Spinal cord ischemia in thoracoabdominal aneurysm surgery: monitoring and conditioning the spinal cord

de Haan, P.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Spinal cord monitoring with Myogenic Motor Evoked Potentials: Early detection of spinal cord ischemia as an integral part of spinal cord protective strategies during thoracoabdominal aneurysm surgery.

Peter de Haan, Cor J. Kalkman, Michael J.H.M. Jacobs.
Abstract

Background  During thoracoabdominal aortic aneurysms (TAAA) surgery, spinal cord ischemia can result in lower limb neurological deficits. Application and adjustment of protective strategies can be guided by techniques that monitor spinal cord function. However, spinal cord monitoring can only improve outcome if ischemia is detected sufficiently rapid (before irreversible damage has occurred) and if function of the ischemia sensitive motoneuronal system is reflected.

Motor evoked potentials  
Motor evoked potentials (MEPs) are a relatively new technique to monitor spinal cord function. Several modalities to elicit and record MEPs are discussed. Motor responses to transcranial or spinal cord stimulation can be recorded from either the epidural space, the peripheral nerve or the muscle (myogenic MEPs). Myogenic MEPs to transcranial stimulation are entirely specific for motor tract conduction, and monitor the vulnerable spinal motoneuronal system. Using this modality ischemia is detected within minutes. In contrast, MEPs recorded from the epidural space reflect axonal conduction, which is relative ischemia resistant. When myogenic and peripheral nerve responses are recorded following spinal cord stimulation, antidromic sensory contamination can not be excluded. Responses to spinal cord stimulation may therefore not be entirely specific for conduction in the motoneuronal system.

Clinical application  
Recent improvements in the technique to elicit myogenic transcranial MEPs include multi-pulse stimulation paradigms and the use of a circumferential cathode. This results in robust and reproducible signals, which are less susceptible to anesthetic interference and allow the use of a constant level of neuromuscular blockade. Using a strategy aimed at maintaining and restoring spinal cord blood supply (distal aortic perfusion, sequential aortic clamping, and segmental artery reattachment), early detection of ischemia with myogenic transcranial MEPs allows protective measures to be applied and adjusted immediately, i.e., reattaching or safely ligating intercostal arteries, or guidance of proximal and distal aortic pressure management.

Conclusion  
In conclusion, during TAAA surgery monitoring myogenic MEPs after transcranial stimulation has become clinically feasible. The fast detection of spinal cord ischemia allows timely guidance of protective measures.
Introduction

Efforts to decrease the incidence of neurological complications after TAAA surgery have been hampered by the lack of a rapidly responsive monitor to assess the adequacy of spinal cord blood supply. With a monitoring technique that allows a short interval between onset and detection of spinal cord ischemia, protective strategies can be applied and adjusted before ischemia has produced irreversible neuronal damage.

Adjuncts to prevent a paraplegia aim to preserve spinal cord perfusion and/or increase spinal cord ischemic tolerance. Retrograde aortic perfusion using atrio-femoral bypass appeared to be protective, especially if sequential aortic clamping was performed. It may also be beneficial to use cerebro spinal fluid (CSF) drainage to prevent a rise in CSF pressure, and a subsequent decrease in perfusion pressure, following aortic cross-clamping. In addition, permanent restoration of spinal cord blood supply is necessary to prevent a paraplegia. This requires revascularisation of segmental arteries. If a period of spinal cord ischemia cannot be avoided, for example if the critical segmental arteries are located between the aortic clamps, ischemic tolerance can be increased by inducing hypothermia.

Somatosensory evoked potentials (SSEPs) are widely used for spinal cord function monitoring during operations that pose a risk for a postoperative paraplegia. In the clinical experience of Cunningham and Laschinger, SSEPs were used to assess adequacy of distal aortic perfusion, and to identify vessels critical to spinal cord blood supply. The major drawback of SSEP monitoring in the clinical setting is the occurrence of false negative results (postoperative paraplegia despite unchanged intraoperative SSEPs). After experimental aortic occlusion in dogs predominant gray matter spinal cord necrosis was observed. The spinal motoneuronal system is located in the anterior horn gray matter and is supplied by the anterior spinal artery. SSEPs monitor conduction in the ascending sensory tracts located in the dorsal part of the spinal cord and supplied by the posterior spinal arteries. Therefore, SSEPs do not reflect motor function and motor tract blood supply, and ischemia limited to the motor tracts or anterior horn may go undetected. In addition, there is a relatively long delay (7 to 30 minutes) between occurrence of ischemia and complete disappearance of SSEPs. Another disadvantage of SSEPs is the low specificity. Crawford reported a false positive rate of 67%, although distal aortic perfusion may improve accuracy.
Modalities to monitor motor evoked potentials

Motor evoked potentials (MEPs) can be elicited by electrical or magnetical transcranial stimulation (tc-MEP). Transcranial stimulation has not yet been FDA approved. Another option to elicited MEPS is supplied by the electrical stimulation of descending motor tracts at the level of the cervical or high thoracic spinal cord with an epidural wire electrode or needle electrodes. Responses can be recorded from the epidural space over the lower lumbar spinal cord (epidural MEPs), the peripheral nerve (neurogenic MEPs) or from limb muscles as compound muscle action potentials (CMAP) using standard EMG techniques (myogenic MEPs) (figure 1). Magnetical transcranial stimulation has the disadvantage over
electrical transcranial stimulation that continuous access to the head is required and small displacements of the magnet result in considerable amplitude variability.

**Myogenic MEPs** Svensson described myogenic MEPs after spinal cord stimulation to be highly sensitive in predicting paraplegia in the pig.7 The limitation of this technique is that invasive electrode placement is required. In addition, the muscle response might be partly elicited by antidromic sensory conduction. As a consequence, this modality is not entirely specific for the spinal cord motoneuronal system. Our Group opted to use recording of myogenic responses after electrical transcranial stimulation (myogenic tc-MEPs). Recording of myogenic tc-MEPs is exclusively specific for motor tract conduction, including the ischemia sensitive anterior horn motor neurons. This modality requires no invasive electrode placement. Intraoperative use of this technique is now clinically feasible and can detect spinal cord ischemia within minutes. The myogenic tc-MEPs will be discussed in the next paragraph.

**Epidural MEPs** The epidural recording of MEPs after electrical transcranial stimulation from the lower lumbar spinal cord (epidural tc-MEPs) is characterized by an initial direct (D-) wave followed by a series of indirect waves. The D-wave is the result of direct activation of pyramidal cells in the motor cortex. The D-wave is relative resistant to anesthetics. Muscle relaxant do not interfere with epidural tc-MEP recording. The main disadvantage of the recording of epidural tc-MEPs is that only conduction in the cortico-spinal tracts is monitored and no information is provided on function of the anterior horn gray matter. Axonal conduction is relative resistant to ischemia.3 Consecutively, it was confirmed that epidural tc-MEPs disappear slow following interruption of spinal cord blood flow.5,10 In experimental aortic occlusion in the rabbit, myogenic responses after transcranial stimulation disappeared within 2 minutes, whereas the epidural recordings required 11 minutes to decrease 50% in amplitude.11 In two studies describing a model of spinal cord ischemia in the dog, epidural responses after transcranial stimulation disappeared in 21 ± 6.6 minutes and 24 ± 4 minutes respectively.5,10 The observed time between onset and detection of spinal cord ischemia with epidural tc-MEPs is be too long to allow prompt interventions. Moreover, epidural tc-MEPs do not provide information about the functional status of the central gray matter. In accordance, epidural tc-MEPs had a low sensitivity (46%) in predicting neurologic deficits after temporary aortic cross-clamping in the dog.10 When epidural MEPs are elicited after spinal cord stimulation at a cervical or high thoracic level (in the literature also described as spinal cord evoked potential (SCEP) or spinal evoked potential) there is no anesthetic interference. However, using this technique the motor tracts are not solely monitored because both ascending and descending tracts are activated. Therefore the spinal response consists of a mixed sensory/motor signal. Conflicting results
with this technique were described. Ischemic spinal cord dysfunction could be detected in 11 to 17 minutes after aortic occlusion in dogs.\(^\text{12}\) In contrast, after progressive ligation of intercostal arteries (including the Adamkiewicz artery) in the dog, epidural MEPs remained unchanged.\(^\text{13}\)

**Neurogenic MEPs** The peripheral nerve response (recorded from the sciatic nerve) to spinal cord stimulation is small (about one μV). Therefore it is necessary to average at least hundred responses in order to obtain a reproducible signal. Although the neurogenic MEP after spinal cord stimulation is relative insensitive to anesthetic interference, this modality is not entirely specific for the motor tracts, because it contains components produced by antidromic conduction in sensory tracts. Accordingly, deficits confined to the motor tracts might not always be detected using neurogenic MEPs. Monitoring neurogenic MEPs after transcranial stimulation is clinically not feasible because of the large number of transcranial stimuli that has to be averaged.

### Myogenic MEPs after transcranial electrical stimulation

Application of myogenic tc-MEPs during TAA surgery has been limited to few clinical centres. The use of this modality was hampered by the fact that many commonly used anesthetics, especially the volatile agents, readily depress myogenic responses.\(^\text{14}\) Anesthetics not only decrease the excitability of cortical motor neurons, but also depress spinal cord motor neuron excitability. Complete neuromuscular blockade is not compatible with myogenic tc-MEP monitoring. If neuromuscular blockers are avoided, patient movement is disconcerting. Another drawback of myogenic tc-MEPs mentioned in initial reports was a high response variability. Many of these problems were recently overcome.

Careful planning and adjustment of the anesthetic technique is necessary. Etomidate, ketamine and opioids hardly depressed myogenic tc-MEP amplitudes.\(^\text{15,16}\) Since tc-MEP amplitude was also influenced by the level of neuromuscular blockade, a stable level of neuromuscular blockade should be maintained. Using a closed-loop vecuronium infusion, we were able to maintain the level of neuromuscular blockade within a narrow range and thus minimize the influence of fluctuations in relaxation level on the variability of the myogenic tc-MEP signal.\(^\text{15,17}\)

Amplitude variability of myogenic tc-MEPs to single transcranial stimulation can be overcome by using multi-pulse transcranial stimulation paradigms. If multiple stimuli are applied with an inter stimulus interval of 2-3 ms, temporal summation of the excitatory postsynaptic potential substantially amplifies myogenic responses and reduces variability.\(^\text{18}\) The use of a circumferential cathode of interconnected EEG electrodes also improves stimulus efficiency.
and increases response amplitude. With the double pulse stimulation paradigm, a circumferential cathode and a continuous level of neuromuscular blockade, the median amplitude recorded from the tibial anterior muscle was 600 μV with a coefficient of variation of 26%. This level of reproducibility allows continuous monitoring of anterior horn function. Multi-pulse transcranial stimulators providing a train of up to ten successive stimuli are now commercially available.

Evoked potential techniques that rely on stimulation and recording from nerves and muscles in the leg lose their predictive value when lower limb ischemia during TAAA surgery occurs, especially when simple aortic cross-clamping without retrograde perfusion is used. Ischemia of the peripheral nerve and muscle will result in loss of myogenic motor responses (and SSEPs) in approximately 30 min after discontinuation of limb perfusion. When retrograde aortic perfusion is employed, at least one leg will be normally perfused, but peripheral ischemia may occur in the leg used for femoral artery cannulation. This limitation could be overcome and reliability of the myogenic tc-MEPs was increased, by inserting a second cannula to perfuse the periphery of the femoral artery used for retrograde bypass.

Figure 2. In a patient with a type II thoraco abdominal aneurysm a technical failure caused temporary interruption of the atrio-femoral bypass flow. The amplitude of the trancranial myogenic motor evoked potentials (myogenic tc-MEPs) of the left and right anterior tibial muscle, the systemic blood pressure and the pressure distal to the clamp are shown versus time. Within minutes after retrograde perfusion pressure decreased to zero, myogenic tc-MEPs demonstrated ischemic changes. Immediately after restoration of bypass flow the responses returned to baseline values.
Clinical application

In our initial clinical experience, myogenic tc-MEPs appeared both safe and accurate. No false positive or false negative monitoring results were observed. Myogenic tc-MEPs were extremely sensitive to spinal cord ischemia, and an interruption of spinal cord blood supply ischemia was detected within minutes (Figure 2). The rapid assessment of the adequacy of spinal cord blood flow with myogenic tc-MEPs offers several advantages in a surgical approach that includes spinal cord protective measures. Retrograde aortic perfusion and sequential aortic clamping allow preservation of spinal cord perfusion while the proximal anastomosis of the graft is being performed. Retrograde aortic perfusion preserved spinal cord integrity if distal aortic pressures were maintained above 60 mmHg. However, in our experience maintaining distal pressure or mean arterial pressure (MAP) above 60 mmHg was not always sufficient. In some patients distal pressure had to be increased above 70 mmHg and MAP had to be maintained above 80 mmHg in order to preserve myogenic tc-MEPs. Therefore pressures necessary to preserve sufficient spinal cord blood flow may vary between patients. Myogenic tc-MEPs proved efficient to determine the pressures required to preserve spinal cord perfusion, and immediate feedback was provided if pressures were increased. Postoperatively in the ICU, MAP was maintained above the pressure that preserved myogenic MEPs during aortic replacement.

If spinal cord ischemia is detected after clamping an aortic segment, critical segmental arteries probably originate from the excluded segment and should be included in the graft in order to permanently restore spinal cord blood supply. We described that an absence of myogenic responses always indicated a paraplegia. Therefore, if myogenic responses disappear during exclusion of an aortic segment and segmental arteries are not readily found, a thorough search is warranted for intercostal or lumbar arteries including an endarterectomy of the aorta.

Another possible use of the myogenic tc-MEPs is the selective application of techniques available to increase ischemic tolerance. The fast detection of ischemia allows a short waiting period after clamping an aortic segment, if ischemia is detected, critical segmental arteries probably arise from that part of the aorta. Clamps can be released and regional or systemic hypothermia can be induced prior to aortic replacement in order to increase ischemic tolerance of the anterior horn motoneuronal system.

In conclusion, monitoring myogenic MEPs after transcranial electrical stimulation is effective in detecting spinal cord ischemia. This technique is sufficiently rapid to allow timely interventions aimed at correcting ischemic conditions and preserving spinal cord blood flow.
Monitoring spinal cord function with motor evoked potentials

References
