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Recent advances in the monitoring of myogenic motor-evoked potentials: development of post-tetanic motor-evoked potentials

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Introduction

Intraoperative monitoring of motor-evoked potentials (MEPs) provides a method for monitoring the functional integrity of descending motor pathways during operations in which there is a risk of brain and spinal cord injury. However, the clinical and experimental use of these techniques has shown that the elicited responses are very sensitive to suppression by most anesthetics and muscular blockade [1]. Furthermore, patients with preoperative neuropathy may have very poor baseline MEPs. Although multipulse stimulation setups have been proposed to improve monitoring reliability [2–5], further improvements in techniques for reliable MEP recording will be required. In this article, we describe recent advances in intraoperative MEP monitoring, with the focus on a recently developed "post-tetanic MEP (p-MEP)" technique.

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A history of the development of MEPs

In 1937, Penfield and Boldrey [6] first reported that limb and face movements in humans could be elicited by the electrical stimulation of the exposed motor cortex at a frequency of 50–60 Hz. In this technique, patients needed to have a craniotomy to stimulate the motor cortex. In 1980, Merton and Morton [7] reported that a high-voltage single electrical stimulus applied over the skull could activate the motor cortex, and consequently, myogenic MEPs could be obtained from the limbs in patients without a craniotomy. These techniques using single pulses for stimulation have been successfully performed in awake subjects. However, MEPs in response to electrical stimulation with a single pulse were very easily suppressed by most anesthetic agents. Early anesthetic techniques were limited to light anesthesia using narcotic-based or ketamine-based anesthesia. To overcome the anesthetic-induced suppression of myogenic MEPs, multiple-stimulus setups, with paired pulses or a train of pulses for stimulation have been introduced [1–5]. When descending impulses are inhibited, the temporal accumulation of several excitatory postsynaptic potentials (EPSPs) is required to bring motor neurons from the resting state to the firing threshold. Kalkman et al. [2] examined the effects of paired transcranial electrical stimulation on myogenic MEPs in anesthetized patients and demonstrated that maximum amplitude augmentation was observed with interstimulus intervals between 2 and 5 ms. When the interstimulus interval was increased to 7 ms, no further augmentation was observed. Subsequently, a short train of electrical pulses over the scalp and exposed motor cortex has been shown to elicit MEPs successfully even under general anesthesia [3,4]. Multipulse transcranial

stimulators providing a train of up to ten stimuli are now available commercially.

Are current techniques for monitoring myogenic MEPs optimal?

Although the intraoperative recording of myogenic MEPs has become feasible since the introduction of multipulse stimulation, several problems regarding myogenic MEP monitoring remain unresolved. First, MEPs in response to multipulse stimulation are still sensitive to suppression by most anesthetics, so that the anesthetic drugs that can be used when MEPs are monitored are limited to those with less suppressive effects on MEPs. In addition, MEPs could not be recorded in most patients with preoperative motor dysfunction, resulting in low success rates of MEP recording and false-positive results in such patients. Second, because the use of neuromuscular blocking agents is limited or precluded when MEPs are to be monitored, transcranial stimulation of the motor cortex usually elicits patients movement, which may interfere with the surgical procedure, especially under microscopy [8]. Furthermore, such movement of patients may predispose the patients to a risk of injury of neck, tongue, lip, and eyes, and the disconnection of catheters, resulting in failure of administration of intravenous anesthetics and, subsequently, intraoperative awareness.

What are post-tetanic MEPs?

Tetanic stimulation of peripheral nerves has been widely used as a method to potentiate muscle response under neuromuscular blockade. During the administration of nondepolarizing neuromuscular blocking agents, tetanic nerve stimulation at 50–100 Hz is followed by a post-tetanic increase in twitch tension. The post-tetanic count after tetanic stimulation at 50 Hz for 5 s has therefore become an accepted technique to quantify the degree of intense neuromuscular blockade under conditions in which responses to single-twitch stimulation are no longer obtained. Considering this phenomenon, we speculated that myogenic MEPs could also be augmented when tetanic stimulation was applied prior to transcranial stimulation of the motor cortex. In 2005, we originally reported a new technique for MEP recording, called "post-tetanic MEP" (p-MEP, Fig. 1), in which the MEP amplitude can be enlarged by tetanic stimulation of the peripheral nerve prior to transcranial stimulation, compared with the amplitude of conventional MEP (c-MEP) [9]. Using this technique, we can successfully enlarge MEP amplitudes under general anesthesia with partial neuromuscular blockade. In the study [9], we determined the appropriate conditions of tetanic stimulation at 50 Hz for p-MEP augmentation as follows; duration of tetanic stimulation, 2–5 s; stimulus intensity of tetanic stimulation, 25–50 mA; and post-tetanic interval until transcranial stimulation, 1–5 s.

Mechanisms of p-MEP augmentation

The exact mechanisms of augmentation in p-MEP are still unclear. However, possible explanations are as follows. First, potentiation of neuromuscular transmission at neuromuscular junctions could be a primary mechanism for p-MEP augmentation. Tetanic stimulation at 50 Hz has been widely recognized to induce an augmentation of subsequent muscle response to peripheral nerve stimulation. The mobilization and enhanced synthesis of acetylcholine can continue during and after cessation of tetanic stimulation, so that, following the end of tetanic stimulation, there is an increase in the fractional release of acetylcholine from the nerve ending.

In addition to peripheral mechanisms at neuromuscular junctions, central mechanisms at the levels of brain and spinal cord may be also be involved in p-MEP

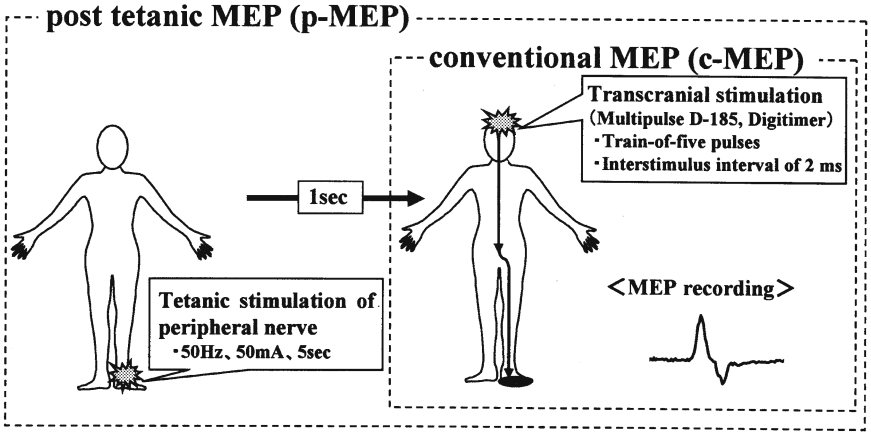

Fig. 1. Techniques for recording post-tetanic motor-evoked potential (*p-MEP*) and conventional MEP (*c-MEP*). For p-MEP recording, tetanic stimulation of peripheral nerve with a duration of 5 s and a stimulus intensity of 50 mA at 50 Hz was performed prior to transcranial stimulation, with a post-tetanic interval of 1 s. *Digitimer*, Welwyn Garden City, UK. (From [10] with permission)

augmentation. The results of a subsequent study from our laboratory showed some evidence of which central mechanisms may be involved in p-MEP augmentation [10]. Originally, we proposed that MEP augmentation by tetanic stimulation of peripheral nerves would be limited to those muscles innervated by nerves with tetanic stimulation (TS muscles). For example, tetanic stimulation of the left tibial nerve was considered to augment MEP only in the TS muscles innervated by the left tibial nerve, including the left abductor hallucis muscle, but not other muscles (non-TS muscles) that are not innervated by the left tibial nerve. However, Hayashi et al. [10] recently demonstrated that tetanic stimulation of the unilateral tibial nerve prior to transcranial stimulation augmented MEP amplitudes from non-TS muscles in the bilateral upper and lower limbs, as well as augmenting MEP amplitudes from TS muscles. These findings suggested that central mechanisms at the levels of spine and brain may be also involved in p-MEP augmentation.

Appropriate levels of neuromuscular blockade for MEP monitoring

Because complete neuromuscular blockade abolishes myogenic MEPs, the concept of partial neuromuscular blockade was invoked for anesthetic management during the monitoring of myogenic MEPs. van Dongen et al. [11] suggested that a stable neuromuscular blockade aimed at 45%–55% of baseline could provide reliable and recordable muscle responses during intraoperative myogenic MEPs. However, this level of neuromuscular blockade elicits movement of the patient in response to transcranial stimulation. The movement of patients may interfere with surgery, especially microscopic surgery, and may induce injury to the cervical spine, tongue, and eyes, for example. The development of MEP methods in which no patient movement is induced in response to transcranial stimulation may therefore be an important clinical challenge. Recently, in a study from our group, Yamamoto et al. [8], using the twitch height (T1) of the abductor hallucis brevis muscle in response to supramaximal electrical stimulation, investigated the appropriate levels of neuromuscular blockade in which p-MEP monitoring was feasible without any patients movement. The results indicated that 1 mV of T1 or 10% of %T1 was an appropriate level of neuromuscular blockade for monitoring p-MEP without patients movement in response to transcranial stimulation under propofol/fentanyl anesthesia. At this level of neuromuscular blockade, microsurgery was feasible without the interruption of surgery as long as p-MEP was used for monitoring. Although we do not recommend this level of neuromuscular blockade as a routine practice, this technique can be used as an alternative tool when patient movement is a problem.

Reliability of p-MEP monitoring

For the reliable monitoring of MEP, high success rates of MEP recording and low false-positive and false-negative rates are required. However, the success rates of baseline MEP recording during general anesthesia have remained unsatisfactory, especially in patients with preoperative neurological dysfunction. Recent reports have indicated that the success rates of baseline MEP recording during spinal surgery were 89%–100% and 30%–50% in patients without and with preoperative motor weakness, respectively [12,13]. In our recent study, the success rates of baseline MEP recording were significantly improved by using p-MEP in patients without and with preoperative motor weakness (c-MEP, 74.5% and 51.7%, respectively; p-MEP, 96.1% and 86.2%, respectively) [14].

A false-positive result of intraoperative MEP was defined as persistent MEP loss or a significant decrease with no new postoperative motor deficits. In fact, false-positive results of intraoperative MEPs have been reported repeatedly, at a range of 0% to 27%, because of the suppressive effects exerted by a variety of factors, including anesthetic agents, neuromuscular blocking agents, hemodynamic changes, temperature, and failure of electrodes [15,16]. In our series of 80 patients undergoing spine and spinal cord surgery, the false-positive rate of MEP monitoring was 4% when c-MEP was used for monitoring; however, when p-MEP was used for monitoring, the false-positive rate was 0% [14]. This study also showed that there were no false-negative results of c-MEP and p-MEP. These results indicate that the application of p-MEPs does not seems to interfere with the accuracy of MEP monitoring, although, for a definitive result, further study with more patients would be required.

Conclusion

Although MEP monitoring under general anesthesia was feasible in most patients without preoperative neurological deficits, the success rates of MEPs and the accuracy of MEP monitoring remained unsatisfactory. The development of techniques to augment MEP responses, such as p-MEP, under general anesthesia may provide the key to further improvements in MEP monitoring. Further studies are required before p-MEP can be used as a routine technique for the intraoperative monitoring of motor function.

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