed be useful in determining the clinical outcome of animals with "closed" spinal cord injuries. In every animal studied, ability to walk returned only if the response never disappeared or returned shortly after injury and persisted. It should be emphasized, therefore, that the most significant finding affecting prognosis was not merely the return of evoked response following injury, but the persistence of this response throughout the first few days following injury. This prognostic sign does not depend upon subtle changes in the amplitude or duration of the cortical evoked potentials but only on the presence or absence of this response, a finding which again emphasizes the possible utility of this method in the clinical setting.

The results of our study differ somewhat from those performed in animals injured with an "open" method. In a previous study all animals with evoked responses present at 3 to 4 hours after injury had significant neurological recovery. The progressive disappearance of the cortical response following the next few hours (Fig. 1C) after injury was not reported. It is possible that this observation is due to the compression of the spinal cord resulting from edema. The time course of these electrophysiological changes is consistent with that of the development of edema following spinal cord injury. If this difference is really due to the fact that the cord injured by the "open" method is decompressed, the procedure may be quite helpful in certain clinical cases.

The results also show that there was little association between the volume of water used to inflate the Fogarty balloon and the severity of the lesion produced. This was probably due to variations in the size of the spinal canal, and the fact that the position of the balloon in the epidural space could not be controlled. Despite this variability, the changes in the cortical evoked responses were specific indicators of the prognosis for each animal.

It seems likely that the changes in the cortical evoked responses are the result of injury to ascending pathways in the dorsal and lateral fasciculi. It has previously been argued that compromised function in at least the posterior columns is necessary to produce a significant effect on cortical responses evoked by peripheral stimulation. Dempsey, et al., Giblin, and Halliday and Wakefield all suggest that the afferents responsible for the primary evoked cortical response travel in the dorsal column-medial lemniscal pathway. Additional experiments by Morin, et al., showed that ascending pathways located in the lateral fasciculi also may be significant in determining the amplitude and duration of the cortical evoked response. Since these pathways are located near the corticospinal routes, the close association between changes in the cortical evoked response and the extent of recovery of voluntary motor function might be expected.

It would be inappropriate to extrapolate the specific findings of this study to the direct evaluation of patients without further investigation. What this experiment has shown, however, is that this simple and clinically applicable technique is useful in
Evaluation of spinal cord injury by cortical evoked potentials

indicating the prognosis following spinal injury in the animals studied. To obtain the specific changes in the cortical evoked response that will be useful clinically, additional experiments on primates and human subjects must be attempted.

References


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