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Effect of peripheral nerve tetanic stimulation on the inter-trial variability and accuracy of transcranial motor-evoked potential in brain surgery

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HIGHLIGHTS

- We compared post-tetanic (p-MEP) and conventional (c-MEP) motor-evoked potentials.
- p-MEP showed lower inter-trial variability, higher amplitude, fewer false-positive alarm signs, and equal sensitivity.
- The p-MEP technique may increase the accuracy of intraoperative MEP monitoring.

ABSTRACT

Objectives: The aim of this study was to evaluate and compare the advantages of post-tetanic motor-evoked potential (p-MEP) and conventional motor-evoked potential (c-MEP) in terms of MEP inter-trial variability and accuracy.
Methods: c-MEP and p-MEP were quantified in subjects who underwent brain surgery. c-MEP was generated by transcranial electrical stimulation (TES). p-MEP was generated using a preconditioning process involving tetanic stimulation at the left tibial nerve followed by TES. The presence of significant MEP deterioration was monitored during major surgical process. An additional 5–8 MEP obtained after major surgical process were used to analyze amplitude parameters such as mean, standard deviation, range, coefficient of variation (CV), and range to mean ratio.
Results: When only irreversible MEP deteriorations were considered as positive results, the false-positive rate was identical for p-MEP and c-MEP. When total MEP deteriorations were considered as positive results, the false-positive rate of p-MEP was lower and p-MEP had higher specificity than c-MEP. The mean amplitude of p-MEP was significantly higher than that of c-MEP. The CV and range to mean ratio of p-MEP were less than those of c-MEP.
Conclusion: The p-MEP technique is useful for augmenting MEP amplitude and reducing inter-trial variability.
Significance: p-MEP has clinical significance as a useful technique for intraoperative monitoring.

1. Introduction

Transcranial muscle motor-evoked potential (Tce-mMEP) has been widely accepted as a major tool for intraoperative monitoring (IOM) of the corticospinal tract during spinal cord or brain surgery (Kawaguchi and Furuya, 2004; Jameson and Sloan, 2012). Tce-mMEP has high sensitivity for prediction of neural damage during surgery. However, it also has limitations, such as high inter-trial variation (Woodforth et al., 1996), inability to generate waveforms in some cases (Nuwer, 2008a,b), and vulnerability to anesthesia (Sloan and Heyer, 2002). Of these, high inter-trial variability is a major obstacle to using Tce-mMEP for IOM, because it interferes with the identification of clear alarm signs of real neural damage during surgery (Calancie and Molano, 2008). Previously, tetanic stimulation of peripheral nerves immediately before

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Tce-mMEP (post-tetanic motor-evoked potential, p-MEP) has been proposed to increase the amplitude of the MEP (Yamamoto et al., 2010). This technique may be more accurate than conventional MEP (c-MEP) during IOM of spinal surgery (Yamamoto et al., 2010) because of enhanced corticomotoneuronal excitability (Kaelin-Lang et al., 2002). To date, the utility of p-MEP has only been evaluated during spinal cord surgery (Kakimoto et al., 2005; Hayashi et al., 2008, 2009; Yamamoto et al., 2008; Sun et al., 2014), and the effect of tetanic stimulation on the inter-trial variability of Tce-mMEP has not been fully evaluated (Yamamoto et al., 2010). We aimed to evaluate the utility of p-MEP compared to c-MEP in terms of inter-trial variability and diagnostic accuracy during brain surgery.

2. Methods

2.1. Patients

This study retrospectively included 29 patients who underwent brain surgery with both c-MEP and p-MEP monitoring during surgery in Seoul National University Hospital, from April 2013 to August 2013. Subject characteristics such as age, gender, and post-operative change of motor power were collected. All patients underwent total intravenous anesthesia with propofol and remifentanil.

Rocuronium, a rapid-onset non-depolarizing neuromuscular blockade, was only used for intubation during the initial period of surgery. Train-of-four (TOF) stimulation was applied to the posterior tibial nerve and recorded at the abductor hallucis muscle (stimulation frequency 1 Hz, intensity 40 mA, and duration 200 ms). The study protocol was approved and supervised by the Institutional Review Boards of the Seoul National University Hospital.

The presence of a postoperative motor deficit was defined as worsening of the Medical Research Council (MRC) motor grade score in any muscle. Postoperative motor deficit was divided into two categories, temporary and permanent deficit. Temporary deficit was defined as the deficit with full recovery within eight weeks after the surgery (Krieg et al., 2012). Permanent deficit was defined as the deficit that lasted >eight weeks after the surgery. The clinical characteristics of patients are summarized in Table 1.

2.2. Intraoperative MEP monitoring

The c-MEP was elicited by transcranial electrical stimulation only. For the p-MEP generation, preconditioning tetanic electrical stimulation on the peripheral nerve (left posterior tibial nerve, 50 mA, 5 s, 50 Hz) was applied 1 s before transcranial electrical stimulation (Kakimoto et al., 2005). For both p-MEP and c-MEP, transcranial electrical stimulation consisted of trains of five square-wave stimuli with a pulse duration of 50 μs, an interval of 2 ms, and an intensity of 300–400 V, using an MEP monitoring system (ECLIPSE, Medtronic, Dublin, Ireland). The C3 anode and C4 cathode pairs were used for stimulation of the left hemisphere, and the reverse arrangement was used for stimulation of the right hemisphere (Klem et al., 1999). Once the suitable intensity was determined, it was not changed during surgery. MEP was recorded at the thenar muscle and abductor hallucis muscle.

During surgery, both c-MEP and p-MEP were recorded repeatedly. In order to avoid the residual effect of prior MEP stimulation, the minimum interval between p-MEP and c-MEP stimulations or vice versa was set at 2 min (Hayashi et al., 2009). MEP recordings were obtained after the disappearance of the neuromuscular blocking effect, confirmed by TOF ratio (T4 to T1 amplitude > 0.9) (Viby-Mogensen, 2000). For both p-MEP and c-MEP, baseline waves were obtained immediately before the start of the main surgical procedure. During surgery, significant MEP deterioration was defined as a decrease of MEP amplitude to <50% of the baseline amplitude (Zhou and Kelly, 2001; Neuloh and Schramm, 2009; Szelenyi et al., 2010). Significant MEP deterioration was regarded as reversible when it recovered and irreversible when it did not recover, at the end of surgery.

2.3. Analysis 1: Analysis of the effect of tetanic stimulation on the inter-trial variability and amplitude of the MEP

We hypothesized that tetanic stimulation of the peripheral nerve would decrease the inter-trial variability and increase the amplitude of MEP in a surgery where neural integrity was preserved. To answer this question, we selected 52 hemispheric MEP stimulations without postoperative motor deficits (Fig. 1). For each hemispheric MEP stimulation, the mean amplitude, standard deviation (SD), range, coefficient of variation, and range to mean ratio of p-MEP and c-MEP were analyzed. The range was defined as the difference between the maximal and minimal amplitudes. The coefficient of variation (CV) was defined as the ratio of the SD to the mean. Subgroup analysis was also performed to evaluate the effect of tetanic stimulation of the peripheral nerve (left tibial

Table 1
Clinical characteristics of patients ($n = 29$).

Clinical features	
Age (mean ± SD)	50.25 ± 17.33
Sex (male, %)	16, 57.1%
Surgery duration (min, mean ± SD)	245.71 ± 92.71
Cause of surgery	
Brain tumor (*n*, %)	24, 85.7%
Cerebral aneurysm (*n*, %)	2, 7.1%
Others (*n*, %)	2, 7.1%
Anesthetics use (range)	
Propofol (μg/ml)	3.3–5.0
Remifentanil (ng/ml)	1.0–6.0
Preoperative motor weakness (n, %)	
MRC grade 3	3, 10.7%
MRC grade 4	2, 7.1%
No weakness	23, 82.1%

SD = standard deviation; MRC = Medical research council.

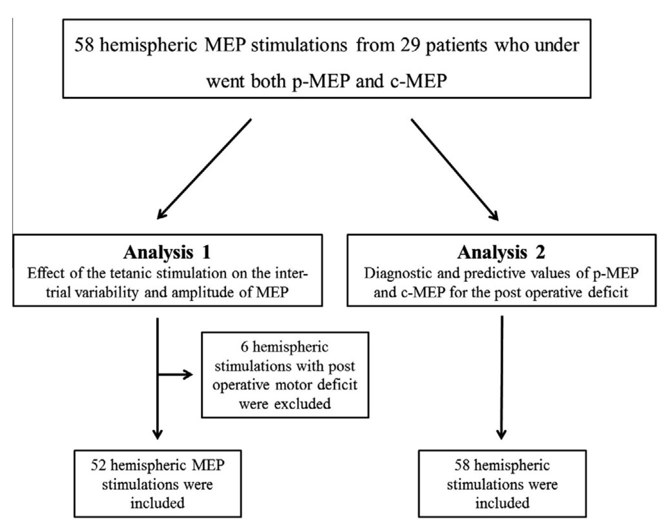

Fig. 1. Flow of subject selection and analysis. For analysis 1, six stimulations with postoperative motor deficit were excluded. Analysis 2 used all 58 MEP stimulations for calculating diagnostic and predictive values. MEP = Motor-evoked potential. c-MEP = Conventional motor-evoked potential. p-MEP = Post-tetanic motor-evoked potential.