Monitoring of a middle latency auditory evoked potential index during postresuscitation care with induced therapeutic hypothermia

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ABSTRACT
A 48-year-old man suddenly suffered a cardiac arrest at the supermarket and underwent bystander cardiopulmonary resuscitation. During transportation to our emergency center, ventricular fibrillation occurred and defibrillation was successful. Restoration of spontaneous circulation (ROSC) with sinus rhythm occurred 12 min after sudden cardiac arrest. On arrival at the emergency center 2 min after ROSC, middle latency auditory evoked potential index (MLAEPi) was measured and MLAEPi monitoring was continued to post-resuscitation care with induced therapeutic hypothermia (TH). This case highlights the usefulness of MLAEPi monitoring during primary care in the emergency center and postresuscitation care, including TH, for predicting neurological outcome.

Key words: resuscitation, cardiopulmonary arrest, monitoring, prognosis

Introduction
Although therapeutic hypothermia (TH) has improved mortality rates and neurological outcomes after resuscitation from sudden cardiac arrest (SCA), predicting survival or neurologic function remains difficult. A processed electroencephalogram (EEG), which computes the bispectral index (BIS), is a non-invasive tool used for monitoring the level of consciousness during anesthesia or critical care sedation. There have been several prior studies concerning the use of the BIS to indicate cerebral function during pre and post-resuscitation care, but results have been inconclusive. (1-3) In addition to the BIS value, auditory evoked potential (AEP) provides a good indication of the level of consciousness during anesthesia. (4) Specifically, measurement of the middle latency auditory evoked potentials (MLAEP) is a non-invasive procedure that is useful for monitoring cerebral function. The aepEX® (1st version; Audiomex, Glasgow, Scotland, UK) is the first available mobile MLAEP monitor. This device continuously generates a MLAEP index (MLAEPi), which is a dimensionless number scaled from 100 (awake) to 0, using differences between successive segments of its amplitude curve. Here we describe successful MLAEPi monitoring of a patient beginning in the emergency center and continuing during post-resuscitation TH induced in the intensive care unit (ICU) of our hospital. To the best of our knowledge, this is the first report of its kind.

Case report
Written informed consent for this report was obtained from the patient. A 48-year-old previously healthy man, weighing 85 kg and having a body mass index of 27.4, suddenly became unconscious at the supermarket and immediately underwent bystander cardiopulmonary resuscitation (CPR). Paramedics arrived 4 min after the collapse, and enlarged pupils, which did not respond to light, were noted; an electrocardiogram (ECG) revealed asystole. He underwent advanced cardiac life support (ACLS). During transportation to our hospital, an ECG showed ventricular fibrillation (VF). Defibrillation was successful, and return of spontaneous circulation (ROSC) with sinus rhythm occurred 12 min after SCA. On arrival at our emergency center 3 min after ROSC, physical examination revealed the following: Glasgow Coma Scale (GCS) score, E1V1M1; blood pressure, 138/74 mmHg; heart rate, 100 beats/min; spontaneous respiratory rate, 16 beats/min; and body temperature (BT), 35.7°C. The initial MLAEPi, measured 4 min after ROSC, was 55; the patient was still unconscious with an abnormal extension response in the extremities.
on painful stimuli. The ECG showed non-specific ST depression, and echocardiography revealed no hypokinesia and normal left ventricular function. Cerebral computed tomography revealed no abnormality. During primary care in the emergency center, no sedative drugs or neuromuscular blockade were administered. After admission to our ICU 1 hour after SCA, TH was introduced. Following premedication with 10 mg of intravenous midazolam, the MLAEPi soon decreased to 28. The deep BT reached 34°C 4 h after the SCA. During induced TH, 0.01 mg/kg/h of midazolam was infused for 29 h, 0.02 mg/kg/h of vecuronium bromide was infused for 23 h, and 0.01 mg/kg/h of fentanyl was infused for 29 h. The MLAEPi remained less than 30 throughout anesthesia administration. Re-warming was begun 28 h after the SCA; the MLAEPi was 24 after termination of the anesthetic (figure 1,2). When deep BT reached 37°C 5 h after re-warming began, the consciousness level improved to a GCS score of E2VtM4, and the MLAEPi increased to 44. The patient’s GCS score was E4VtM5 60 h post-SCA; he was extubated, and the MLAEPi increased to 64. TH was uneventful; 84 h post-SCA, he was neurologically normal, as defined by a Pittsburgh cerebral performance category of 1, and the MLAEPi was 82. The patient was discharged 41 days after SCA.

**Discussion**

To the best of our knowledge, this is the first report of an SCA patient receiving MLAEPi monitoring in an emergency center and ICU setting. Results suggest that MLAEPi measurement can help with the prediction of neurological outcome and survival throughout primary care in the emergency center and post-resuscitation care in the ICU. Although a major goal for SCA resuscitation is to improve post-resuscitation neurological function, most comatose survivors sustain anoxic brain damage. Induction of TH is currently the only treatment that improves survival rates and neurological recovery in comatose survivors of SCA resuscitation. (5,6) Therefore, informative monitoring throughout, from initial resuscitation before TH induction to post-resuscitation care, is essential. However, effective indicators of cerebral function remain to be identified. The BIS index is a monitoring tool obtained by processing the EEG wave form, which is composed of the combination of a time domain, frequency domain, and second-order spectral subparameters. For SCA patients, the efficacy of BIS index use remains controversial. Shibata et al. suggested its use after resuscitation to predict post-resuscitation outcomes. (1) Conversely, Fatovich et al. and Chollet-Xémard et al. reported that the BIS index was
a poor marker of cerebral perfusion or cerebral function in the prehospital or emergency setting during CPR. (2,3)
The MLAEP was derived from the AEP, and it reflects the morphology of the MLAEP curves. The aepEX identifies the positive Pa wave and the negative Nb wave of the MLAEP after auditory stimuli, and the MLAEPi is calculated from the consistent changes, of decreased amplitude and increased latency, resulting in each wave. It is difficult to analyze waves in real time in an emergency situation using the MLAEP, which is usually obtained intermittently. However, the aepEX, which is a mobile monitor, is easy to use, is battery operated, and allows rescuers to provide consistent assessment of MLAEP while performing any life-saving activities, or while transporting a patient within the hospital. Recent studies reported the efficacy of MLAEPi use in operative and ICU settings. (7,8) Doi et al. demonstrated that the MLAEPi was a better indicator of the depth of sedation than BIS or other EEG-based monitoring methods. (7) The MLAEPi was a better indicator of sedation depth than the BIS or any other EEG-based monitoring method and demonstrated 100% specificity for MLAEPi cut-offs of 37 and 61 for unconsciousness and for being awake during anesthesia, respectively. (8) In the present study, the MLAEPi during induced TH anesthetic administration was always less than 30 and the patient was unconsciousness. However, after re-warming, the MLAEPi increased to 82, which was higher than the initial value (55), and there was a good outcome. Although correlation with the MLAEPi at the time of collapse or on arrival at the emergency center remain to be evaluated, this case highlights the usefulness of MLAEPi monitoring during primary and post-resuscitation care, including TH, for predicting neurological outcome.

In conclusion, use of MLAEPi monitoring, which involves consideration of simple numerical values, is recommended for prediction of post-resuscitation outcome in SCA patients. Larger studies to further evaluate the MLAEPi in the SCA patient population are essential.

REFERENCES