Spinal evoked potentials in the primate: neural substrate

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Summated responses evoked by peripheral nerve stimulation were recorded from electrodes located in the epidural and subdural spaces anterior and posterior to the monkey spinal cord. Segmental microsurgical resection of the dorsal columns both at the thoracic and cervical levels resulted in total obliteration of the response recorded rostral to these lesions. Isolated segmental dorsal column preservation did not significantly alter response latency or wave form recorded at the rostral electrodes. Bilateral cervical dorsolateral column resection also resulted in no discernible alterations of these responses. These data indicate that spinal evoked potentials recorded from levels rostral to their root entry zones arise almost exclusively from the dorsal columns.

KEY WORDS □9 spinal evoked response □9 neural substrate □9 dorsal column

NUMEROUS investigations indicate that analysis of spinal cord electrical recordings offers a means of objectively assessing spinal cord integrity. In 1946, Pool performed an electrospinogram (ESG) from intrathecal recording electrodes in a paraplegic patient. Subsequent studies suggested that the random electrical activity of the ESG arises from segmental neuronal pools tonically maintained by afferent impulses. This lack of specificity and the susceptibility of the ESG to a variety of exogenous and supraspinal influences have supported the contention that spinal cord potentials evoked by peripheral nerve stimulation (SEP) offer a superior method of diagnostic and prognostic evaluation.

The inclusion of signal-averaging techniques increased the feasibility of such examinations and numerous studies of summated SEP's recorded from skin, epidural, or intrathecal electrodes have been reported. Liberson, et al., recording from surface electrodes, suggested that the SEP in man might arise from the dorsal roots, cauda equina, spinal cord, or cerebellum. Cracco, with similar recording methods, suggested that such summated responses arose from multiple spinal cord afferent pathways. In non-primate laboratory preparations, Happel, et al., and others agreed with this interpretation but were unable to further delineate the specific pathways. Shimoji, et al., re-evaluated the nature of the summated SEP and felt that it was necessary to use epidural electrodes in humans to overcome the attenuation and distortion of surface recordings. Similar recording methods were employed by Caccia, et al., who verified the diagnostic value of SEP's in defining dorsal root or root entry zone disorders. However,
the prognostic and diagnostic information derived from the SEP conducted over distances within the spinal cord has not been as clearly defined. A major constituent of this limitation has been the inconclusive definition of the anatomic substrate from which these responses originate. It is generally considered that these responses arise from primary and non-primary fibers located in multiple afferent pathways. Therefore, this present study was undertaken to evaluate the relative contributions of the various spinal cord tracts in the monkey to the averaged SEP as it is conducted through the cord.

Materials and Methods

Experiments were carried out in 10 stump-tail macaque monkeys (Macaca arctoides). Seven animals underwent five-level cervicothoracic laminectomies under sodium thiamylal (10 mg/kg) anesthesia with placement of bipolar electrodes in the midline dorsal epidural or the subdural spaces at the limits of the operative sites. The electrodes were three platinum iridium discs, 0.025 mm thick, 2 mm in diameter, and 4 mm apart on center, embedded in Dacron-reinforced Silastic, 0.25 mm thick. Flexible stainless steel, Teflon-coated leads were brought out for recording. Identical electrodes were placed bilaterally over sensorimotor cortices and fixed to the skull with dental cement. Two animals had a cervical laminectomy with midline dorsal epidural electrode placement at the C2-3 and C6-7 levels. Additionally, these animals had anterior resection of C2-4 vertebral bodies with electrode placement in the ventral epidural space. The leads of the ventral electrode were incorporated into a vertebral body prosthesis of dental cement.

After a 3- to 4-day recovery period, all animals in the series were anesthetized with ketamine hydrochloride (20 mg/kg). After intubation, they were placed on a volume respirator and paralyzed with 0.8 mg pancuronium/100 ml lactated Ringer's solution. Anesthesia was maintained by an intravenous infusion of ketamine hydrochloride (4 mg/kg) which was discontinued approximately 10 minutes before recording. All surgical sites were infiltrated with 1% Xylocaine (lidocaine) solution. Numerous evaluations in our laboratory have shown minimal alterations in the monkey spinal or cortical evoked responses during ketamine anesthesia at the above dosage levels. Enhancement of the primary and short-term depression of the secondary components of these responses frequently occurs but is rapidly reversed after infusion is discontinued for approximately 5 minutes. We have found with this route of administration, analgesia as manifested by withdrawal to painful stimuli persists for an additional 20 to 25 minutes. The sciatic nerve was stimulated transcutaneously. Rectangular pulses of 0.2 ms duration were applied at 4 Hz with intensities well above those required to obtain a motor response in the hind limb. These stimuli do not appear to cause discomfort in small animals, nor have they been reported as unpleasant by human patients. Similar techniques were used for stimulation of upper-limb peripheral nerves. The spinal cord was exposed through the previous laminectomy sites. Following sciatic and median nerve stimulation, spinal cord evoked potentials were assessed to obtain maximum responses. Evoked potentials were retrieved with an evoked potential measurement system.* The system incorporates two channels of photic isolated differential amplification with a frequency response from 1 to 1000 Hz and a 100 decibel common mode rejection. Two current stimulators, variable from 0 to 15 mA, and a 1024 sampling point averaging program (eight bits for each sample) are part of the system's programmable processor. This dual system allowed for simultaneous recordings from the dorsal and ventral cervical electrodes. The number of sweeps for each recording was kept at 250 except in the long-term studies, where 500 sweeps were averaged. Electrode impedance was maintained between 800 and 1500 Ω. Rectal temperature was maintained between 98° and 100° F, and continuous blood pressure measurements were carried out through a Silastic femoral artery catheter. Microsurgical techniques were used for segmental selective spinal cord resections. Serial sections of the cervical and thoracic cord stained for cell and fiber were examined to determine the extent of the lesions. The

*CTC-2000 Evoked Potential Measurement System manufactured by Clinical Technology Corporation, Kansas City, Missouri.
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**Fig. 1.** *Left:* Photomicrograph showing an almost total dorsal column resection (DCX) in an animal sacrificed 3 hours after resection. Weil, × 6. *Center and Right:* Evoked potential responses to sciatic nerve stimulation recorded from the dorsal epidural space cephalad and caudal to the segmental dorsal column resection. Recordings cephalad to DCX show almost total absence of evoked activity and maintenance caudal to the resection. The two lower illustrations show the relatively intact evoked potentials secondary to sensorimotor cortex stimulation recorded from the dorsal epidural space above and below the level of DCX indicating the intact physiological integrity of the lateral columns. Stimulus and beginning of responses at *arrows.*

Animals were divided into categories depending on the site of the lesion and length of follow-up review.

**Results**

**Acute Dorsal Column Resection**

Four animals had acute segmental dorsal column resection; one of these had undergone a previous bilateral ventral column ablation, unassociated with any SEP alterations. The dorsal column lesions were judged to be histologically complete in three animals. The remainder of the spinal cord appeared intact in the complete dorsal column lesion group except for the previously noted ventral column lesion and one instance of a minor unilateral dorsolateral column injury. One animal was judged to have an incomplete lesion because of the presence of a small residuum of deep midline dorsal column fibers. In the complete lesions, the amplitude of the responses evoked by sciatic nerve stimulation and recorded from the dorsal epidural space cephalad to the area of resection was almost totally reduced. The response changes in these three animals were consistent and essentially identical to those shown in Fig. 1. In the animal demonstrating the small midline dorsal column remnant, recordings showed persistence of a response approximately 10% of control amplitude occurring at control latency. Post-resection recordings remained unchanged in all animals over a 3-hour period. Responses evoked by sensorimotor cortex stimulation recorded from the dorsal epidural space cephalad and caudal to the area of resection remained intact in all four animals.

The cervical experiments involved two monkeys. Both animals had bilateral dorsolateral column resection at the C-3 level as the initial cord lesions. These ablations, which were subsequently judged to be histologically complete, did not result in any significant...
alterations in the responses evoked by sciatic and median nerve stimulation recorded cephalad to the area of resection. Recordings from the ventral and dorsal epidural electrodes had similar latencies and wave forms. Although the ventral recordings were less complex, these responses appear to represent spread in a volume conductor. Follow-up dorsal column resection at the C-4 level resulted in almost total loss of evoked activity recorded from electrodes cephalad to the resections (Fig. 2). No significant variability was noted in the histological evaluations or post-resection recordings in these two preparations.

Chronic Dorsal Column Resection

Two monkeys were evaluated for 6 and 7 weeks, respectively, following segmental upper thoracic dorsal column resection. Serial histological sections of the lesions were very similar, with both preparations showing almost total resection except for a few small fragments of residual dorsal column. The remainder of the cord appeared intact except for a small unilateral area of dorsolateral column injury in one animal. Responses evoked by sciatic nerve stimulation and recorded from the dorsal cord surface cephalad to the resection were unobtainable in the immediate post-resection period. However, both preparations showed a similar degree of minute response recovery on the day following surgical resection. In the animal followed for 6 weeks, this hardly discernible element of response recovery remained an inconsistent finding without further improvement. The second animal, however, showed an increased degree of response recovery at control latency which reached its maximum extent 4 weeks after resection. No further recovery occurred up to the termination of the experiment at the seventh week. This series of response alterations is illustrated in Fig. 3; the degree of response recovery shown occurring at the seventh week was the same as that noted on the fourth post-resection week. In both animals, stimulation of the sensorimotor cortex immediately after dorsal column resection and in the subsequent follow-up recordings showed no significant changes in the responses recorded above and below the area of resection (Fig. 3).
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**FIG. 3.** Left: Photomicrograph showing almost complete dorsal column resection (DCX) and a minor degree of unilateral dorsolateral column degeneration in an animal sacrificed at the seventh week. Weil, × 6. Center and Right: The DCX resulted in immediate loss of evoked activity to sciatic nerve stimulation recorded from the dorsal epidural space cephalad to the level of resection. A degree of recovery of the amplitude of the primary response occurring at control latency was noted, and remained unchanged up to the seventh week.

**Isolated Dorsal Column Preservation**

Two animals underwent segmental resection of the upper thoracic cord with sparing of the dorsal columns. In both animals, histological sections verified the isolated dorsal column preservation with only minor evidence of structural damage. Immediately after surgical resection, the amplitude of the dorsal cord response was moderately reduced in one animal, but recovery to control occurred within 15 to 45 minutes (Fig. 4). The apparent latency increase of the cord response to sciatic nerve stimulation following resection seen in Fig. 4 connotes an experimental variation of 4% and is most likely secondary to the surgical manipulation. In the second animal, evoked responses to lum-
bar cord stimulation and recorded rostral to the area of resection showed no alterations in latency or wave form during the surgical procedure or follow-up period (Fig. 4).

**Bilateral Anterior Column Resection**

Two animals underwent bilateral anterior column resection without any evidence of response alterations except for moderate amplitude depression of the second inflection of the primary complex in one animal. This change was incomplete and the responses remained stable over a 4-week follow-up period. Histological examination showed the lesions to be complete and similar.

**Discussion**

The SEP following peripheral nerve stimulation is conducted into the spinal cord exclusively through the dorsal roots. This response is, therefore, sensory in nature and has been shown to be unaffected by motor neuron activity. At the area of entrance into the cord, a large amplitude response is recorded with a wave form of varying complexity. Such wave forms most likely result from the activation of a large interneuronal pool with contributions from the asynchronous discharge of different groups of dorsal horn neurons as the potentials spread along divergent pathways. In the present experiments, our recordings were made from the dorsal surface of the cord well above these segments in which the stimulated afferent fibers entered the spinal cord.

Although Ertekin suggested that SEP recorded in caudal-rostral transmission originated from the dorsal columns, other investigators have indicated that afferent fibers outside of the dorsal columns contribute to the response. Liberson, et al., and Cracco suggested that in man such responses arose from multiple spinal cord afferent pathways. In the present experiments, our recordings were made from the dorsal surface of the cord well above these segments in which the stimulated afferent fibers entered the spinal cord.

Although Ertekin suggested that SEP recorded in caudal-rostral transmission originated from the dorsal columns, other investigators have indicated that afferent fibers outside of the dorsal columns contribute to the response. Liberson, et al., and Cracco suggested that in man such responses arose from multiple spinal cord afferent pathways. This contention has been supported by certain laboratory investigations in the cat. Le Blanc, et al., noted an inconsistent decrease in response amplitude at upper cervical levels not exceeding 50% following dorsal column resection. Form and latency were unaltered. Sarnowski, et al., supported these findings, and suggested that a significant amount of spinal evoked activity in the cat originated from pathways in the dorsolateral columns. In support of this concept, other investigators have suggested a potential contribution by a dorsolaterally located spino-cervical tract of the cat to the evoked response following peripheral nerve stimulation. The existence of this tract, however, has not been definitely established in primates.

Our observations in the monkey do not support these conclusions, but instead suggest that the SEP as it is conducted through the monkey cord is essentially dependent upon the dorsal columns. The almost complete loss of the SEP after dorsal column resection and its preservation in the monkeys with isolated dorsal columns supports this concept. The absence of significant response alterations in the isolated dorsal column preparations also does not support the proposal that supraspinal or spinal feedback mechanisms influence the character of the SEP recorded rostral to the responsible root entry zone.

Although one monkey with a dorsal column resection that was followed for 7 weeks showed a small degree of unsustained response recovery, the absence of such findings in another similar preparation and its occurrence at control latency suggests improved function in residual dorsal column elements rather than transmission over alternate pathways. In the cervical preparation, the absence of response alterations after bilateral dorsolateral column resection indicates that tracts in this location do not contribute to the SEP in the monkey. The corresponding response obliteration from both dorsal and ventral electrodes following cervical dorsal column resection offers additional support to the importance of the dorsal columns in SEP transmission. These findings also suggest that ventral cervical recordings represent volume-conducted potentials from a more dorsally positioned generator, rather than reflecting interneuronal activity or conduction in more ventrally located tracts.

Although the localization of primate spinal evoked activity to the dorsal columns may imply a restriction in the application of this examination, this conclusion is not fully warranted. The diagnostic value of the SEP in differentiating compressive from intrinsic myelopathies has been noted. Evidence has also been presented that indicates a correlation between response abnormalities and the severity of spinal cord trauma. Preliminary laboratory and clinical studies of SEP alterations at the site of spinal cord injury
Spinal evoked potentials in primates suggest that certain changes may be reliable diagnostic and prognostic indicators of the degree of the trauma. In this regard, future investigations will more clearly delineate the value of the SEP in the assessment of functional spinal cord integrity.

References


This research was supported, in part, by the Office of Naval Research Contract No. N00014-77-C-0749.

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