Intraoperative Detection of Spinal Cord Ischemia Using Somatosensory Cortical Evoked Potentials during Thoracic Aortic Occlusion

John G. Coles, M.D., Gregory J. Wilson, M.D., Anders F. Sima, M.D., Petr Klement, D.V.M., and Gordon A. Tait, Ph.D.

ABSTRACT Paraplegia remains a devastating and unpredictable complication of surgical procedures requiring temporary occlusion of the thoracic aorta, interruption of important spinal radicular vessels, or both. Intraoperative monitoring of the physiological integrity of the spinal cord should permit the early detection of spinal cord ischemia, the judicious and timely institution of corrective measures, including bypass or shunting, and the preservation of important intercostal arteries in appropriate circumstances. A model of spinal cord ischemia was created by temporary proximal and distal occlusion of the canine thoracic aorta. Serial measurement of somatosensory cortical evoked potentials (SCEP) generated by peripheral nerve stimulation, reflecting the status of long-tract neural conduction, was used to monitor alterations in spinal cord function during ischemia. Twelve animals subjected to aortic occlusion demonstrated a characteristic time-related deterioration of the SCEP with virtual extinction of the signal at a mean interval (+ standard error of the mean) of 12.4 ± 1.5 minutes. Six animals in which reperfusion was established immediately following the loss of the SCEP (Group 1) demonstrated complete recovery without neurological sequelae, as assessed by clinical and histological criteria. In 6 animals (Group 2), the period of aortic occlusion was extended for an additional 15 minutes following loss of the SCEP (27.3 ± 2.3 minutes); postoperatively, 4 of 6 animals sustained major neurological lesions characterized by spastic paraplegia and histological evidence of spinal cord infarction (Group 1 versus Group 2, p < 0.05).

We conclude that distinctive alterations in the SCEP are indicative of reversible ischemic spinal cord dysfunction. On-line monitoring of spinal cord function using the technique of SCEP provides a rational basis for determining operative strategy during surgical procedures on the thoracic aorta.

Perioperative spinal cord infarction continues to occur with disturbing frequency following resection of thoracic aortic aneurysms. The reported incidence of paraplegia complicating the surgical repair of acute traumatic injury to the thoracic aorta ranges from 0 to 23% [1–6]. Moreover, ischemic spinal cord injury remains a major hazard following any procedure involving temporary aortic occlusion or the interruption of important radicular vessels, or both [7, 8].

The intraoperative recognition of spinal cord ischemia during periods of aortic occlusion would identify the need for specific technical adjuncts designed to circumvent the development of irreversible neurological injury. The technique of measuring the cortical evoked response generated by peripheral nerve stimulation using signal enhancement techniques has been successfully applied clinically as a means of monitoring the functional integrity of the spinal cord during orthopedic procedures involving mechanical distraction of the spine. In the present study, we investigated the concept that measurement of the somatosensory cortical evoked potential (SCEP), reflecting the fidelity of neural transmission in the spinal cord, could be exploited as a means of detecting ischemic spinal cord dysfunction during periods of aortic occlusion.

With regard to the clinical utility of evoked response monitoring in the context of surgical procedures on the thoracic aorta, it would be critically important to determine if distinctive alterations in this electrophysiological prop-
erty induced by spinal cord ischemia preceded the development of irreversible neurological injury. Under these circumstances, direct assessment of the functional integrity of the spinal cord provided by intraoperative SCEP monitoring should allow the opportunity for early detection and reversal of ischemic spinal cord injury during surgical procedures on the thoracic aorta.

Material and Methods

Experimental Preparation

Experiments were performed on 12 adult mongrel dogs (22 to 30 kg). Following induction with sodium pentobarbital (25 mg per kilogram of body weight) and endotracheal intubation, anesthesia was maintained with enflurane (0.75 to 1.0%). Under sterile operating conditions, a left sixth interspace skin incision with a double intercostal incision through the fourth and eighth intercostal spaces provided access to both the proximal and distal regions of the descending thoracic aorta.

The induction of spinal cord ischemia was accomplished by temporary occlusion of the proximal thoracic aorta, the left subclavian artery, and the distal thoracic aorta at the level of the diaphragmatic hiatus (Fig 1). This method of aortic occlusion creates a reduction in spinal cord blood flow which consistently results in spinal cord infarction if maintained for a 30-minute period at normothermia [9]. Heparin sulfate (1 mg/kg) was administered prior to aortic occlusion and was reversed with protamine sulfate (1 mg/kg) following release of the vascular clamps.

Recording of the SCEP

SCEPs were generated by electrical stimulation of the sciatic nerve and recorded with electroencephalographic (EEG) scalp electrodes positioned over the primary somesthetic projection of the contralateral hemisphere (Fig 2). Following exposure of the sciatic nerve in the left popliteal fossa, bipolar stimulation* was performed using two J-shaped electrodes applied directly around the nerve at an inter-polar distance of 1 cm. Repetitive stimuli (N = 100 to 150) using a 10 V square-wave stimulus of 5 msec duration at a frequency of 1.2 Hz elicited a consistent pattern of SCEPs.

The evoked electrical potentials were recorded with a single parasagittal vertex electrode referenced to the inion. The signal was led to a single-ended, ac-coupled EEG preamplifier,* which was interfaced with a computerized signal averager.† The latter unit further amplified and filtered the signal using a bandpass filter nominally set at 1 to 3,000 Hz prior to processing. The digitizing rate of the signal averager permitted acquisition of 256 data points during the poststimulus analysis period of 400 to 500 msec corresponding to a temporal resolution of 1.56 to 1.95 msec dwell time per point. A poststimulus analysis time of 400 to 500 msec allowed recording of both the short-latency (primary) and long-latency (secondary and tertiary) components of the cortical evoked response.

The signal averaging process permitted extraction of the low-level signal from the background EEG and random electrical noise by

*Grass Model 79 amplifier.
†Nicolet Model CA-1000 signal averager, Nicolet Biomedical Instruments, Madison, WI 53711.
summing repeated sweeps of data that were time-locked to the stimulus pulse. A trigger signal from the pulse generator, initiated with each pulse, synchronized acquisition of the SCEP by the averaging computer. The composite signal was permanently recorded from the oscilloscopic display of the signal averager by means of a Polaroid camera. The peak-to-peak amplitude and latency of the primary and secondary components of the evoked response were measured with a calibrated cursor on the computer oscilloscope or directly from the photographed recording.

**Experimental Protocol**

Superimposition of two independently collected averages confirmed the integrity of the SCEP prior to aortic occlusion in each experiment. Measurement of the SCEP was repeated at 3-minute intervals during the period of aortic occlusion beginning 1 minute following the onset of occlusion, and at 5, 15, and 30 minutes following release of the clamps (reperfusion). Approximately 2 to 2.5 minutes, measured from the start of each time interval, were required to generate each summated recording.

The duration of aortic occlusion was determined in each experiment by the results from on-line recording of the SCEP. In Group 1 (6 animals), aortic occlusion was maintained until substantial attenuation was evident in both the primary and secondary components of the evoked response, after which reperfusion was immediately established. For purposes of analysis, a 50% or greater reduction in the peak-to-peak amplitude of the primary or secondary component of the evoked response was considered indicative of substantial attenuation (or loss) of the corresponding signal. In Group 2 (6 animals), the period of aortic occlusion was extended for an additional 15 minutes following 50% or greater attenuation of the SCEP.

Following removal of the vascular clamps and completion of the SCEP measurements, the chest was closed without postoperative tube drainage. All animals were recovered for assessment of functional neurological recovery and eventual histological examination of the spinal cord. The status of neurological function, determined at 24 hours and 7 days postoperatively, was designated according to Tarlov's [10] criteria for grading the recovery of hind limb motor function: 0 = no voluntary movement; 1 = perceptible movement of joints; 2 = good movements at joints but inability to stand; 3 = ability to stand and walk; and 4 = complete recovery. Sensory testing involving the response to painful stimuli presented to the hind limb was performed at the same postoperative time intervals. All animals were killed 7 days postoperatively, and the thoracic, lumbar, and sacral segments of the spinal cords, including the cauda equina, were explanted. The specimens were sectioned at 2 to 4 cm intervals, prepared for light microscopy, and examined by one of us (A.F.S.), a neuropathologist, without knowledge of the group assignment.

**Statistical Analysis**

The Student t test for paired data was used in computing the p value for comparison of the ischemic intervals at which loss of the primary and secondary components of the SCEP occurred. Fisher's exact test was used to detect significant differences in proportions with respect to outcomes between the two groups. The results of continuous observations are expressed as the mean ± standard error of the mean (SEM).

**Results**

Figure 3 depicts a typical preocclusion tracing of the SCEP. The characteristic features of the
SCEP consist of an early positive response (SCEP<sub>1</sub>; peak latency = 18.5 ± 1.0 msec), followed by a secondary positive response (SCEP<sub>2</sub>; peak latency = 79.1 ± 8.0 msec) of greater amplitude and duration and a series of long-latency tertiary waves of variable configuration.

Following the induction of spinal cord ischemia, a progressive time-related attenuation of the evoked response was observed in all experiments (Fig 4). Substantial (>50%) diminution in the amplitude of the SCEP<sub>1</sub> occurred after 4.0 ± 1.2 minutes of ischemia and preceded a similar reduction in amplitude of the SCEP<sub>2</sub>, which occurred at 12.6 ± 1.6 minutes (p < 0.005). Thus, loss of the early component of the evoked response, SCEP<sub>1</sub>, was the most sensitive indicator of ischemic spinal cord dysfunction.

Following substantial loss of both the SCEP<sub>1</sub> and SCEP<sub>2</sub> components of the evoked response, reperfusion was established at 12.4 ± 1.5 minutes in Group 1 animals, whereas the ischemic interval was extended for an additional 15-minute period to 27.3 ± 2.3 minutes in Group 2 animals. Group 1 animals uniformly recovered, without clinical evidence of neurological injury as assessed at 24 hours and 7 days postoperatively. In contrast, 4 of 6 Group 2 animals sustained a significant perioperative motor lesion (Group 1 versus Group 2, p < 0.05 by Fischer's exact test). Three of the 4 affected animals demonstrated a complete spastic paraplegia, evident at 24 hours with no improvement at 7 days. The other affected animal demonstrated only grade 2 motor function (good movements at joints but inability to stand) at 24 hours, improving to grade 3 motor function (ability to stand and walk) at 7 days postoperatively.

Although the results of postoperative sen-
sory testing were difficult to quantify, painful stimuli presented to the hind limb evoked a normal withdrawal response in all 6 Group 1 animals as well as the 2 Group 2 animals without motor impairment. Furthermore, a positive response to painful stimuli also was elicited in 2 of 4 animals with complete motor lesions, implying a degree of dissociation in the extent of involvement of the motor and sensory pathways. The clinical findings were paralleled by the status of the SCEP, following 30 minutes of reperfusion, which showed substantial recovery (>50% of preocclusion amplitude) in 9 of 10 animals with preservation of sensory function.

The results of the histological evaluation substantiated the clinical findings. The spinal cords from the animals with complete motor lesions demonstrated areas of extensive infarction involving the gray matter in the distal lumbar and proximal sacral segments (Fig 5A). The corresponding white matter revealed more subtle changes consisting of limited demyelination and gliosis affecting principally the ventral and lateral columns. These histological findings sharply contrast with those of Group 1 and the 2 unaffected Group 2 animals, which were limited to a minimal degree of neuron loss and gliosis involving the central gray matter of the lumbosacral cord (Fig 5B).

Comment
The prevention of ischemic injury to the spinal cord during repair of lesions of the descending thoracic aorta remains a challenging surgical problem. Temporary occlusion of the thoracic aorta, in the absence of adequate collateral vessels or effective bypass, may compromise spinal cord blood flow indirectly as a result of a critical reduction in distal aortic perfusion. The risk of perioperative spinal cord infarction is increased by the necessity for concomitant resection or exclusion of spinal radicular vessels, irrespective of the adequacy of distal aortic perfusion. Furthermore, inability to localize the origin of important radicular vessels in individual patients precludes the use of a systematic operative strategy that will uniformly prevent a critical reduction in spinal cord perfusion during periods of aortic occlusion.

Intraoperative recognition and reversal of spinal cord ischemia has not been successfully accomplished during the performance of surgical procedures on the thoracic aorta. The results of the present study suggest that serial measurement of SCEPs, indicative of the status of conductivity in the neuraxis, could be exploited as a means of detecting ischemic spinal cord dysfunction during occlusion of the thoracic aorta. A characteristic time-related deterioration in the evoked response was observed following the induction of spinal cord ischemia, with virtual cessation of neural transmission...
within a 12-minute period. This finding is consonant with that of Kobrine and colleagues, who measured the evoked response in monkeys using direct dural recordings from the cervicomedullary region [11] and the somatosensory cortex [12]. These investigators noted the onset of electrical silence following 8 to 18 minutes of profound ischemia induced by controlled exsanguination to below the limits of circulatory autoregulation in the spinal cord.

The available evidence indicates that the earliest surface-positive potential (SCEP) in animals is generated by the ascending afferent volley in the lemnisco-thalamocortical pathways and the contralateral primary sensory cortex, and is analogous to the more complex short-latency cortical evoked response observed in recordings done in humans [13]. The precise neuroanatomical substrate of the secondary component (SCEP₂) and subsequent long-latency components of the animal (and human) evoked response, characterized by diffuse and symmetrical cortical radiation, remain to be completely delineated [14, 15].

In the present study, a consistent finding was the rapid loss of the earliest surface-positive potential (SCEP₁) following induction of spinal cord ischemia, which preceded eventual loss of the secondary and tertiary components of the evoked response. The reason for the more rapid loss of the initial component of the evoked response, which represents the earliest indication of ischemic spinal cord dysfunction, is unknown. Selective loss of the initial deflection of the cortical evoked response has been recorded in patients with documented vascular lesions involving the thalamus [16]. It may be speculated that altered spinal cord conduction during ischemia selectively increases the latency of the SCEP, which then becomes buried, as a result of temporal dispersion, in the more conspicuous secondary component of the evoked response.

Intraoperative monitoring of spinal cord function with SCEPs has been used successfully in the detection of injurious mechanical distraction of the spinal cord during the correction of scoliosis by Harrington instrumentation [17, 18], and during decompression and stabilization procedures following traumatic lesions of the thoracic spine [19]. Our results indicate that distinctive alterations in the SCEP are associated with ischemic dysfunction of the spinal cord occasioned by temporary occlusion of the thoracic aorta. Spinal cord ischemic injury of sufficient degree to result in abolition of the cortical evoked response, if promptly followed by restoration of spinal cord perfusion, was uniformly compatible with complete recovery of neurological function. Thus, the early recognition of spinal cord ischemia using on-line measurement of SCEP allows the opportunity for rational intervention with corrective measures designed to enhance spinal cord perfusion during surgical procedures on the thoracic aorta.

In this context, the development of characteristic changes in the SCEP following cross-clamping of the thoracic aorta would indicate the need for adjunctive measures, such as bypass or a shunt, to improve perfusion distal to the cross-clamped aortic segment and, indirectly, to the spinal cord. Recovery of the SCEP following this intervention would indicate that the intended procedure could be completed without the risk of perioperative spinal cord infarction. Conversely, failure to recover the normal pattern of the SCEP would constitute strong circumstantial evidence that spinal cord blood flow is inadequate because an important spinal radicular vessel, typically the arteria radicularis magna [20, 21], has been excluded from systemic perfusion as a result of the position of the vascular clamps. Given this exigency, and lacking specific information relating to the level of origin of the arteria radicularis magna, reimplantation of a segment of posterior aortic wall from which several intercostal arteries originate would be imperative in order to prevent irreversible spinal cord injury. Available experimental evidence suggests that the efficacy of intercostal reimplantation would be enhanced by the induction of even modest levels of systemic hypothermia [12, 22-24], since the time required to complete such a procedure may exceed the tolerable period of normothermic ischemia of the corresponding segment of the spinal cord [25].
Alternatively, evidence of spinal cord ischemia despite effective distal aortic perfusion may justify abandonment of the intended procedure, given the risks and uncertainty attending random reimplantation of intercostal vessels. Angiographic demonstration of the arteria radicularis magna by selective catheterization [26] could then be performed electively as an interval procedure prior to definitive repair of the lesion at a second operation. Under these circumstances, precise knowledge of the level of origin of major spinal arteries would allow reimplantation or preservation of the appropriate intercostal vessels, thus minimizing the risk of perioperative spinal cord infarction.

Theoretically, an ischemic lesion of the spinal cord could selectively involve the motor neurons in the gray matter without apparent perturbation in the SCEP, which is principally mediated through posterior column pathways located in the white matter [27]. In the present study, this dissociative type of injury was evident in 2 animals subjected to extended aortic occlusion following loss of the evoked response; they sustained major motor lesions in association with preservation of sensory function and substantial recovery of the reperfusion evoked response. This finding suggests that a reduction in spinal cord blood flow of sufficient severity to produce isolated infarction of motor pathways is associated with at least temporary ischemic dysfunction of the somatosensory pathways and corresponding abnormalities in the evoked response.

These results demonstrate that the characteristics of the SCEP can be profitably analyzed to provide useful information regarding the functional status of the spinal somatosensory system under conditions of aortic occlusion. We conclude that the concept of spinal cord monitoring may assume an important role in the prevention of ischemic injury to the spinal cord during surgical procedures on the thoracic aorta.

References

Discussion

Dr. Joseph N. Cunningham (New York, NY): I congratulate Dr. Coles and his group on a fine study. At New York University we have performed laboratory experimentation very similar to that which Dr. Coles and his group have so convincingly presented today. On the basis of our findings we have routinely applied these techniques directly in the operating room for the past several weeks for all surgery performed on the thoracic aorta.

We now have accumulated 6 consecutive patients who underwent large resections of descending thoracic or thoracoabdominal aneurysms. In 5 of them, somatosensory evoked potentials began to disappear within 3 minutes following application of a proximal cross-clamp. All potentials were completely gone at 9 minutes. This also occurred in the sixth patient, but in the first 5, reversal of the somatosensory evoked potentials could be obtained by use of a shunt or femorofemoral bypass. In the sixth patient, a critical intercostal artery was reimplanted, resulting in immediate return of the somatosensory evoked potentials to normal.

We believe that both from the standpoint of the patient’s welfare with regard to prevention of paraplegia, and with respect to the obvious medicolegal implications, the time has come for continuous monitoring of evoked potentials in the operating room during aortic cross-clamping to become part of routine hospital policy.

Dr. Coles: I was very interested in your comments, Dr. Cunningham. At present we have no clinical experience with this technique but would like to congratulate you for demonstrating the potential clinical utility of spinal cord monitoring. We hope that our results have provided some experimental validation for the concept of spinal cord monitoring during surgical procedures on the thoracic aorta.