Journal of Clinical Monitoring and Computing (2019) 33:471–479
https://doi.org/10.1007/s10877-018-0182-8

ORIGINAL RESEARCH

Effect of neuromuscular blockade on transcranial electric motor evoked potentials during surgical correction for idiopathic scoliosis under total intravenous anesthesia

Hai-yan Liu[1] · Tian-jiao Xia[2] · Ze-zhang Zhu[3] · Xing Zhao[1] · Yue Qian[1] · Zheng-liang Ma[1] · Xiao-ping Gu[1]

Received: 20 March 2018 / Accepted: 10 July 2018 / Published online: 20 July 2018

Abstract
Transcranial electric motor evoked potentials (TCeMEPs) play an important role in reducing the risk of iatrogenic paraplegia. TCeMEPs could be obviously suppressed by neuromuscular blockade (NMB). The aims of this study were to examine the effects of NMB on TCeMEPs and to determine an appropriate level of partial neuromuscular blockade (pNMB) for TCeMEPs during surgical correction of idiopathic scoliosis under total intravenous anesthesia (TIVA). All patients were maintained with TIVA. The pNMB levels were classified into five phases: one or two train-of-four (TOF) counts (TOF_1); three TOF counts, or T_4/T_1 (TOFR, $T_{1,4}$, first or four twitch height of TOF) ≤ 15% (TOF_2); TOFR at 16–25% (TOF_3); TOFR at 26–50% (TOF_4); and TOFR at 51–75% (TOF_5). No neuromuscular blockade (nNMB) was achieved when TOFR was more than 75%. The absolute and relative latency, amplitude and area under curve (AUC), efficacy of TCeMEPs and rate of unexpected movement were compared among these phases. Neither the amplitude and AUC nor the efficacy of TCeMEPs were affected at TOF_{4-5} of abductor halluces muscles TCeMEPs (AH-TCeMEPs) or at TOF_{3-5} of tibialis anterior muscles TCeMEPs (TA-TCeMEPs) compared with nNMB. However, the rate of unexpected movement was increased significantly at TOF_5 and nNMB compared with TOF_1 and TOF_4. The application of pNMB with TOFR aimed at 26–50% for AH-TCeMEPs or 16–50% for TA-TCeMEPs seems to be an appropriate regimen for TCeMEPs during surgical correction for idiopathic scoliosis under TIVA.

Keywords Transcranial electric motor evoked potentials · Partial neuromuscular blockade · Idiopathic scoliosis · Total intravenous anesthesia

1 Introduction

Patients undergoing surgical correction for idiopathic scoliosis are at high risk of neural complications associated with spinal cord injury [1]. Intraoperative neurophysiological monitoring of transcranial electric motor evoked potentials (TCeMEPs), which reflect real-time neural transmission through the entire motor pathway, including corticospinal motor tracts [2–4], has recently emerged as an effective way to reduce the risk of iatrogenic paraplegia in most

✉ Xiao-ping Gu
xiaopinggu@nju.edu.cn

Hai-yan Liu
drliuhaiyan@163.com

Tian-jiao Xia
annextj@126.com

Ze-zhang Zhu
zhuzezhang@126.com

Xing Zhao
leilei00617@163.com

Yue Qian
money890713moon@163.com

Zheng-liang Ma
mazhengliang1964@nju.edu.cn

[1] Department of Anesthesiology, Affiliated Drum Tower Hospital of Medical Department of Nanjing University, 321 Zhong Shan Road, Nanjing, Jiangsu 210008, People's Republic of China

[2] Medical Department of Nanjing University, Nanjing, People's Republic of China

[3] Department of Orthopaedic Surgery, Affiliated Drum Tower Hospital of Medical Department of Nanjing University, Nanjing, People's Republic of China

leading spine centers. It has been reported that TCeMEPs are affected by multiple factors, such as body temperature, blood pressure, depth of anesthesia and neuromuscular blockade (NMB) [5–8]. Despite many efforts in both anesthetics and neurophysiological monitoring techniques that have improved the stability of TCeMEPs, the depressant effects of NMB on TCeMEPs can barely be avoided due to interference with the neuromuscular junction [9–11].

Opponents of anesthesia without NMB insist that complete omission of NMB could increase the difficulty of the surgical procedure as well as the complexity of anesthetic management [12, 13]. Partial neuromuscular blockade (pNMB) seems to be more preferable to surgeons, neurophysiologists, and anesthesiologists during surgical correction for idiopathic scoliosis. However, the appropriate level of pNMB for TCeMEPs during surgery for idiopathic scoliosis remains controversial. The controversy may be largely attributable to confounding factors, such as the type of surgery or the choice of anesthetics [14, 15]. Therefore, this study was conducted to examine the effects of NMB on TCeMEPs and to determine an appropriate level of pNMB for TCeMEPs during surgical correction of idiopathic scoliosis under total intravenous anesthesia (TIVA).

2 Materials and methods

2.1 Patients

After Institutional Review Board approval, the research team reviewed the TCeMEPs and anesthesia records of patients with idiopathic scoliosis who presented for posterior spinal fusion surgery from January 1, 2016 to October 30, 2016. The inclusion criteria were as follows: (1) age 10–30 years, (2) diagnosis of idiopathic scoliosis and (3) American Society of Anesthesiologists (ASA) physical status was between I and II. The exclusion criteria were as follows: (1) any cases with other types of scoliosis, such as neuromuscular scoliosis; (2) any cases associated with existing sensory or motor neurologic deficits; (3) morbid obesity (BMI > 40 kg m^{-2}); (4) history of previous surgical treatment for scoliosis; and (5) history of severe cardiopulmonary disease, such as pulmonary hypertension.

2.2 Anesthesia regimen

All patients were maintained with TIVA. No premedication was administered. After establishing intravenous access, general anesthesia was induced with midazolam (2 mg) and propofol (1–3 mg kg^{-1}). Cisatracurium (0.2 mg kg^{-1}) and fentanyl (2–4 μg kg^{-1}) were used to facilitate tracheal intubation. After tracheal intubation, anesthesia was maintained with intravenous infusions of propofol at 80–120 μg^{-1} kg^{-1} min^{-1}, remifentanil at 0.2–1 μg^{-1} kg^{-1} min^{-1}, dexmedetomidine at 0.2 μg^{-1} kg^{-1} h^{-1} and cisatracurium at 2.0–4.0 μg^{-1} kg^{-1} min^{-1}. A continuous infusion of cisatracurium was started at an initial rate of 4.0 μg^{-1} kg^{-1} min^{-1} and titrated to maintain intraoperative pNMB. The mean arterial pressure (MAP) was maintained within ± 20% of the basal MAP of each patient. The Bispectral Index (BIS) was kept in the 40–60 range. Rectal temperature was controlled within 35.5–37 °C, and end-tidal carbon dioxide was maintained within 35–45 mmHg.

2.3 Monitoring the intraoperative neuromuscular blockade

Neuromuscular function was evaluated by acceleromyography utilizing the commercially available device TOF-Watch (Organon Corporation, Oss, KN). Two electrodes from the device were placed over the ulnar nerve, and the response to nerve stimulation was measured using a small piezo electrode acceleration transducer placed distally on the volar side of the thumb. The theory behind acceleromyography was based on Newton's second law of motion: force = mass × acceleration. When mass is constant, acceleration is directly proportional to force [16]. The degree of NMB was typically quantified by train-of-four (TOF) electrical stimulation, which was monitoring of four supramaximal stimuli (2 Hz) given every 0.5 s. As muscle relaxation increased, the forth response (T_4) was lost, then the third (T_3), the second (T_2) and, finally, the first twitch (T_1). Thus, the number of twitches (zero, one, two or three) was used to estimate NMB. The ratio of T_4/T_1 (TOFR) was displayed to evaluate NMB when four responses were present. The intraoperative pNMB levels were classified into 5 phases: one or two TOF counts (TOF_1); three TOF counts, or TOFR ≤ 15% (TOF_2); TOFR at 16–25% (TOF_3); TOFR at 26–50% (TOF_4); or TOFR at 51–75% (TOF_5). No neuromuscular blockade (nNMB) was achieved when TOFR was more than 75%.

2.4 Monitoring the transcranial electric motor evoked potentials

TCeMEPs were triggered using a Xltek Protektor IOM (XLTEK Corporation, Oakville, CA). The stimulating electrodes of TCeMEPs were inserted subcutaneously over the motor cortex regions of C3 and C4 (International 10–20 system), where the compound muscle action potential (CMAP) was recorded from abductor halluces muscles (AH-TCeMEPs) and from tibialis anterior muscles (TA-TCeMEPs) bilaterally in the lower extremities. Transcranial stimulation consisted of a train of nine electrical pulses with pulse duration of 0.2–0.5 ms and stimulus intensity of

400 V. The recording parameters were: sweep = 150 ms, sensitivity = 100 μV/division, and bandpass = 30–1000 Hz. The absolute amplitude of TCeMEPs was evaluated by measuring the voltage from the lowest trough to the highest peak, while the absolute latency was defined as the span between the onset of the stimulation in a given sequence and the first assessable amplitude. Additionally, the absolute AUC of TCeMEPs, which was defined as a function of the total motor neuron activity over a particular temporal domain, was calculated [17]. Relative parameter of TCeMEPs on each pNMB phase was determined by comparing the absolute latency, amplitude and AUC to the nNMB baseline (which was preset at a value of 1). TCeMEPs were considered to be feasible if amplitude was above 50 mV [18]. TCeMEPs responses were considered false-positive if the amplitude of one or more of the muscle responses declined by ≥ 80% compared with the baseline that was independent of perioperative neurological deficits [19].

2.5 Statistical analysis

All statistical analyses were performed using SPSS 21.0 software (IBM Corporation., Armonk, NY). Measured continuous variables are summarized as the mean (SD) or median (IQR). ANOVA was performed to compare the anesthetic parameters among the six phases. Differences in absolute TCeMEP latency between the left and right side were identified using paired *t* test, while differences in absolute amplitude and AUC were determined by Wilcoxon signed rank test. The relative TCeMEP parameters of multiple pNMB were compared with the nNMB baseline using Wilcoxon signed rank test. Incidence data was compared using the χ^2 test or Fisher's exact test according to the expected counts. In all cases, a p-value of < 0.05 was considered significant.

3 Results

A total of 62 patients who underwent surgery for idiopathic scoliosis were included in the study. There was no new onset of postoperative neurological dysfunction. Reliable TCeMEP baselines were obtained in all patients, including seven patients for solo AH-TCeMEPs modality, 4 patients for solo TA-TCeMEPs modality and 51 patients for both modalities. The baseline characteristics for the total study population were outlined in Table 1. The comparison of anesthetic parameters among pNMB phases and nNMB phase was shown in Fig. 1. There was no significant difference among six phases during intraoperative TCeMEPs monitoring regarding the measured temperature, BIS and mean arterial pressure.

No significant differences were observed between the left side and right side in terms of the absolute latency, amplitude and AUC for both AH-TCeMEPs and TA-TCeMEPs modalities, respectively (Tables 2, 3). The latency of AH-TCeMEPs and TA-TCeMEPs were significantly extended at TOF_1 compared with nNMB, while no dramatic changes were observed at TOF_{2-5} (Fig. 2a, d). The amplitude and AUC of AH-TCeMEPs showed a significant decrease at TOF_{1-3} compared with nNMB. However, the parameters were not significantly changed at TOF_{4-5} (Fig. 2b, c). Statistically significant reductions were achieved at TOF_{1-2} with regard to the amplitude and AUC of TA-TCeMEPs compared with nNMB. However, the amplitude and AUC of TA-TCeMEPs did not differ between TOF_{3-5} and nNMB (Fig. 2e, f).

Efficacy of TCeMEPs involves feasibility and false-positive rate. The changes of feasibility and false-positive rate were in accordance with that of amplitude and AUC (Fig. 3). The feasibility of AH-TCeMEPs exhibited a sharp decrease at TOF_{1-3} compared with nNMB, and the false-positive rate was higher. No significant differences were observed between TOF_{4-5} and nNMB with regard to the feasibility and false-positive rate of AH-TCeMEPs. However, the feasibility rate of TA-TCeMEPs was significantly lower at TOF_{1-2} compared with nNMB, while the false-positive rate was higher. The feasibility and false-positive rate of TA-TCeMEPs did not differ between TOF_{3-5} and nNMB.

Throughout the study, unexpected movement was observed in 1 patient (1.6%) at TOF_3, 2 patients (3.2%) at TOF_4, 33 patients (53.2%) at TOF_5 and 54 patients (87.1%) at nNMB. The incidence of unexpected movement showed a significant increase at TOF_5 and nNMB compared with TOF_1 and TOF_4. No statistical changes were observed among TOF_1 to TOF_4 with regard to the rate of unexpected movement (Fig. 4).

Table 1 Characteristics of patients with idiopathic scoliosis undergoing posterior spinal fusion surgery (n = 62)

Demographics	Mean ± SD	Range
Age (year)	15.8 ± 3.3	11–26
Gender		
Male/female	11/51	
Weight (kg)	47.8 ± 6.3	31–62
Height (cm)	161.7 ± 7.8	145–182
BMI (kg m^{-2})	18.3 ± 2.3	14.2–25.9
Number of levels fused	9.6 ± 2.7	5–13
Preoperative cobb angle (°)	51.3 ± 10.3	40–82
Surgery time (min)	205.9 ± 47.2	130–325
Estimated blood loss (mL)	843.5 ± 415.3	200–1700
Autologous blood transfused (mL)	317.0 ± 192.1	0–750
Urine output (mL)	912.9 ± 320.1	200–1800
Fluid infusion volume (mL)	2541.1 ± 556.7	1500–3600

Values are mean (SD)

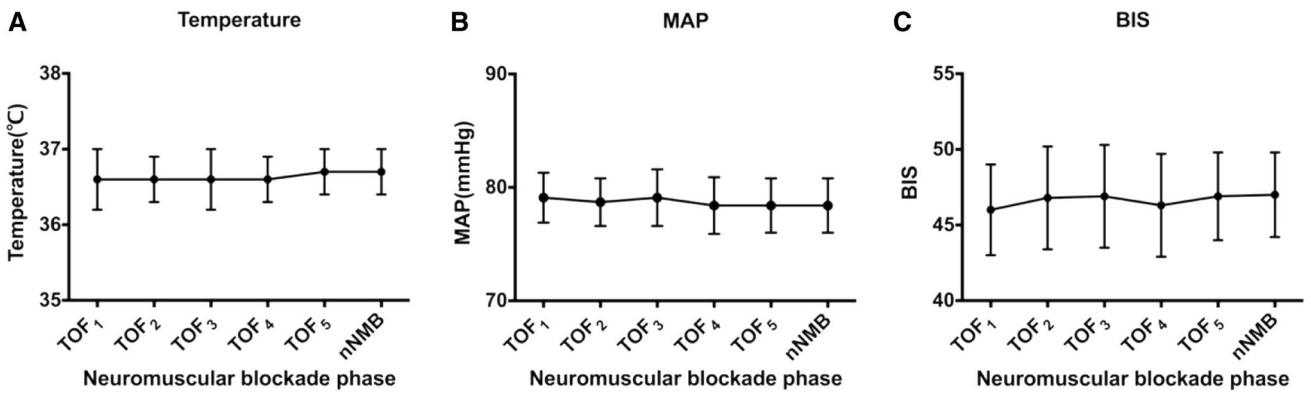

Fig. 1 Comparison of anesthetic parameters (**a** temperature, **b** MAP, **c** BIS) among pNMB phases and nNMB phase during TCeMEPs monitoring. *pNMB* partial neuromuscular blockade, TOF_1 one or two TOF counts, TOF_2 three TOF counts or TOFR ≤ 15%, TOF_3 TOFR at 16–25%, TOF_4 TOFR at 26–50%, TOF_5 TOFR at 51–75%, *nNMB* TOFR > 75%, *MAP* mean arterial pressure, *BIS* bispectral index. No significant difference among groups

4 Discussion

In this study, the research team investigated the effectiveness of varying levels of NMB with focus on the parameters and efficacy of TCeMEPs monitoring. Concomitantly, exploration of its effects on the unexpected movement during surgical correction of idiopathic scoliosis under total intravenous anesthesia was also conducted. The results of this retrospective study demonstrated that in patients with idiopathic scoliosis, the parameters of AH-TCeMEPs could be recorded at TOFR of 26–50% and those of TA-TCeMEPs could be recorded at TOFR of 16–50% (much like nNMB) without interfering with the efficacy of TCeMEPs monitoring or increasing the risk of unexpected movement.

The first clinical application of pNMB in TCeMEPs monitoring was reported in patients undergoing lumbar laminectomy/discectomy or lumbar spinal fusion, which demonstrated that TCeMEPs could be recorded at pNMB with T_1 twitch height of 5–15% [13]. Another clinical study reported that a stable pNMB phase aimed at T_1 twitch height of 45–55%, rather than 5–15%, of baseline provided reliable and recordable muscle responses sufficiently robust for TCeMEPs monitoring in aortic surgery [14]. In addition, the application of a stable level of pNMB with TOFR aimed at 50–75% was proven to be beneficial for intraoperative facial nerve monitoring [15]. The most plausible explanation for the controversial results was an overly simplistic classification of partial neuromuscular blockade, which did not account for the varying effects of pNMB on TCeMEPs monitoring. Indeed, Kalkman [13] only maintained pNMB aimed at T_1 twitch height of 5–15%, whereas additional classification of pNMB aimed at T_1 twitch height of 45–55% by van Dongen [14] led to contrasting results. Cengiz [15] drew another different conclusion when obtaining pNMB aimed at TOFR of 50 or 75%. In the current study, the neuromuscular blockade was classified into six phases exactly, through the reversal of the neuromuscular relaxation. The results showed that the application of a stable level of pNMB with TOFR aimed at 26–50% for AH-TCeMEPs or 16–50% for TA-TCeMEPs seems to be an appropriate regimen for TCeMEPs monitoring during surgical correction for scoliosis.

The reductions in amplitude and AUC probably represent reductions in number and timing of excited motor units responding to transcranial electric stimulation [14, 20]. Previously, Sloan [20] reported that the amplitude of TCeMEPs was not reduced to the same extent as was the NMB increase. Similarly, statistically significant reductions in AH-TCeMEPs were not achieved until TOFR was less than 26%, while reductions in TA-TCeMEPs were not achieved until TOFR was less than 16% in the current study. Additionally, the decreased amplitude of TCeMEPs may contribute to potential pitfalls in monitoring failure rate and false-positive results, which negatively affect the efficacy of TCeMEPs monitoring. The effects of pNMB on the false-positive results of TCeMEPs monitoring were evaluated by Kim [21], who concluded that there was no significant difference between pNMB aimed at T_1 twitch height of 50% and nNMB. By comparison, in the current study, the incidence of monitoring failure and false-positive results were not increased significantly until TOFR was less than 26% for the AH-TCeMEPs modality and TOFR was less than 16% for the TA-TCeMEPs modality.

However, low doses or avoidance of NMB may not be conducive to smooth surgical procedures when considering the increased risk of unexpected movement [13, 15]. Indeed, the influence of nNMB on TCeMEPs monitoring has been evaluated by Cengiz [15], who demonstrated that there were more slight movements or coughs with additional treatment of isoflurane under nNMB compared with

Table 2 Comparison of absolute parameters for AH-TCeMEPs modality between the left side and right side during different neuromuscular blockade phases (n = 62)

NMB phase	Latency (ms)			Amplitude (μV)			AUC (ms μV)		
	L	R	p value	L	R	p value	L	R	p value
TOF_1	39.38 (3.30)	39.98 (4.06)	0.898	101.70 (76.15–139.05 [50.10–212.20])	108.30 (71.85–139.25 [51.00–267.70])	0.829	1397.50 (1106.80–1968.80 [634.30–4566.70])	1633.30 (1128.20–1955.45 [631.60–4250.00])	0.534
TOF_2	38.22 (3.06)	38.29 (3.47)	0.935	162.10 (98.65–272.40 [52.70–437.60])	163.30 (128.55–253.20 [50.00–394.50])	0.514	3000.00 (1583.35–4150.00 [632.10–6833.30])	2600.00 (1891.65–4116.65 [599.10–6066.70])	0.495
TOF_3	38.24 (3.95)	38.25 (3.38)	0.122	225.10 (150.05–369.75 [60.00–558.70])	228.40 (146.50–329.55 [54.40–475.50])	0.772	3600.00 (2083.35–6000.00 [646.60–8700.00])	3233.30 (2041.00–5733.30 [676.50–8450.00])	0.866
TOF_4	38.26 (3.76)	38.26 (3.90)	0.995	319.50 (263.55–542.55 [76.00–814.90])	372.90 (229.35–527.80 [96.00–838.50])	0.417	6366.70 (3724.35–8710.00 [1117.00–11950.00])	7266.70 (3420.85–8450.00 [947.30–12750.00])	0.678
TOF_5	38.25 (3.53)	38.30 (3.84)	0.737	396.70 (231.60–534.10 [85.20–873.30])	373.60 (223.65–538.35 [94.40–957.30])	0.429	6560.00 (3300.00–9108.35 [1349.50–12850.00])	6600.00 (3050.00–8175.00 [934.60–14560.00])	0.715
nNMB	38.30 (3.92)	38.27 (4.09)	0.897	357.00 (275.05–571.95 [67.70–786.80])	435.50 (252.50–520.35 [91.70–1060.60])	0.725	7283.30 (4226.70–9145.85 [806.70–15600.00])	6966.7 (3953.35–8691.70 [1030.20–15455.60])	0.847

Values are mean (SD) or median (IQR [range])

Data were presented as mean (SD) or median (IQR)

AH-TCeMEPs abductor halluces muscles TCeMEPs, *NMB* neuromuscular blockade, *AUC* area under curve, *L* left side, *R* right side, TOF_1, one or two TOF counts, TOF_2 three TOF counts or TOFR ≤ 15%, TOF_3, TOFR at 16–25%; TOF_4, TOFR at 26–50%; TOF_5, TOFR at 51–75%; nNMB, TOFR > 75%

Table 3 Comparison of absolute parameters for TA-TCeMEPs modality between the left side and right side during different neuromuscular blockade phases

NMB phase	Latency (ms)			Amplitude (μV)			AUC (ms μV)		
	L	R	p value	L	R	p value	L	R	p value
TOF_1	28.56 (4.75)	28.82 (5.27)	0.107	100.60 (76.33–122.95 [52.10–176.20])	114.10 (68.03–152.13 [50.80–241.60])	0.133	1183.70 (973.38–1587.03 [644.00–2321.60])	1258.35 (765.90–1838.80 [634.70–3016.70])	0.372
TOF_2	27.46 (4.61)	27.36 (4.65)	0.870	159.75 (133.58–214.28 [50.10–343.70])	192.20 (140.30–240.83 [51.20–374.10])	0.470	2050.00 (1766.68–2970.80 [608.40–3866.70])	2187.50 (1724.98–2940.93 [549.20–4200.00])	0.789
TOF_3	27.83 (4.35)	27.66 (4.13)	0.569	322.10 (261.68–407.95 [52.60–778.80])	404.90 (299.60–566.23 [52.90–911.70])	0.148	4728.35 (3657.98–6408.30 [800.00–9866.70])	5749.25 (4060.43–7762.53 [915.40–9366.70])	0.720
TOF_4	27.73 (4.33)	27.66 (4.32)	0.819	310.30 (231.58–383.18 [54.20–855.70])	390.75 (267.20–630.25 [63.50–803.30])	0.260	4525.00 (3183.33–5937.50 [627.30–10600.00])	5180.35 (3237.50–8300.00 [840.90–11100.00])	0.747
TOF_5	27.85 (4.56)	27.75 (4.55)	0.744	301.55 (239.40–399.18 [83.30–889.20])	403.5 (264.03–604.55 [53.50–846.10])	0.828	4383.35 (3531.25–5100.83 [923.50–11650.00])	6508.35 (3024.98–7966.68 [759.60–11780.00])	0.833
nNMB	27.78 (4.47)	27.81 (4.67)	0.927	288.40 (212.53–449.28 [84.30–888.70])	464.25 (254.00–582.35 [52.00–850.00])	0.639	4233.35 (2974.98–7012.50 [934.10–11500.00])	7208.35 (3587.48–8299.98 [873.10–12650.00])	0.757

Values are mean (SD) or median (IQR [range])

Data were presented as mean (SD) or median (IQR)

TA-TCeMEPs tibialis anterior muscles TCeMEPs, *NMB* neuromuscular blockade, *AUC* area under curve, *L* left side, *R* right side, TOF_1 one or two TOF counts, TOF_2 three TOF counts or TOFR ≤ 15%, TOF_3 TOFR at 16–25%, TOF_4 TOFR at 26–50%, TOF_5 TOFR at 51–75%, *nNMB* TOFR > 75%

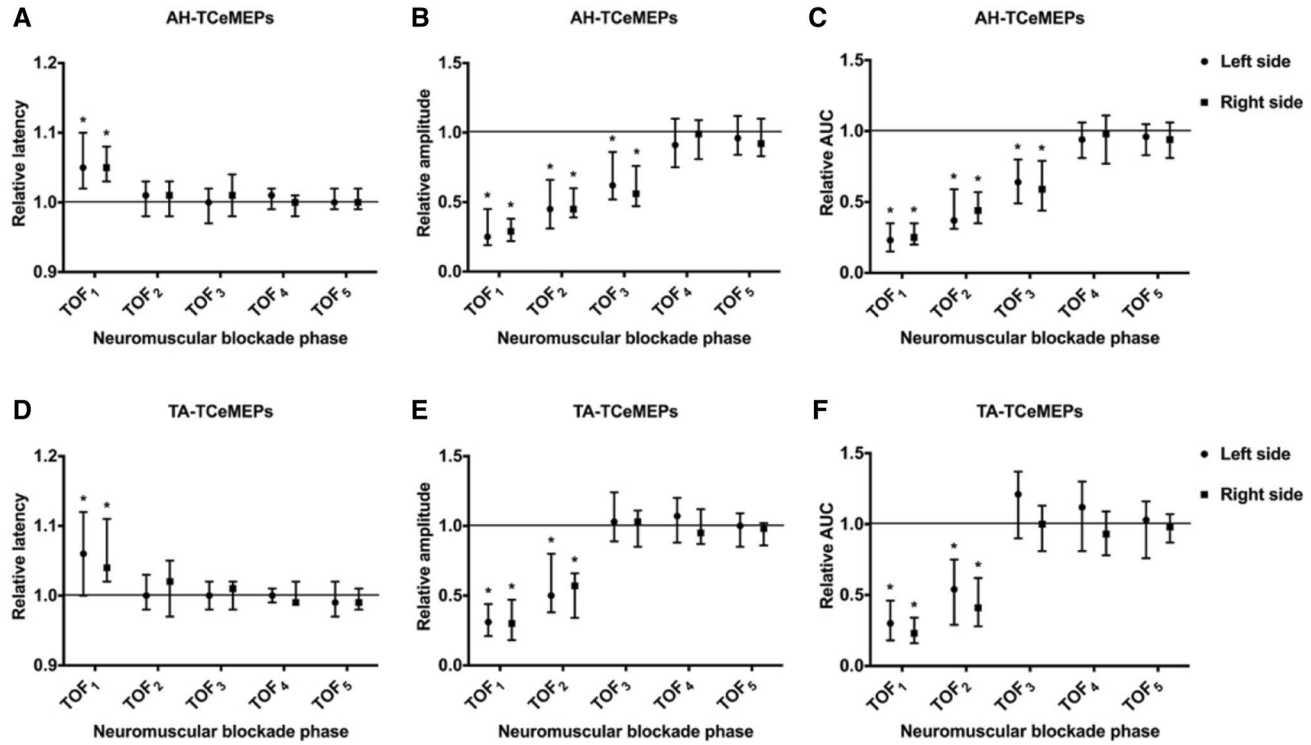

Fig. 2 Comparison of relative TCeMEPs parameters (left side: filled circle, right side: filled square) of multiple pNMB with nNMB baseline during TCeMEPs monitoring. Relative parameter of TCeMEPs on each pNMB phase was determined by referring the absolute latency, amplitude and AUC to the nNMB baseline (which was preset a value of 1). **P* indicates statistically significant different from that of nNMB. *AH-TCeMEPs* abductor halluces muscles TCeMEPs, *TA-TCeMEPs* tibialis anterior muscles TCeMEPs, *AUC* area under curve, *pNMB* partial neuromuscular blockade, TOF_1 one or two TOF counts, TOF_2 three TOF counts or TOFR ≤ 15%; TOF_3 TOFR at 16–25%, TOF_4 TOFR at 26–50%, TOF_5 TOFR at 51–75%; nNMB, TOFR > 75%

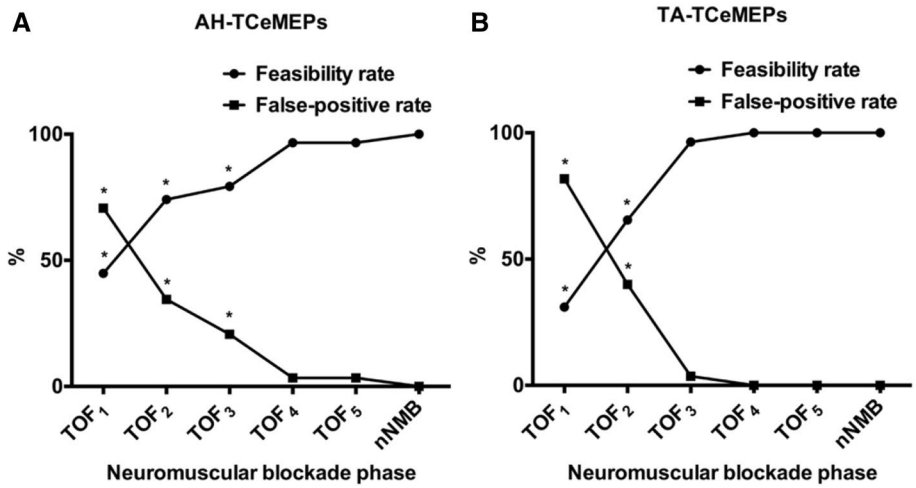

Fig. 3 Efficacy (feasibility rate: filled circle, false-positive rate: filled square) of TCeMEPs among pNMB phases and nNMB phase during TCeMEPs monitoring. **P* indicates significantly different from that of nNMB. *AH-TCeMEPs* abductor halluces muscles TCeMEPs, *TA-TCeMEPs* tibialis anterior muscles TCeMEPs, *AUC* area under curve, *pNMB* partial neuromuscular blockade, TOF_1 one or two TOF counts, TOF_2 three TOF counts or TOFR ≤ 15%; TOF_3 TOFR at 16–25%, TOF_4 TOFR at 26–50%, TOF_5 TOFR at 51–75%; nNMB, TOFR > 75%

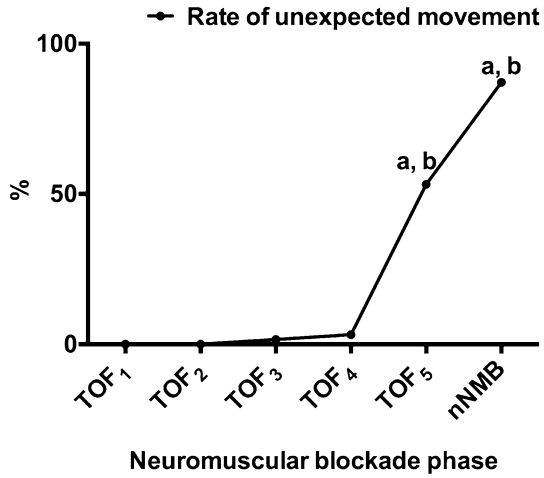

Fig. 4 The rate of unexpected movement among pNMB phases and nNMB phase during TCeMEPs monitoring. [a]*P* indicates significantly different from that of TOF_1; [b]*P* indicates significantly different from that of TOF_4. *pNMB* partial neuromuscular blockade, TOF_1 one or two TOF counts, TOF_2 three TOF counts or TOFR ≤ 15%; TOF_3 TOFR at 16–25%, TOF_4 TOFR at 26–50%, TOF_5 TOFR at 51–75%; nNMB, TOFR > 75%

pNMB. In a recent retrospective study involving 220 craniotomies for aneurysm clipping, Hemmer [22] observed that seven patients exhibited unacceptable movement with TCeMEPs monitoring in the absence of neuromuscular blocking drugs. The results of the current study agreed with the previous studies, which demonstrated the incidence rate of unexpected movement was significantly higher under nNMB. Additionally, the maintenance of some pNMB phases may not eliminate the risk of unexpected movement, and Yamatomo [23] reported that pNMB aimed at T_1 twitch height of 45–55% may elicit patient movement and interfere with surgery. In the current study, the incidence rate of unexpected movement was not decreased significantly until TOFR was less than 50%.

Interestingly, the results of the current study demonstrated a difference in the appropriate level of pNMB for AH-TCeMEPs compared to TA-TCeMEPs. This difference is possibly due to incongruent sensitivities of the involved muscle groups to neuromuscular blockade agents. Similarly, van Dongen [14] also demonstrated major differences in sensitivity to neuromuscular blocking drugs among muscle groups (tibialis anterior muscle vs extensor digitorum communis muscle) due to the unique physical and structural features, as well as the unique intrinsic physiological and biochemical properties, of each muscle. When only one modality can be used, TA-TCeMEPs seems to be more appropriate for surgical correction of idiopathic scoliosis, considering the wider range of pNMB for TCeMEPs monitoring. If AH-TCeMEPs and TA-TCeMEPs can be used in combination, pNMB aimed at 26–50% is recommended, as this level of pNMB can cover both of them and lead to the most acceptable level of unexpected movement.

In a previous study, Mahmoud [24] concluded that there was no significant difference between the left and right sides of the body in the nNMB state. However, Schwartz [25] observed differential sensitivity to neuromuscular blocking drugs for homologous muscles on the two sides of the body during pNMB phases. In the current study, no statistical difference existed between left and right sides of TCeMEPs monitoring among the six periods of NMB. It was confirmed that pNMB was feasible for intraoperative monitoring without interfering with the symmetry of TCeMEPs.

Other factors that could confound the interpretation of the differences between multiple pNMB phases and nNMB phase were analyzed. The temperature [26] and depth of anesthesia [5] were not changed throughout the study period, and the hemodynamics [27] of the patients were tightly controlled. The only factor that changed among the phases was the neuromuscular blockade.

In summary, the effects of varying levels of NMB on TCeMEPs monitoring and the risk of unexpected movement during surgical correction for idiopathic scoliosis under total intravenous anesthesia were investigated. The results demonstrate that the application of a stable level of pNMB with TOFR aimed at 26–50% for AH-TCeMEPs or 16–50% for TA-TCeMEPs seems to be an appropriate regimen for TCeMEPs monitoring. This regimen also seems adequate to avoid suboptimal operating conditions during surgical correction for idiopathic scoliosis under total intravenous anesthesia.

Acknowledgements The study was funded by the National Natural Science Foundation (81371207), the Key Talent's of 13th Five-year Plan for Strengthening Health of Jiangsu Province (ZDRCA2016069), the Key Talent's Project in Medical Science of Jiangsu Province (RC2011006), the Fundamental Research Funds for the Central Universities (0214-14380338), the Natural Science Foundation of Jiangsu Province of China (BK20170654) and the National Natural Science Foundation (81701371). We thank Hua-ye Xu, Jie Chen, Fen Song and Shi-he Cui, who are anesthetists in the department of Anesthesiology, Affiliated Drum Tower Hospital of Medical Department of Nanjing University. We also thank Jun-yin Qiu, neurologist in the department of Orthopaedic Surgery, Affiliated Drum Tower Hospital of Medical Department of Nanjing University for her invaluable assistance in collecting the data in this study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Vitale MG, Moore DW, Matsumoto H, Emerson RG, Booker WA, Gomez JA, Gallo EJ, Hyman JE, Roye DP Jr. Risk factors for

spinal cord injury during surgery for spinal deformity. J Bone Joint Surg. 2010;92(1):64–71. https://doi.org/10.2106/jbjs.h.01839.
2. Neira VM, Ghaffari K, Bulusu S, Moroz PJ, Jarvis JG, Barrowman N, Splinter W. Diagnostic accuracy of neuromonitoring for identification of new neurologic deficits in pediatric spinal fusion surgery. Anesth Analg. 2016;123(6):1556–66. https://doi.org/10.1213/ane.0000000000001503.
3. Pastorelli F, Di Silvestre M, Plasmati R, Michelucci R, Greggi T, Morigi A, Bacchin MR, Bonarelli S, Cioni A, Vommaro F, Fini N, Lolli F, Parisini P. The prevention of neural complications in the surgical treatment of scoliosis: the role of the neurophysiological intraoperative monitoring. Eur Spine J. 2011;20(Suppl 1):105–14. https://doi.org/10.1007/s00586-011-1756-z.
4. Thuet ED, Winscher JC, Padberg AM, Bridwell KH, Lenke LG, Dobbs MB, Schootman M, Luhmann SJ. Validity and reliability of intraoperative monitoring in pediatric spinal deformity surgery: a 23-year experience of 3436 surgical cases. Spine. 2010;35(20):1880–6. https://doi.org/10.1097/BRS.0b013e3181e53434.
5. Ohtaki S, Akiyama Y, Kanno A, Noshiro S, Hayase T, Yamakage M, Mikuni N. The influence of depth of anesthesia on motor evoked potential response during awake craniotomy. J Neurosurg. 2017;126(1):260–5. https://doi.org/10.3171/2015.11.jns151291.
6. Lieberman JA, Feiner J, Lyon R, Rollins MD. Effect of hemorrhage and hypotension on transcranial motor-evoked potentials in swine. Anesthesiology. 2013;119(5):1109–19. https://doi.org/10.1097/ALN.0b013e31829d4a92.
7. Sakamoto T, Kawaguchi M, Kakimoto M, Inoue S, Takahashi M, Furuya H. The effect of hypothermia on myogenic motor-evoked potentials to electrical stimulation with a single pulse and a train of pulses under propofol/ketamine/fentanyl anesthesia in rabbits. Anesth Analg. 2003;96(6):1692–7 (**table of contents**).
8. Sloan TB, Heyer EJ. Anesthesia for intraoperative neurophysiologic monitoring of the spinal cord. J Clin Neurophysiol. 2002;19(5):430–43.
9. Tsutsui S, Iwasaki H, Yamada H, Hashizume H, Minamide A, Nakagawa Y, Nishi H, Yoshida M. Augmentation of motor evoked potentials using multi-train transcranial electrical stimulation in intraoperative neurophysiologic monitoring during spinal surgery. J Clin Monit Comput. 2015;29(1):35–9. https://doi.org/10.1007/s10877-014-9565-7.
10. Yang J, Huang Z, Shu H, Chen Y, Sun X, Liu W, Dou Y, Xie C, Lin X, Hu Y. Improving successful rate of transcranial electrical motor-evoked potentials monitoring during spinal surgery in young children. Eur Spine J. 2012;21(5):980–4. https://doi.org/10.1007/s00586-011-1995-z.
11. Azabou E, Manel V, Andre-obadia N, Fischer C, Mauguiere F, Peiffer C, Lofaso F, Shils JL. Optimal parameters of transcranial electrical stimulation for intraoperative monitoring of motor evoked potentials of the tibialis anterior muscle during pediatric scoliosis surgery. Clin Neurophysiol. 2013;43(4):243–50. https://doi.org/10.1016/j.neucli.2013.08.001.
12. Mendiratta A, Emerson RG. Neurophysiologic intraoperative monitoring of scoliosis surgery. J Clin Neurophysiol. 2009;26(2):62–9. https://doi.org/10.1097/WNP.0b013e31819f9049.
13. Kalkman CJ, Drummond JC, Kennelly NA, Patel PM, Partridge BL. Intraoperative monitoring of tibialis anterior muscle motor evoked responses to transcranial electrical stimulation during partial neuromuscular blockade. Anesth Analg. 1992;75(4):584–9.
14. van Dongen EP, ter Beek HT, Schepens MA, Morshuis WJ, Langemeijer HJ, de Boer A, Boezeman EH. Within-patient variability of myogenic motor-evoked potentials to multipulse transcranial electrical stimulation during two levels of partial neuromuscular blockade in aortic surgery. Anesth Analg. 1999;88(1):22–7.
15. Cengiz M, Ganidagli S, Alatas N, San I, Baysal Z. Partial neuromuscular blockage levels with mivacurium during mastoidectomy allows intraoperative facial nerve monitoring. ORL. 2008;70(4):236–241. https://doi.org/10.1159/000130871.
16. Claudius C, Viby-Mogensen J. Acceleromyography for use in scientific and clinical practice: a systematic review of the evidence. Anesthesiology. 2008;108(6):1117–40. https://doi.org/10.1097/ALN.0b013e318173f62f.
17. Leon-Sarmiento FE, Rizzo-Sierra CV, Leon-Ariza JS, Leon-Ariza DS, Sobota R, Prada DG. A new neurometric dissection of the area-under-curve-associated jiggle of the motor evoked potential induced by transcranial magnetic stimulation. Physiol Behav. 2015;141:111–9. https://doi.org/10.1016/j.physbeh.2015.01.014.
18. Tamkus AA, Rice KS, Kim HL. Differential rates of false-positive findings in transcranial electric motor evoked potential monitoring when using inhalational anesthesia versus total intravenous anesthesia during spine surgeries. Spine J. 2014;14(8):1440–6. https://doi.org/10.1016/j.spinee.2013.08.037.
19. Zhuang Q, Wang S, Zhang J, Zhao H, Wang Y, Tian Y, Zhao Y, Li S, Weng X, Qiu G, Shen J. How to make the best use of intraoperative motor evoked potential monitoring? Experience in 1162 consecutive spinal deformity surgical procedures. Spine. 2014;39(24):E1425–32. https://doi.org/10.1097/brs.0000000000000589.
20. Sloan TB, Erian R. Effect of vecuronium-induced neuromuscular blockade on cortical motor evoked potentials. Anesthesiology. 1993;78(5):966–73.
21. Kim WH, Lee JJ, Lee SM, Park MN, Park SK, Seo DW, Chung IS. Comparison of motor-evoked potentials monitoring in response to transcranial electrical stimulation in subjects undergoing neurosurgery with partial vs no neuromuscular block. Br J Anaesth. 2013;110(4):567–76. https://doi.org/10.1093/bja/aes395.
22. Hemmer LB, Zeeni C, Bebawy JF, Bendok BR, Cotton MA, Shah NB, Gupta DK, Koht A. The incidence of unacceptable movement with motor evoked potentials during craniotomy for aneurysm clipping. World Neurosurg. 2014;81(1):99–104. https://doi.org/10.1016/j.wneu.2012.05.034.
23. Yamamoto Y, Kawaguchi M, Hayashi H, Horiuchi T, Inoue S, Nakase H, Sakaki T, Furuya H. The effects of the neuromuscular blockade levels on amplitudes of posttetanic motor-evoked potentials and movement in response to transcranial stimulation in patients receiving propofol and fentanyl anesthesia. Anesth Analg. 2008;106(3):930–4. https://doi.org/10.1213/ane.0b013e3181617508 (**table of contents**).
24. Mahmoud M, Sadhasivam S, Salisbury S, Nick TG, Schnell B, Sestokas AK, Wiggins C, Samuels P, Kabalin T, McAuliffe J. Susceptibility of transcranial electric motor-evoked potentials to varying targeted blood levels of dexmedetomidine during spine surgery. Anesthesiology. 2010;112(6):1364–73. https://doi.org/10.1097/ALN.0b013e3181d74f55.
25. Schwartz DM, Sestokas AK, Dormans JP, Vaccaro AR, Hilibrand AS, Flynn JM, Li PM, Shah SA, Welch W, Drummond DS, Albert TJ. Transcranial electric motor evoked potential monitoring during spine surgery: is it safe? Spine. 2011;36(13):1046–9. https://doi.org/10.1097/BRS.0b013e3181ecbe77.
26. Oro J, Haghighi SS. Effects of altering core body temperature on somatosensory and motor evoked potentials in rats. Spine. 1992;17(5):498–503.
27. Schwartz DM, Auerbach JD, Dormans JP, Flynn J, Drummond DS, Bowe JA, Laufer S, Shah SA, Bowen JR, Pizzutillo PD, Jones KJ, Drummond DS. Neurophysiological detection of impending spinal cord injury during scoliosis surgery. J Bone Joint Surg. 2007;89(11):2440–9. https://doi.org/10.2106/jbjs.f.01476.