Hajime KUMAGAI*, Kazumasa ORIHASHI, Mitsuhiro ISAKA, Makoto HAMAISHI and Taijiro SUEDA

Department of Surgery, Division of Clinical Medical Science, Graduate School of Biomedical Sciences, Hiroshima University, Japan

ABSTRACT

To investigate the feasibility of a novel recording method for trans-intercostal evoked spinal cord potentials (Tic-ESCPs) and the properties of the waveforms, the potentials were recorded and analyzed in an animal model. In two beagle dogs, Tic-ESCPs were recorded at the left twelfth intercostal to fourth lumbar nerves following stimulation at the left eleventh intercostal nerve, either with or without the use of a muscle relaxant. The amplitude and latency of the Tic-ESCP waves were then measured and compared with those of conventional transcranial spinal motor evoked potentials (MEPs). Tic-ESCPs could be obtained at any nerve, with or without the use of a muscle relaxant. The Tic-ESCP waveform was clear and simple, consisting of a small positive (P1) wave and a subsequent large negative (N1) wave. As the site of recording moved farther from the stimulation site, the N1 amplitudes were reduced and the P1 latency was prolonged. Under muscle relaxation, the N1 amplitudes were reduced, and the P1 latencies were shorter. As compared with MEPs, Tic-ESCPs could be evoked by a weaker stimulus, the N1 amplitude was smaller, and the P1 latency was shorter. Tic-ESCP recording was feasible either with or without the use of a muscle relaxant. The Tic-ESCPs showed simple and clear waveforms with smaller stimulations. Therefore, Tic-ESCPs may be useful for intraoperative spinal cord monitoring.

Key words: Intercostal nerve stimulation, Evoked spinal cord potential monitoring, Thoracoabdominal region

Paraplegia resulting from spinal cord ischemia is one of the most important problems in thoracoabdominal aortic aneurysm (TAAA) surgeries. Electrophysiological diagnostic methods such as transcranial spinal motor evoked potentials (MEPs) and somatosensory evoked spinal cord potentials (SEPs) have been used for evaluating spinal cord function during TAAA surgeries^{1,6,11)}. MEPs are specific to the motor pathway, and MEP monitoring has been reported to be useful for reducing postoperative paraplegia^{3,9,10}. However, we have recognized drawbacks in MEP monitoring. For example, MEPs contain various components that arise from the pathway between the site of stimulation and the site of recording, thus making data analysis difficult, and the recording can be susceptible to various noises and artifacts. The placement of the electrode into the epidural space for MEP monitoring is also invasive, and may cause an epidural hematoma. The latter problem limits the use of MEP monitoring because an increased number of patients are under anticoagulant or anti-platelet therapy for coronary stents or valve prosthesis.

Recently, we have proposed the use of transintercostal evoked spinal cord potentials (Tic-ESCPs), in which the intercostal nerve is stimulated and an evoked potential is recorded at an intercostal or lumbar nerve inside the body, since these nerves are readily accessible by surgeons in the operative field. If Tic-ESCP monitoring is feasible, the placement of epidural electrodes is not necessary. Furthermore, the waveform is simple and specific to thoracoabdominal region, and thus the recording will be less susceptible to noises or artifacts.

As an initial step, this study was designed to: 1) confirm the feasibility of Tic-ESCP recordings; and 2) examine the properties of Tic-ESCP waveforms in an animal model.

^{*}Address for correspondence: Hajime Kumagai, MD

Department of Surgery, Division of Clinical Medical Science, Graduate School of Biomedical Sciences, Hiroshima University, 1–2–3 Kasumi, Minami-ku, Hiroshima 734–8551, Japan

MATERIALS AND METHODS

Animal Preparations

All animals received humane care in compliance with "Principles of Laboratory Animal Care" formulated by the Institute of Laboratory Animal Resources and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources and published by the National Institute of Health. The study protocol was approved by the Guiding Principles on Animal Experimentations in Research Facilities for Laboratory Animal Science, School of Medicine, Hiroshima University.

Anesthesia and Blood Pressure Monitoring

Two adult beagle dogs weighing 8.5 and 9.0 kg were studied. Anesthesia was induced with intramuscular injections of ketamine hydrochloride (0.3 ml/kg) and atropine sulfate (0.5 mg). Lactated solution was continuously infused Ringer's through a 20-gauge plastic cannula inserted into a right forelimb vein. After an intravenous injection of thiamylal sodium (15 mg/kg), endotracheal intubation was performed. General anesthesia was maintained with isoflurane carried by oxygen (2 liters/min) mixed with nitrous oxide (4 liters/min) using volume-controlled mechanical ventilation. The concentration of isoflurane was fixed at 1.5%during the monitoring. This concentration represented a good balance between monitoring and the depth of anesthesia. Ventilation was controlled according to blood gas analysis data collected at 37°C, and electrocardiograms were continuously monitored. The rectal temperature was kept at 37°C using a warm blanket.

The proximal blood pressure (PAP) was monitored at a right forelimb artery, and was maintained at approximately 85 mmHg by means of a pressure control system as previously reported⁵) by allowing the blood to circulate freely between the dog and a reservoir.

Measurements of Evoked Spinal Cord Potentials

On the right lateral decubitus position, a thoracotomy and a laparotomy were performed between the T10 and L5 vertebral levels. Tic-ESCPs were recorded from the left twelfth intercostal nerve to the fourth lumbar nerve after the left eleventh intercostal nerve was stimulated (Fig. 1). A hook type bipolar platinum electrode with a 7 mm interval was placed 3 cm from the left eleventh intercostal nerve root. The left eleventh intercostal nerve was then electrically stimulated (intensity, 1–13 mA; pulse duration, 0.1–0.5 msec; pulse rate, 4.0 Hz; single-pulse; and filter, 150 Hz-1.5 kHz). The Tic-ESCPs were averaged for a total of 50 impulses (without a muscle relaxant) and for 100 impulses (with a muscle relaxant) for each recording, using a Nicolet Viking Quest system (Nicolet



Fig. 1. Schema of the operative field This schema shows the operative field on a recording at the first lumbar nerve with stimulation at the eleventh intercostal nerve.

Biomedical, Inc., Madison, WI). The intensity of stimulation was determined as 1.3 times of the threshold for nerve stimulation. The Tic-ESCPs were recorded by a unipolar electrode. A needle type platinum electrode was placed under the skin in the thigh as a reference electrode. The Tic-ESCPs were first recorded without any muscle relaxant, and then again after 0.5 mg of pancronium bromide was given. All recorded data were saved on a hard-disk for off-line analysis.

In order to compare the Tic-ESCPs with the MEPs, the MEP data (n=6) obtained from a previous study⁵⁾ were used. Stimuli (intensity, 100 mA; pulse duration, 0.5 ms; pulse rate, 4.0 Hz; single-pulse; filter, 20 Hz–1.5 kHz) were applied to bilateral temporal scalp regions using two needle type electrodes, and the evoked potentials were recorded with a linear electrode (unipolar) placed in the lumbar epidural space (L5) after a laminectomy. The MEPs were averaged for 50 impulses per recording under muscle relaxation using the same system as the Tic-ESCPs.

RESULTS

Tic-ESCP Waveforms

Figure 2 shows the Tic-ESCPs recorded between T12 and L4 without and with the use of a muscle relaxant. The Tic-ESCP waveform consisted of a small positive (P1) and subsequent large negative (N1) wave in both conditions. Each wave and latency was defined as shown in Fig. 3 and upward deflection in the Tic-ESCP waveform was defined as negative in this study. The waveforms were more clearly recorded from the adjacent intercostal nerve than from distant lumbar nerves. In the condition without a muscle relaxant, the small P1 wave was unclear because the



Fig. 2. Changes in trans-intercostal evoked spinal cord potentials

This shows the waveforms recorded at the twelfth intercostal nerve and, the first, second, third and fourth lumbar nerves with stimulation at the eleventh intercostal nerve. Waveforms are recorded by a unipolar electrode. Waveforms on the left side are recorded without the use of a muscle relaxant and those on the right side with the use of a muscle relaxant. The N1 amplitudes reduce progressively according to the distance from the stimulation site.



Fig. 3. Evaluation of Tic-ESCP waveform Tic-ESCP waveform is measured by the N1 amplitude and the P1 and N1 latency. Upward deflection in the waveform is deflection as negative.

N1 wave was large. The amplitude of Tic-ESCPs was measured as that of the N1 wave because the baseline of the Tic-ESCP waveform was stable and the waveform had little artifact by stimulation. The latency of Tic-ESCPs was measured as the P1 and N1 latency.

Tic-ESCP Amplitudes and Latencies

Without the use of a muscle relaxant, the stimulus intensity was 0.1–1.0 mA and duration was 0.1–0.2 msec. After a muscle relaxant was given, the stimulus intensity and duration varied according to the distance between the stimulating and recording sites. The intensity was 1.0-1.4 mA and the duration was 0.02-0.1 msec at a distance of one vertebral body, but was 4.7-13.0 mA and 0.1–0.5 msec at a distance of two to five vertebral bodies. Figure 4 shows the changes in the N1 amplitude and the P1 latency. The N1 amplitude was reduced, and the P1 latency was prolonged progressively according to the distance from the stimulating site. The N1 amplitudes were much smaller with the use of a muscle relaxant as compared with those without the use of a muscle relaxant. The P1 latencies with the use of a muscle relaxant were also shorter than those without the use of a muscle relaxant.

The stimulus intensity and duration of MEPs were about 7–20 times and 1–5 times, respectively, of those of the Tic-ESCPs with the use of muscle relaxant. The averaged N1 amplitude of the MEPs at L4 was $12.1 \pm 5.3 \mu$ V. The averaged N1 amplitudes of the Tic-ESCPs at L4 without and with the use of a muscle relaxant were about 2.5 fold and two thirds of those of the corresponding MEP values, respectively. The averaged P1 latency of the MEPs was 4.08 ± 0.40 msec; the latency of the MEPs was longer than that of the Tic-ESCPs.



Changes in P1 Latencies



Fig. 4. Changes in N1 amplitudes and P1 latencies These show N1 amplitudes (upper) and P1 latencies (lower) on each level between T12 and L4 with bipolar and unipolar recording. N1 amplitudes and P1 latencies are recorded without (-) and with (+) the use of a muscle relaxant.

DISCUSSION

This study has demonstrated that: 1) Tic-ESCP recording specific to the thoracoabdominal region is feasible in dogs; 2) the waveform is simple and consists of a small P1 wave followed by a large N1 wave; 3) monitoring can be performed with or without the use of a muscle relaxant; and 4) it requires a smaller stimulus than MEP recording.

This is the first report of topical ESCPs recorded in the operative field. There have been reports of somatosensory evoked potentials as ascending spinal cord potentials, recorded from the cortex and spinal cord following intercostal stimulation in orthopedic surgery $^{2,4)}$. In these methods, the sites of stimulation and recording were the body surface or epidural space. In Tic-ESCP monitoring, the nerves were readily accessible in the operative field, and the electrodes could be directly attached to the nerves. This monitoring might be used for the segmental diagnosis of motor pathway lesions. The waveforms were simple and clear, consisting of a small P1 and a large N1 wave, probably due to the short length of the pathway.

There are several reports that suggest a specific conduction pathway for Tic-ESCPs. Ogura et al reported MEPs recorded from the bilateral paravertebral muscles and tibialis anterior muscles using cervical skin surface stimulation⁷. They



Fig. 5. Schema of conduction pathway of intercostal nerve stimulation

This shows the speculated electrical conduction pathway. Activation in the intercostal nerve is conducted to the posterior funiculus of the spinal cord, transmitted to the anterior funiculus via interneurons, descends along the motor pathway, is conducted to the lower anterior funiculus, then is transmitted to the α -motor neuron with anterior horn cells to the lumbar nerve.

demonstrated that the latency of the amplitude gradually prolonged as the recording site moved further from the stimulation site. Okuma et al reported that anti-phase cervical spinal cord potentials were recorded from the anterior and posterior funiculi by stimulating the median nerve or spinal cord⁸⁾ suggesting the presence of conduction via interneurons between the posterior and anterior funiculi. Figure 5 shows a schematic of the most probable conduction pathway in Tic-ESCP monitoring. Activation in the intercostal nerve is conducted to the posterior funiculus of the spinal cord, transmitted to the anterior funiculus via interneurons, descends along the motor pathway, is then conducted to the lower anterior funiculus, and is transmitted to the α -motor neuron with the anterior horn cells to the lumbar nerve. Thus, Tic-ESCPs reflect the conduction along the motor pathway in the thoracoabdominal region between the two electrodes.

Conventional MEPs have been used because the motor pathway can be evaluated and muscle relaxants can be used during monitoring. The MEPs can be monitored without muscle relaxants as well. The MEPs appear to be less affected by muscle relaxants than Tic-ESCPs. Tic-ESCPs can be susceptible to direct conduction of stimulation via the muscle because the distance between the stimulating and recording sites is short. Thus use of muscle relaxants is advised. However, MEP monitoring is not feasible in emergency operations because it necessitates the placement of an electrode into the epidural space which may be potentially complicated with an epidural hematoma. It is also susceptible to electrical noises, and the waveforms are composed of multiple waves because of the long conduction pathway. Tic-ESCP monitoring has several advantages. First, the waveforms of the Tic-ESCPs are simple and may be less susceptible to external noise because they reflect activation over a short segment of the spinal cord. Second, preoperative preparations such as the epidural placement of an electrode are not necessary for Tic-ESCPs. It is available not only in emergency cases, but also in patients undergoing anticoagulant or anti-platelet therapy. Third, muscle relaxants can be used and the neuronal potentials can be evaluated without muscle interference. Although the amplitude is small, the waveform is simple and clear, thus facilitating wave analysis. Fourth, a smaller stimulus is needed because of the direct stimulation onto the nerve in Tic-ESCPs.

Although the placement of the electrode is easy, it necessitates the exposure of the intercostal nerve, and may potentially damage the vessels and nerves. We observed that the amplitude varied according to the contact of the electrode to the nerves. The nerves can also be damaged by manipulation, cooling and drying. Thus, careful manipulations are needed while setting the electrode and during monitoring. A large aortic aneurysm may interfere with the placement of an electrode close to the nerve root, and an upper intercostal nerve may be needed. In order to be applicable in a clinical setting, a new electrode must be devised to enhance the stability and safety of the monitoring protocol.

CONCLUSION

Tic-ESCPs may be useful for spinal cord monitoring, and provide simple and clear waveforms with smaller stimuli. The development of better electrodes, and the changes of the ESCPs under spinal ischemia need to be studied.

ACKNOWLEDGEMENTS

This work was supported by a Grant-in aid from the Japanese Ministry of Education, Science and Culture. The authors thank Mr. Kazunori Iwase for his excellent technical assistance.

> (Received January 16, 2006) (Accepted February 16, 2006)

REFERENCES

- Cunningham, J.N. Jr., Laschinger, J.C., Merkin, H.A., Nathan, I.M., Colvin, S., Ransohoff, J. and Spencer, F.C. 1982. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience. Ann. Surg. 196: 285–296.
- Dreyfuss, P., Dumitru, D. and Prewitt-Buchanan, L. 1993. Intercostal somatosensoryevoked potentials: a new technique. Am. J. Phys. Med. Rehabil. 72: 144–150.
- 3. Jacobs, M.J., Meylaerts, S.A., de Haan, P., de Mol, B.A. and Kalkman, C.J. 1999. Strategies to prevent neurologic deficit based on motor-evoked potentials in type I and II thoracoabdominal aortic

aneurysm repair. J. Vasc. Surg. 29: 48-57.

- Kaneko, K., Kawai, S., Huchigami, Y., Itoh, T. and Hashida, T. 1993. Experimental and clinical studies on spinal cord potential evoked by stimulation of intercostal nerve. Sekitsuisekizui 6: 293–298.
- Kumagai, H., Sugawara, Y., Isaka, M., Okada, K., Orihashi, K. and Sueda, T. 2005. Cold saline injection attenuates motor-evoked potential in the spinal cord by cortical electrical stimulation in the dog. Hiroshima J. Med. Sci. 54: 77–82.
- Meylaerts, S.A., Jacobs, M.J., van Iterson, V., De Haan, P. and Kalkman, C.J. 1999. Comparison of transcranial motor evoked potentials and somatosensory evoked potentials during thoracoabdominal aortic aneurysm repair. Ann. Surg. 230: 742–749.
- Ogura, T., Takeshita, H., Hase, H., Hayashida, T., Mori, M. and Kubo, T. 2003. Evaluation of descending spinal cord tracts in patients with thoracic cord lesions using motor evoked potentials recorded from the paravertebral and lower limb muscles. J. Spinal Disord & Techniques. 16: 163–170.
- Okuma, T. 1987. Level diagnosis of cervical myelopathy using evoked spinal cord action potentials —Clinical and experimental studies—. J. Jpn. Orthop. Assoc. 61: 477–489.
- Sueda, T., Morita, S., Okada, K., Orihashi, K., Shikata, H. and Matsuura, Y. 2000. Selective intercostal arterial perfusion during thoracoabdominal aortic aneurysm surgery. Ann. Thorac. Surg. 70: 44–47.
- Sugawara, Y., Kumagai, H. and Sueda, T. 2005. A novel canine spinal cord ischemia model with reproducible neurologic outcomes. Surgery Today 35: 649–652.
- Svensson, L.G., Patel, V., Robinson, M.F., Ueda, T., Roehm, J.O. Jr. and Crawford, E.S. 1991. Influence of preservation or perfusion of intraoperatively identified spinal cord blood supply on spinal motor evoked potentials and paraplegia after aortic surgery. J. Vasc. Surg. 13: 355–365.