



Updated review on the use of neuromuscular blockade during intraoperative motor-evoked potential monitoring in the modern anesthesia era

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Abstract

Transcranial electrical stimulation motor-evoked potentials (Tc-MEP) monitoring is a common practice in neurosurgery to prevent postoperative neurological damage. However, the use of neuromuscular blocking agents (NMBAs) during Tc-MEP monitoring is a subject of controversy. In addition, the effectiveness of sugammadex, a selective reversal agent, in the context of Tc-MEP monitoring requires further investigation. This review aimed to clarify the considerations involved in achieving optimal Tc-MEP monitoring while ensuring patient safety. Preoperative patient selection, comorbidity assessment, motor power evaluation, and the nature of the planned surgery are critical factors. Accurate paralysis assessment, continuous NMBA infusion, and post-tetanic stimulation techniques are essential for achieving optimal partial NMB. The decision to administer an NMB during Tc-MEP monitoring necessitates a careful evaluation of the balance between accuracy and potential complications. This review emphasizes the challenges associated with NMB administration during Tc-MEP monitoring and highlights the need for personalized patient assessment.

Keywords Neuromuscular blockade · Transcranial electrical stimulation motor-evoked potentials · Spine surgery · Brain surgery

Introduction

Intraoperative monitoring of motor-evoked potentials (MEP) has been widely used for over 40 years to prevent postoperative motor deficits in various surgeries [1–9]. However, the use of neuromuscular blocking agents (NMBAs) during transcranial electrical stimulation MEP (Tc-MEP) monitoring is a topic of debate, and the role of sugammadex as a reversal agent requires further investigation.

This review aimed to provide a comprehensive understanding of the considerations involved in Tc-MEP monitoring while prioritizing patient safety. We discussed the challenges associated with NMBA use during Tc-MEP monitoring and emphasized the need for personalized patient

assessment. Furthermore, we explored the potential benefits of sugammadex as a reversal agent in Tc-MEP monitoring. An improved understanding of these considerations will enhance Tc-MEP monitoring practices and patient outcomes in neurosurgical procedures.

Degree of NMB during Tc-MEP monitoring

How to assess the extent of blockade?

Two primary methods, acceleromyography and electromyography [10–15], assess neuromuscular block (NMB) at the neuromuscular junction (NMJ). Acceleromyography measures train-of-four (TOF) response, widely used for practicality. Electromyography measures M-response (T1 in mV), which is ideal for NMB monitoring but a challenging baseline in a real-world setting. Kalkman et al. [16] found that M-response persisted when mechanical TOF was abolished, suggesting it as a marker during varying NMB levels. Yamamoto et al. [17] observed comparable NMB degrees using

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1 mV of T1 and 10% of %T1 during MEP monitoring, favoring T1 for its practicality.

How important is it to check the degree of NMB before recording baseline MEPs?

According to a 2018 consensus statement, recommendations regarding routine quantitative neuromuscular monitoring during anesthesia are increasing [18]. This is crucial because residual neuromuscular effects can impact the accuracy of MEP interpretation until the time of stimulation. Therefore, appropriate monitoring and administering reversal drugs at suitable doses are essential to prevent this interference.

In an observational study [19], 240 patients receiving NMBA during elective procedures were examined. Those with intraoperative monitoring showed no residual NMB (rNMB), regardless of the reversal agent. On contrast, the non-monitored group exhibited rNMB despite sugammadex administration, highlighting the importance of NMB monitoring and proper reversal agent use. Applying this insight to scenarios requiring MEP monitoring, techniques like TOF can play a comparable role. Effective NMB monitoring establishes a dependable MEP baseline by minimizing rNMB.

Rocuronium (ROC), an intermediate-acting NMBA, is subject to variations in metabolism and elimination across patients. High ROC doses, often utilized to expedite rapid sequence endotracheal intubation, can result in a 50–300% prolongation of NMB when compared with standard doses (1–2 95% effective dose) [15]. A case report of a 12-year-old [20] weighing 56 kg had multiple comorbidities that required posterior spinal fusion surgery (T4–L4 levels), illustrated the challenges of inducing profound NMB even 90 min following 0.9 mg/kg ROC administration. The surgery had to be postponed due to the inability to determine the baseline MEP. The clinicians decided to determine the baseline MEP after administering sugammadex. Additionally, a retrospective analysis of Japanese patients [21] showed prolonged recovery times with a TOFR of 0.75 in 44.3% of patients undergoing intracranial aneurysm clipping following ROC administration for intubation (0.5–1.0 mg/kg based on total body weight). A prolonged recovery time was defined as ≥ 120 min and was significantly correlated with ROC dosage based on ideal body weight. These studies highlight the necessity of quantitative monitoring to identify patients with residual paralysis and the need for reversal.

Factors associated with the residual effect of NMBA

A Japanese observational study [22] on patients undergoing spine surgery showed that the ROC dose, mean blood pressure, hepatic function, and patient age significantly influenced the TOFR. Moreover [14], hypothermia, certain

antibiotics, furosemide, local anesthetics, acidosis, and magnesium can also increase the blockade. NMB duration may also be affected by anti-epileptic medications, with the acute use of phenytoin increasing blockade and the chronic use decreasing it. In addition, the sensitivity of various muscle groups to neuromuscular blockers varies [23], which can lead to unpredictable intraoperative neurophysiological recordings [24, 25]. These findings highlight the importance of monitoring and adjusting NMBA and reversal agents based on patient-specific factors to prevent perioperative adverse outcomes.

Role of sugammadex in Tc-MEP monitoring

Efficacy comparison to neostigmine

Cochrane et al. [26, 27] found that sugammadex (2–4 mg/kg) resulted in 16× faster recovery than neostigmine, achieving TOFR > 0.9 in ~ 3 min.

Benefits of MEP monitoring

Sugammadex emerges as a pivotal asset in MEP monitoring scenarios, addressing the threat of rNMB and ensuring the establishment of a dependable baseline MEP before surgical incision. Formerly [28, 29], strategies like deep anesthesia or high-dose opiates were employed to circumvent NMB, whereas NMBA now offer improved intubation quality and reduced complications. The preparatory phase for MEP monitoring, spanning 30–90 min [11, 13–15] encompassing procedures such as line placements and patient positioning, can be susceptible to NMB absence-associated issues like movement, bronchospasm, or hypotension, necessitating escalated anesthetic dosages [29, 30]. Sugammadex's efficacy in enhancing neuromuscular recovery and mitigating movement during these critical junctures is robustly evidenced. Research underscores its capacity to improve Tc-MEP amplitudes and hasten the initiation of MEP monitoring [31, 32]. This is particularly valuable for patients with conditions like cervical myelopathy, often characterized by sensory and motor deficits. They confront challenges in establishing baseline MEPs [23]. Here, sugammadex's deployment proves instrumental, enabling early MEP baselines, timely injury detection, and repositioning [22, 23, 33–35].

Appropriate dose of sugammadex reversal

Sugammadex's effective reversal requires a higher dose for deeper neuromuscular blockade. To reverse moderate NMB (two twitches in response to TOF stimulation), a recommended dose is 2 mg/kg [36]. Unlike ROC dosing based

on ideal weight, sugammadex's dose should use actual body weight. For obese patients, the ideal weight-based ROC dose might not suffice, necessitating a higher sugammadex dose [37, 38].

Possible adverse effects after sugammadex reversal

While sugammadex brings substantial advantages, prudent consideration of potential complications is warranted. Notably, patient movement remains a concern, and administering additional doses of rocuronium post-sugammadex reversal could lead to delayed re-onset of NMB [39]. Therefore, precise dosing is pivotal for effective reversal [40]. While minor side effects like nausea are prevalent, severe reactions [10, 41–44] such as bradycardia and anaphylaxis are rare. In making informed clinical decisions, a meticulous weighing of improved MEP monitoring benefits against potential drawbacks is imperative.

No-NMB versus p-NMB during MEP monitoring

Complete NMB is not ideal for intraoperative Tc-MEP monitoring during brain and spine surgery as it can negatively impact MEP amplitude and increase inter-trial variability [45, 46]. Consequently, previous reviews and studies have recommended avoiding NMBAs during MEP monitoring to ensure the accuracy and reliability of Tc-MEPs [47–52].

On the other hand, certain institutions opt to maintain partial NMB (p-NMB) [10, 16, 41–44]. Avoiding NMBAs during MEP monitoring may require increased anesthetic use, leading to unwanted deep anesthesia and associated problems, such as hypotension, shock, and delayed emergence [53]. Although the relationship between anesthetic depth and long-term survival remains unclear, numerous literature reviews indicate a correlation between deep anesthesia and unfavorable outcomes [54–56].

A previous study showed that the no-NMB group required a significantly higher remifentanyl dose and had a lower mean arterial pressure than the p-NMB group during neurosurgery [52]. However, the clinically acceptable lowest mean level was observed, and there was no increased incidence of hypotension, bradycardia, or vasopressor demand. Another study reported that a higher dose of both remifentanyl and propofol reduced the risk of movement during craniotomy in the absence of NMB [57]. Increasing the propofol dose is not advisable due to its potential to suppress MEP amplitude in a dose-dependent manner and cause bradycardia and hypotension [57–59]. However, Kim et al. [51] observed no significant difference in the incidence of bradycardia between the p-NMB and no-NMB groups receiving propofol- and remifentanyl-based anesthesia during cerebral aneurysmal

clipping surgery. In addition, most cases of bradycardia were effectively treated with bolus administration of vagolytic agents. Intraoperative hypotension can be managed by continuously infusing approximately 500 µg/h of phenylephrine [60].

Safety concerns during Tc-MEP monitoring: no-NMB versus p-NMB

Unacceptable movement

One of the main safety concerns associated with no-NMB during MEP monitoring is the risk of unexpected patient movement. Advocates of p-NMB argue that the absence of NMB could make exposure to the surgical field challenging, particularly during spine surgery [16, 42, 44, 61]. Hemmer et al. found that the incidence rate of unacceptable movements during MEP monitoring in craniotomy for aneurysm clipping without NMB was only 3.2% (however, the movement was not classified from a surgeon's perspective) [62]. Other studies [63–65] have reported that recording during microsurgery was impossible in 6–10% of cases due to electrostimulation-induced muscle contraction. Quiñones-Hinojosa et al. [66] also reported that without NMB, MEPs elicited patient movement, and surgical pauses were required for MEP monitoring to avoid potential movement during microsurgery. Liu et al. [67] observed that the incidence of unexpected movements did not significantly decrease until the TOFR was < 50%.

However, previous studies [52, 53] have reported no significant difference in the incidence of spontaneous movements during neurosurgery between the partial- and no-NMB groups. Moreover, propofol/remifentanyl-based anesthesia can effectively immobilize patients in both the p-NMB and no-NMB groups. These findings suggest that propofol/remifentanyl-based total intravenous anesthesia without NMB is a safe and viable option for patients undergoing cerebral aneurysm clipping surgery, potentially improving the accuracy of MEP monitoring.

Bite injury

The mechanism underlying the occurrence of jaw clenching during Tc-MEP monitoring may involve both corticobulbar activations with pulse trains and direct stimulation of the muscle or trigeminal nerve since jaw clenching has been observed with single pulses. Therefore, it is possible that C3/4 Tc-MEP may produce stronger jaw clenching than C1/2 Tc-MEP as the electrodes are closer to the facial motor cortex, jaw muscles, and trigeminal nerves. Nevertheless, it should be noted that C3/4 application may be more effective, particularly in patients with preoperative motor deficits [68].

Two case reports [68, 69] have documented instances of patients with preoperative motor deficits due to spinal cord tumors requiring intraoperative MEP monitoring with C3/4 application. In both cases, only a single dose of ROC was administered for intubation without additional dosing, and the occurrence of armored tube perforation was noted despite the use of a recommended gauze bite block, ultimately necessitating emergency re-intubation during the surgery.

A recent retrospective study in Japan [70] examined 194 patients who underwent neurosurgical procedures with Tc-MEP monitoring and C3/4 application. The incidence of bite injuries, as assessed by oral surgeons, was 6.5% higher than the previously reported rates (0.13–0.69%) [61, 71]. The study also revealed that patients with severe movement during Tc-MEP monitoring, graded by a neurosurgeon, without continuous NMB, were significantly more likely to experience bite injuries.

p-NMB use during MEP monitoring in spine surgery

Table 1 provides a comprehensive overview of the utilization of p-NMB during MEP monitoring in spine surgery. The first clinical application of p-NMB in Tc-MEP monitoring was reported by Kalkman et al. [16], who demonstrated the ability to record Tc-MEPs at p-NMB with T1 twitch height ranging from 5 to 15%. Similarly, Nagle et al. [72] reviewed 116 cases in which MEPs were monitored in 99 cases (85%) while maintaining T1 at 10% of baseline. In 1996, Lang et al. [41] reported that the MEP amplitude decreased by 50–60% when the T1 twitch height dropped to 20% of the controls. Another clinical study [73] aimed to maintain the T1 twitch height at 30–55% of baseline and demonstrated no false negative or false positive results under a continuous infusion of muscle relaxants to maintain a consistent level of muscle relaxation.

The lack of a clear consensus on the appropriate degree of NMB during MEP monitoring may be attributed to the oversimplified classification of p-NMB in previous studies. The previous classification failed to consider the diverse effects of p-NMB on Tc-MEP monitoring, leading to inconclusive results. To address this issue, a 2019 study [67] classified NMB into six distinct phases based on the reversal of neuromuscular relaxation. The study found that maintaining TOFR at 26–50% for abductor hallucis (AH) Tc-MEPs or 16–50% for tibialis anterior (TA) Tc-MEPs may be suitable for Tc-MEP monitoring during surgical scoliosis correction.

Another study by Kim et al. [52] showed that no-NMB was better than the three p-NMB grades in terms of MEP amplitude and variability. However, the recommended T_2/T_c is 0.5 when p-NMB is used for MEP monitoring since the

false-positive results of Tc-MEPs in the p-NMB group were not significantly higher than those in the no-NMB group. In addition, Liu et al. [67] observed that the incidence of monitoring failure and false-positive results did not increase significantly until the TOFR was < 26% during AH-Tc-MEP monitoring and < 16% during TA-Tc-MEPs monitoring.

Zhang et al. [74] aimed to identify the ideal ROC dose for spinal surgery. The study included 120 patients, with 40 patients in each of the three groups receiving varying doses of ROC. Unexpected body movements and breathing recovery were observed in six patients who received 6.0 mcg/kg/min of ROC. However, no movement or spontaneous breathing recovery was observed in the other two groups who received higher doses of ROC (9 and 12 mcg/kg/min). In addition, as the ROC dose increased, MEP amplitude decreased. The results indicated that a ROC dose of 9.0 mcg/kg/min provides optimal muscle relaxation without any side effects.

Selner et al. [75] recently published the first report on the feasibility of complete NMB (TOF count = 0) in 24 patients undergoing cervical and lumbar spinal surgery. The study showed that at least three of four measurable MEP limb responses were achievable, and 70.8% of patients had measurable responses in all four limbs. The clarity of the signals was reliable, with 82% of thenar-hypothenar responses and 62% of AH responses showing robustness. Interestingly, the absence of Tc-MEPs did not correlate with the degree of NMB, even in patients with 4/5 strength. This contrasts with the finding of a previous study [76], which showed that MEPs were difficult to obtain in patients with a preoperative strength of 3/5 or less without NMB. These findings suggest that the relationship between amplitude and motor weakness during full NMB may be less significant than that expected for a small degree of weakness.

p-NMB use during MEP monitoring in brain surgery

The use of p-NMB for MEP monitoring during brain surgery is limited compared with that during spine surgery (as shown in Table 2). This is because the presence of NMB necessitates a higher stimulus intensity [77], particularly in patients with preoperative muscle weakness, which activates deep subcortical motor pathways, bypassing higher cortical levels, leading to the generation of myogenic MEPs in contralateral limbs despite possible cortical ischemia [63]. Furthermore, subcortical motor pathway ischemia may be missed if corticospinal tract activation occurs more caudally [63, 65, 68, 78, 79]. To minimize the risk of cervical injury from movement due to a three-point fixed pin and other movement-related complications [62], such as bucking-induced brain edema and interruption of microscope use,

Table 1 Previous studies on p-NMB during Tc-MEP monitoring in spine surgery

Author and year of publication	Number of patients (N), type of surgery	Stimulation intensity	Degree of NMB blockade	Induction and intubation	NMB during MEP	Anesthetic maintenance	Muscles for recording	MEP amplitude/success rate during p-NMB
Kalkman et al. 1992	N = 11, lumbar spinal surgery	500–700 V	1–2 TOF count %T1 = 5–15% of control	Sufentanil, etomidate, SUX	VEC bolus 0.05 mg/kg then continuous infusion with 0.05 mg/kg/h	Sufentanil, N ₂ O	TA	Mean amplitude 0.59 ± 0.36 mV (100% recordable)
Ubags et al. 1996	N = 14, spine surgery	300–1200 V	%T1 = 25% of control	Sufentanil, etomidate, VEC 0.1 mg/kg	VEC continuous infusion	Sufentanil, etomidate, ketamine, N ₂ O	TA	Median amplitude 281 μV (100% recordable)
Nagle et al. 1996	N = 116, spine surgery	Constant-current of 2–40 mA	%T1 = 10% of control	At the discretion of the attending anesthesiologist	VEC continuous infusion	Narcotics, N ₂ O, ISO or HAL	Qu, TA, EBV	Recorded in 99 cases (85%)
Lang et al. 1996	N = 40, spine surgery	600–700 V	%T1 = 20% of control	Sufentanil, etomidate, SUX	VEC bolus then continuous infusion	Sufentanil, N ₂ O	TA	100% recordable
Yamamoto et al. 2008	N = 15, spine surgery	p-MEP: 50 mA for 5 s started prior to transcranial stimulation	T1 = 0.8–1.2 mV or %T1 = 10% of control	Fentanyl, propofol, VEC 0.1 mg/kg	VEC bolus 0.1 mg/kg then continuous infusion	Fentanyl, propofol	AH	100% recordable with p-MEP technique
Kim et al. 2013	N = 120, spine surgery	Mean 400 V	Group A: 2 TOF counts Group B: %T1 = 50% of control Group C: %T2 = 50% of control Group D: no-NMB	Remifentanyl, propofol, ROC	VEC 0.1 mg/kg bolus then continuous infusion	Remifentanyl, propofol	APB, TA	Median amplitudes (left TA): Group A 0.23 mV Group B 0.44 mV Group C 0.28 mV Group D 0.75 mV
Liu et al. 2019	N = 62, posterior spinal fusion surgery	400	p-NMB levels (5 phases) TOF ₁ : 1–2 TOF count TOF ₂ : 3 TOF counts TOF ₃ : TOFR 16–25% TOF ₄ : TOFR 26–50% TOF ₅ : TOFR 51–75% nNMB: TOFR > 75%	Midazolam, fentanyl, propofol, CIS (0.2 mg/kg)	CIS 2–4 mcg/kg/min with an initial rate of 4 mcg/kg/min	Propofol, remifentanyl, DEX	AH, TA	Significant reductions of amplitudes at TOF _{1–2} of TA compared with nNMB

Table 1 (continued)

Author and year of publication	Number of patients (N), type of surgery	Stimulation intensity	Degree of NMB blockade	Induction and intubation	NMB during MEP	Anesthetic maintenance	Muscles for recording	MEP amplitude/success rate during p-NMB
Zhang et al. 2022	N = 120 (40 in each group), spine surgery	220	Group A = 2–4 TOF counts Group B = 2 TOF count Group C = 0 TOF count	Midazolam, propofol, sufentanil, lidocaine, ROC 0.6 mg/kg	Group A: 6 mcg/kg/min Group B: 9 mcg/kg/min Group C: 12 mcg/kg/min	Propofol, remifentanyl	APB, TA	Median amplitudes (left APB) before spinal canal decompression Group A: 277 uV Group B: 332 uV Group C: 211 uV
Selner et al. 2022	N = 24, cervical and lumbar spinal surgery	Mean 175.6 mA	95% block or TOF count = 0 or %T1 = 0.1–3.8% of control	Propofol, remifentanyl, ROC 0.6 mg/kg	ROC at 5 mcg/kg/min (continuous infusion)	Propofol, remifentanyl	APB, AH	At least 3 or 4 measurable MEP limbs in all patients

NMB neuromuscular blockade, p-NMB partial NMB, MEP motor evoked potential, Tc-MEP transcranial electrical stimulation motor-evoked potential, CMAP compound muscle action potentials, CIS cisatracurium, ROC rocuronium, VEC vecuronium, SUX succinylcholine, DEX dexmedetomidine, N₂O nitrous oxide, T1 amplitude of CMAP, %T1 percentage of T1 of control value before NMB was administered, p-MEP post-tetanic MEP, no NMB no NMB was used, APB abductor pollicis brevis, AH abductor hallucis, Qu quadriceps, EBV extensor digitorum brevis, TA tibialis anterior, TOFR train-of-four ratio, TOF train-of-four

the lowest possible stimulation intensity is recommended [59, 64, 80, 81].

Kim et al. [51] aimed to compare the diagnostic accuracy of MEP monitoring during cerebral aneurysm surgery under no-NMB versus p-NMB conditions. MEPs were successfully recorded in both groups without significant differences in the stimulation intensity used; however, the false-negative MEP results were significantly lower in the no-NMB group ($P = 0.02$). Moreover, the MEP signals of the upper and lower extremities could be achieved with approximately 250 V of stimulation without inducing patient movement or the need to paralyze the patient. There were no significant differences in the mean amplitudes at baseline and post-MEP in both upper and lower extremities between the two conditions, except in the post-MEP amplitude in the left abductor pollicis brevis ($P = 0.009$).

Lee et al. [81] retrospectively analyzed 768 patients undergoing craniotomy with MEP monitoring under p-NMB. After successfully obtaining the baseline MEP recording, the rate of ROC infusion was increased and decreased by 0.1/mg/kg/h (= 1.67 mcg/kg/min) on encountering unexpected movement or if the MEP amplitude was too small, respectively, maintaining a TOF count of 2/4–3/4. The authors reported a high incidence of unacceptable movements (36%), which included a wider range of movements, even those that could be considered slightly dangerous.

Notably, another study [53] compared the effect of continuous infusion (group I) and an intermittent bolus (group B) of ROC among 80 patients undergoing elective cerebral intervention due to an aneurysm. The mean stimulus intensity was not different among the two groups, while the TOF counts and incidence of involuntary movement and spontaneous breathing recovery were significantly higher in group B. Although the difference was not statistically significant, group B had four patients (5%) with unexpected movement; a small dose of NMBA was injected to resume the operation. A ROC dose administered at 5 mcg/kg/min via infusion was sufficient to maintain the TOF count between 1 and 2 during coil embolization. MEP monitoring was successfully performed in both groups, and the MEP variability, calculated based on the coefficient of variation and mean MEP amplitudes of all limbs, was significantly lower in group I.

Techniques to enhance Tc-MEP amplitudes

MEP monitoring under anesthesia conditions requires multiple pulses of Tc-MEP because a single pulse is usually insufficient for activating the motor neuron. The optimal interpulse interval for generating muscle MEPs is typically 2–4 ms, with some patients requiring a train of three pulses and others requiring more.

Table 2 Previous studies on p-NMB during Tc-MEP monitoring in brain surgery

Author and year of publication	Number of patients (N), type of surgery	Stimulation intensity	Degree of NMB blockade	Induction and intubation	NMB during MEP	Anesthetic maintenance	Muscles for recording	Amplitude	Unacceptable body movement
Sekimoto et al. 2006	N = 36, brain tumor resection	< 200 mA	%T1 = 40–50% of control	Propofol, fentanyl, VEC (0.1 mg/kg)	Continuous infusion of VEC 1.6 ± 0.4 mg/h	N ₂ O, propofol, fentanyl, with HAL, ISO or SEV	APB, TA	Volatile anesthetics depressed the amplitude to 20% of control by maintaining the possible MEP monitoring	N/A
Kim et al. 2016	N = 685, intracranial aneurysm clipping	Mean 265.6 V	%T1 = 40–50% of control	Fentanyl, propofol, remifentanyl, ROC (0.8–1.0 mg/kg) or SUX (0.8–1.2 mg/kg)	Continuous infusion of ROC (dose N/A)	Propofol and remifentanyl	TA, AH, APB	Mean amplitude (left APB) 2502 uV	None in both no-NMB and p-NMB groups
Ko et al. 2018	N = 80, cerebral coil embolization	Mean 400 V	TOF count = 1–2	Propofol, remifentanyl, ROC (0.6 mg/kg)	Group I: continuous infusion of ROC5 mcg/kg/min Group B: bolus ROC 0.1 mg/kg as needed	Propofol and remifentanyl	APB, VA, EHL, AH	Mean amplitude (left APB) Group I: 1383 mV Group B: 2798 mV	Only in group B (18.8%, p = 0.06)
Lee et al. 2021	N = 768, brain tumor and vascular surgery	100–400 V	TOF count = 2–3	Propofol, remifentanyl, ROC (0.6 mg/kg)	Continuous infusion of ROC 0.3 mg/kg/h	Propofol and remifentanyl	APB, ADQ	N/A	278 patients (36.2%)

NMB neuromuscular blockade, p-NMB partial NMB, MEP motor-evoked potential, Tc-MEP transcranial electrical stimulation motor-evoked potential, CMAP compound muscle action potentials, HAL halothane, ISO isoflurane, SEV sevoflurane, TOF train-of-four. Group B bolus group, Group I infusion group, APB abductor pollicis brevis, ADQ abductor digiti quinti, AH abductor hallucis, VA vastus lateralis, Qu quadriceps, EHL extensor hallucis longus, EBV extensor digitorum brevis, TA tibialis anterior

Despite recent advancements in multipulse stimulation setups that have made intraoperative recording of muscle MEPs possible, several factors still affect muscle MEP responses, such as preoperative muscular weakness, variability in muscle response, and the influence of anesthetics and NMBAs. Therefore, techniques to increase the MEP amplitude during monitoring are desirable.

Inghilleri et al. [82] noted that paired stimulation improved monitoring by facilitating the accumulation of excitatory postsynaptic potentials at the anterior horn motor neuron level. MEP monitoring can improve greatly using a short train of stimulations spaced 2–5 ms apart [83, 84]. This technique allows the first stimulus to lower the excitation threshold of the motor neuron pool, facilitating depolarization by the second stimulus. Ubag et al. [85] proposed an alternative strategy, which involves using a circumferential cathode configuration consisting of Fz, F3, F4, A1, and A2 (compared with a single cathode at Fz), with the anode positioned at Cz. This approach was found to significantly increase the tc-MER amplitude.

In 2008, Kakimoto et al. [86] proposed a new technique called “post-tetanic MEPs” (p-MEPs), which utilizes tetanic stimulation of peripheral nerves to amplify *compound muscle action potential* (CMAP) amplitudes prior to transcranial stimulation. The technique is based on the fact that post-tetanic count after tetanic stimulation at 50 Hz for 5 s can be used to quantify the degree of intense NMB when there are no responses to single-twitch stimulation [87–89]. The p-MEP technique [86] involves tetanic stimulation of peripheral nerves at 25–50 mA for 3–5 s, 1–2 s before transcranial stimulation, and can improve the success rate of baseline MEP measurements and decrease false positives and false negatives during p-MEP monitoring compared with those during conventional Tc-MEP (c-MEP) monitoring [90].

Recent studies have confirmed that tetanic stimulation of the unilateral tibial nerve before transcranial stimulation is sufficient to augment CMAP amplitudes in both bilateral upper and lower extremities [91]. However, optimum CMAP augmentation is achieved when the corresponding nerve receives tetanic stimulation. Moreover, tetanic stimulation of multiple nerves provides better CMAP augmentation than that obtained on stimulation of a single nerve [92]. This technique improves the excitability of the anterior horn cells [93] and can improve the reliability of intraoperative MEP monitoring.

Conclusion

The decision to induce NMB during MEP monitoring is complex and involves striking a delicate balance between the accuracy of MEP recordings and the risk of complications. Careful preoperative patient selection, focusing on assessing

comorbidities, motor power, and the type of surgery to be performed, is crucial. To optimize the use of p-NMB, it is necessary to monitor the degree of paralysis, maintain constant paralysis levels, and implement post-tetanic stimulation techniques.

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Declarations

Conflict of interest The authors have no conflict of interest to declare.

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