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Comparison of motor-evoked potentials monitoring in response to transcranial electrical stimulation in subjects undergoing neurosurgery with partial *vs* no neuromuscular block†

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Editor's key points

- Motor-evoked potential monitoring is commonly performed during neurosurgery to monitor the integrity of the motor pathways.
- Maintenance of neuromuscular block after tracheal intubation can interfere with MEP monitoring.
- Some anaesthetists nonetheless maintain partial neuromuscular block during MEP monitoring to prevent evoked and spontaneous movements.
- The authors compared MEP amplitudes and variability during different degrees of partial neuromuscular block.

Background. There have been no evidence-based comparisons of motor-evoked potential (MEP) monitoring with no and partial neuromuscular block (NMB). We compared the effects of different levels of NMB including no NMB on MEP parameters.

Methods. MEP-monitored 120 patients undergoing neurosurgery were enrolled. The patients were randomly allocated to four groups: Group A was to maintain two train-of-four (TOF) counts; Group B was to maintain a T_1/Tc of 0.5; Group C was to maintain a T_2/Tc of 0.5 ($T_{1,2}$, first or second twitch height of TOF; Tc, control twitch height); Group D did not maintain NMB. The mean MEP amplitude, coefficient of variation (CV), the incidence of spontaneous respiration or movement, the efficacy of MEP, and haemodynamic parameters were compared.

Results. The median [inter-quartile range (IQR)] amplitudes of the left leg for Groups A, B, C, and D were 0.23 (0.15–0.57), 0.44 (0.19–0.79), 0.28 (0.15–0.75), and 0.75 (0.39–1.35) mV, respectively. The median (IQR) CVs of the left leg were 71.1 (56.9–88.8), 76.1 (54.2–93.1), 59.8 (48.6–95.6), and 25.2 (17.3–35.0), respectively. The differences between groups of the mean amplitudes of the left arm and both legs were statistically significant (Kruskal–Wallis test, $P=0.011$ for the left leg). For all limbs, the differences between groups of the CVs were significant ($P<0.001$, for the left leg). Other parameters were not different.

Conclusions. If NMB is used during MEP monitoring, a target T_2/Tc of 0.5 is recommended. In terms of the MEP amplitude and variability, no NMB was more desirable than any level of partial NMB.

Keywords: motor-evoked potentials; neuromuscular block; neurosurgery; vecuronium

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While muscle relaxation is not desirable for intraoperative motor-evoked potential (MEP) monitoring during neurosurgery, some surgeons, neurophysiologists, and anaesthesiologists still prefer to use the continuous infusion of neuromuscular blocking agents to maintain partial neuromuscular block (NMB).[1–7] Those who advocate for partial NMB insist that the complete omission of NMB could result in problems such as difficulty in exposing the surgical field, especially during spine surgery, and also the risk of unexpected patient movement.[2 5 6] However, most institutions do not use neuromuscular blocking agents during MEP[8–11] as NMB can reduce the MEP amplitude.[12 13]

Authors who have advocated partial NMB recommend a blockade with T_1 between 5% and 50% of baseline or one or two twitches in a train-of-four (TOF) electrical stimulation of the ulnar nerve.[5–7 14–17] However, in our experience, these levels of NMB seem to cause significant depression and fluctuation in the MEP amplitude and some controversy exists regarding the allowable degree of muscle relaxation for MEP monitoring.[6] There have been no evidence-based comparisons of partial NMB and no NMB on MEP monitoring amplitude, variability, or efficacy. Additional data on anaesthetic parameters such as spontaneous patient movement and haemodynamics are similarly unavailable. As such, there is

† This article is accompanied by Editorial III.

a need to determine the allowable degree of partial NMB during MEP and to compare these effects with those observed when not maintaining NMB.

Towards this purpose, we evaluated the effects of various levels of controlled muscle relaxation, including no NMB, on MEP parameters, efficacy, and other anaesthetic parameters.

Methods

Patients

This study was approved by the Samsung Medical Centre Institutional Review Board (2011-04-010) and registered at www.clinicaltrials.gov (protocol ID NCT01388868). All patients provided informed consent. Between June 2011 and February 2012, patients were enrolled in this prospective randomized study if they were receiving MEP monitoring while undergoing cerebral aneurysm clipping or if they were having tumours removed through craniotomies or spinal laminectomies. Patients were excluded from the study if they had an ASA physical status classification of III or greater. Those who could not undergo MEP monitoring due to central or peripheral neuromuscular diseases such as cerebral palsy, myasthenia gravis, acute spinal injury, or neurologic shock were also excluded from the present study.

General anaesthesia and study protocol

Anaesthesia was induced by i.v. propofol (4–6 μg ml^{-1}) with remifentanil (2–4 ng ml^{-1}) through a target-controlled infusion pump (Orchestra^{TM}, Fresenius Vial, France). After induction, tracheal intubation was facilitated with rocuronium (0.6 mg kg^{-1}). Before rocuronium administration, the baseline twitch response was established with a neuromuscular transmission module (M-NMT Module$^{®}$, Datex-Ohmeda Inc., Helsinki, Finland). This module automatically searched for the stimulus current to achieve the maximum response of the adductor pollicis muscle. The maximum electromyographic amplitude of T_1 before rocuronium administration was considered to be the control response (Tc). Anaesthesia was maintained with propofol and remifentanil infusions through the Orchestra pump. Remifentanil was titrated at a dose range of 2–5 ng ml^{-1} to control the haemodynamic response to the surgical procedure within a 20% range of its preoperative value, and propofol was infused at a dose range of 3–6 μg ml^{-1}. The remifentanil dose was adjusted by 1 ng ml^{-1} until the mean arterial pressure was maintained within the target range and did not decrease below 2 ng ml^{-1}. The mean arterial pressure during the surgery was recorded every 5 min and was compared between the groups. Hypotension was defined as a decrease in the mean arterial pressure of more than 20% of the preoperative value or below 55 mm Hg and was treated by repeated 5 mg i.v. ephedrine bolus doses. Vasopressor infusion (phenylephrine 0.3–1.0 μg kg^{-1} min^{-1}) was given if three or more ephedrine bolus doses were required. If bradycardia ($<$60 beats min^{-1}) developed, 0.5 mg of atropine was administered. All patients were administered 4 ml kg^{-1} h^{-1} of lactated Ringer's solution during surgery, and blood loss was replaced by Voluven$^{®}$ (Fresenius Kabi, Bad Homburg, Germany). The use of these drugs was compared between the groups. Continuous end-tidal CO_2 monitoring was performed and maintained within a range of 4.0–4.7 kPa. Intraoperative monitoring included continuous ECG, pulse oximetry, arterial pressure (via arterial line and non-invasive arterial pressure cuff), and oesophageal temperature. The monitoring of transcranial electrophysiology for major brain or spinal cord surgery was performed by recording MEP and somatosensory-evoked potentials. The muscle being recorded for TOF and MEP was kept warm to maintain body temperature with a warm blanket.

Subjects were randomly allocated into one of the four groups and were given doses of the neuromuscular blocking agent vecuronium adjusted every 15 min according to the group's NMB target. For the groups receiving partial NMB, the goals were as follows: Group A was to maintain a two-count response of TOF stimulation of the ulnar nerve; Group B was to maintain a 0.5 twitch height of the first evoked response of TOF stimulation (T_1) compared with the control twitch (Tc); Group C was to maintain a 0.5 twitch height of the second evoked response of TOF stimulation (T_2) compared with Tc. Group D did not receive vecuronium infusion.

The primary outcome measurement of the present study was the MEP amplitude, and also the coefficient of variation (CV, %) of all measured MEP amplitudes. This CV was calculated as the standard deviation (SD) of the MEP amplitude divided by the mean value. The MEP amplitude was obtained and recorded by the neurophysiologists (i) at baseline after the rocuronium was administered (TOF count of 4 and T_1/Tc of about 75%) and before the vecuronium infusion was started and (ii) at 15 min intervals throughout the period of MEP monitoring (Fig. 1).

Other variables measured and compared among the groups during surgery were (i) the incidence of patient spontaneous movements or respiration during MEP monitoring, (ii) any positive MEP changes during the surgery, (iii) the new onset of postoperative neurological dysfunction, (iv) the doses of anaesthetics administered, and (v) the continuous end-tidal CO_2 measurements. Spontaneous movement was reported by the attending surgeon, who was blinded to the study group of the patient. The anaesthesiologist then measured and recorded whether the movement occurred during microscopic (e.g. removal of tumour or clipping of aneurysm) or macroscopic (e.g. dissection of the surgical field) surgery. Spontaneous respiration was reported by the attending anaesthetists.

The response of the adductor pollicis brevis muscle to TOF stimulation of the ulnar nerve by the NMT module was monitored every 15 min, and the infusion dose of vecuronium was adjusted according to the target of the partial NMB group. In Group D, no neuromuscular blocking agent was infused after the intubating dose of rocuronium. After the surgery, the neurosurgeon evaluated the presence of neurological dysfunction, and neurophysiologists evaluated its correlation with intraoperative positive changes in MEP. Reductions in the MEP amplitude of $>$50% or a loss of MEP for three consecutive

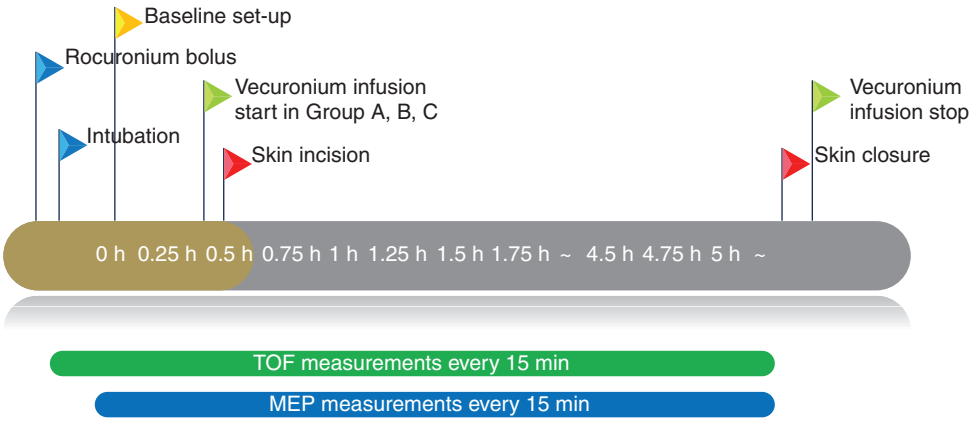

Fig 1 A flow diagram showing the time course of the measurements obtained in the present study.

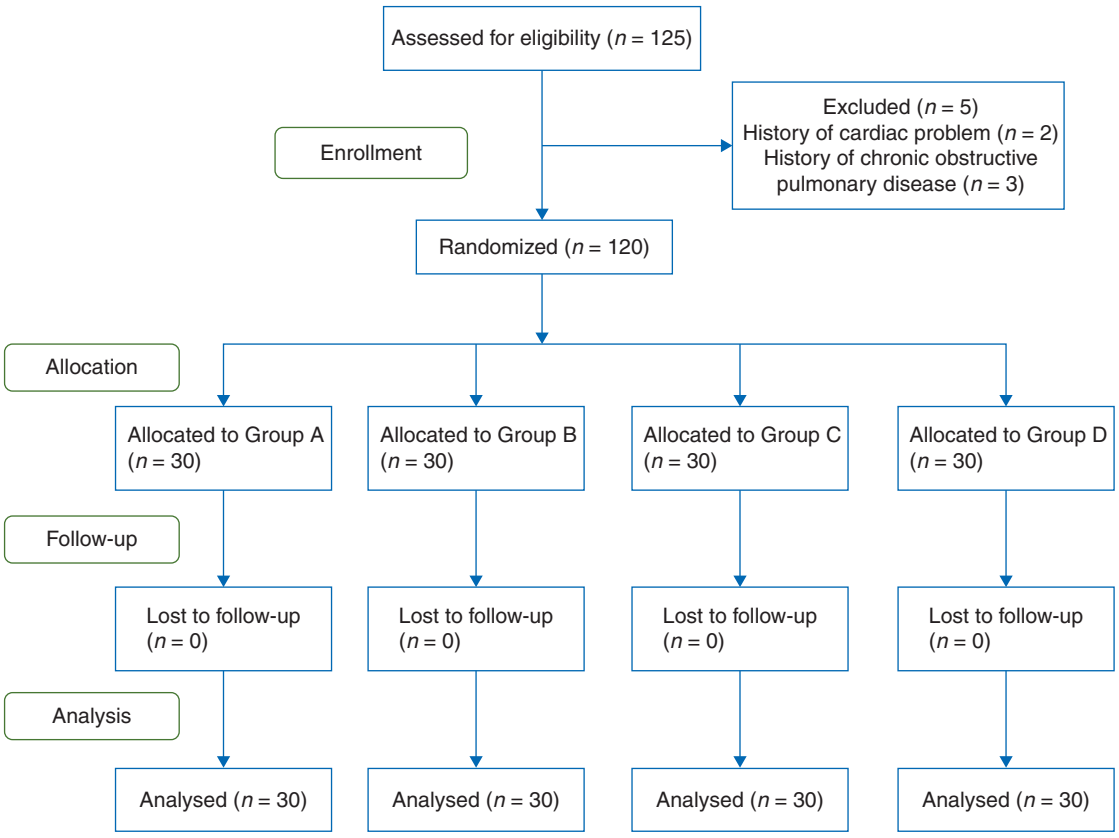

Fig 2 Study design according to CONSORT 2010 flow diagram.

trials were considered to be positive MEP changes, indicating impairment of the functional integrity of the motor pathway.

Acquisition of MEP

Neuromonitoring subdermal needle electrodes (Xi'an Friendship Med Electronics Co., Shaanxi, China) were positioned and secured after intubation by a neurophysiologist, who was blinded to the study group of the patient. Myogenic MEPs were acquired by electrical stimulation of the scalp, and the peripheral responses from target muscles were recorded. MEPs were triggered using a Xltek Protektor IOM (Optima Medical Ltd, London, UK) that delivered electrical stimulus pulse trains (pulse width=50 μs, n=5, interpulse interval=2

Table 1 Comparison of patient characteristics and perioperative clinical variables. Values are mean (SD), mean (range), or median (IQR). BMI, body mass index. Surgery types are the case numbers of (i) craniotomy and tumour removal, (ii) cerebral aneurysm clipping, and (iii) spinal laminectomy sequentially. [a]Significantly different from that of Group A; [b]significantly different from that of Group B; [c]significantly different from that of Group C; [d]significantly different from that of Group D. *P*-values are results of one-way analysis of variance or the Kruskal–Wallis test according to the normality of the data for continuous variables, and χ^2 test for incidence variables

	Group A (*n*=30)	Group B (*n*=30)	Group C (*n*=30)	Group D (*n*=30)	*P*-value
Gender (M/F)	13/17	12/18	14/16	13/17	0.965
Age (yr)	51 (17–80)	47 (19–83)	51 (13–78)	47 (13–75)	0.576
Weight (kg)	65 (13)	64 (10)	61 (13)	62 (9)	0.530
Height (cm)	165 (160–167)[c]	162 (158–164)	157 (155–161)[a,d]	163 (162–164)[c]	0.009
BMI (kg m^{-2})	24.6 (3.2)	24.4 (3.1)	23.6 (3.4)	23.7 (2.6)	0.473
Surgery time (min)	183 (152–229)	175 (107–305)	190 (90–243)	242 (143–298)	0.213
Surgery type (*n*)	11/10/9	11/9/10	13/10/7	12/10/8	0.989
Mean propofol dose (μg ml^{-1})	4.3 (0.6)	4.3 (0.7)	4.3 (0.7)	4.6 (0.6)	0.215
Mean remifentanil dose (ng ml^{-1})	2.5 (0.8)[d]	2.8 (0.9)	2.5 (1.0)[d]	3.2 (0.8)[a,c]	0.007
Mean vecuronium dose (μg kg^{-1} min^{-1})	0.78 (0.22)	0.77 (0.23)	0.61 (0.18)[a,b]	—	—
Mean end-tidal CO_2 (kPa)	4.4 (0.2)	4.3 (0.2)	4.4 (0.2)[d]	4.3 (0.2)[c]	0.045

Table 2 Comparison of MEP parameters among the groups. Values are median (IQR) or number. [a]Significantly different from that of Group A; [b]significantly different from that of Group B; [c]significantly different from that of Group C; [d]significantly different from that of Group D. *P*-values are the results of the Kruskal–Wallis test for continuous variables and Fisher's exact test for categorical variables among the four groups. MEP, motor-evoked potential monitoring; APB, abductor pollicis brevis; TA, tibialis anterior. The mean amplitude means the average of all the amplitude values at all time points. The CV of MEP amplitude (%) means the SD of MEP amplitude divided by the mean MEP amplitude value. *This case of brain tumour removal was correlated with the positive intraoperative MEP change

	Group A	Group B	Group C	Group D	*P*-value
Mean stimulus intensity (V)	400 (400–400)	400 (388–400)	400 (400–400)	400 (350–400)	0.626
Baseline MEP amplitude (mV)					
Right arm (APB)	0.79 (0.05–1.51)	0.99 (0.64–1.16)	0.51 (0.33–1.05)	0.87 (0.30–1.23)	0.391
Left arm (APB)	0.67 (0.28–1.28)	0.70 (0.43–1.14)	0.65 (0.43–0.72)	0.86 (0.48–1.42)	0.253
Right leg (TA)	0.28 (0.11–0.57)[c]	0.18 (0.06–0.73)	0.10 (0.05–0.20)[a,d]	0.35 (0.09–0.96)[c]	0.067
Left leg (TA)	0.12 (0.04–0.35)[d]	0.10 (0.04–0.58)[d]	0.14 (0.05–0.38)[d]	0.67 (0.25–0.97)[a,b,c]	0.001
Mean MEP amplitude (mV)					
Right arm (APB)	0.87 (0.33–1.42)	0.81 (0.53–1.14)	0.93 (0.31–2.02)	0.77 (0.47–1.90)	0.811
Left arm (APB)	0.84 (0.44–1.15)[d]	0.72 (0.38–0.94)[c,d]	1.15 (0.61–1.58)[b]	1.14 (0.51–1.92)[a,b]	0.007
Right leg (TA)	0.16 (0.06–0.57)[b,c,d]	0.53 (0.16–0.80)[a]	0.50 (0.37–0.82)[a]	0.90 (0.19–1.40)[a]	0.002
Left leg (TA)	0.23 (0.15–0.57)[d]	0.44 (0.19–0.79)	0.28 (0.15–0.75)[d]	0.75 (0.39–1.35)[a,c]	0.011
Coefficient of variation (CV) (%)					
Right arm (APB)	57.2 (36.5–104.5)[c,d]	61.9 (45.8–83.3)[d]	41.0 (21.9–73.4)[a]	36.0 (23.0–53.4)[a,b]	0.002
Left arm (APB)	74.9 (48.4–119.4)[c,d]	59.4 (32.5–87.9)[d]	42.7 (20.2–72.3)[a]	42.9 (13.1–56.1)[a,b]	<0.001
Right leg (TA)	76.5 (49.0–93.8)[d]	75.0 (49.7–123.3)[d]	60.1 (53.1–92.9)[d]	24.6 (12.6–76.8)[a,b,c]	<0.001
Left leg (TA)	71.1 (56.9–88.8)[d]	76.1 (54.2–93.1)[d]	59.8 (48.6–95.6)[d]	25.2 (17.3–35.0)[a,b,c]	<0.001
Preoperative neurological dysfunction (*n*)	3	1	1	2	0.834
Postoperative neurological dysfunction (*n*)	4	1	1	2	0.522
Newly onset postoperative neurological dysfunction (*n*)	1*	0	0	0	0.999
Positive MEP change during surgery (*n*)	4	2	1	2	0.625
Incidence of spontaneous movement (*n*)	1	0	1	1	0.999
Incidence of spontaneous respiration (*n*)	2	1	2	1	0.999

ms, 500 Hz) between two needle-type electrodes placed over the motor cortex region at C3 and C4 (international 10–20 system).[18–20] Recording of the MEP was accomplished by placing pairs of subdermal needle electrodes in target muscle groups in all four extremities and by observing the electromyographic responses. MEPs were recorded using

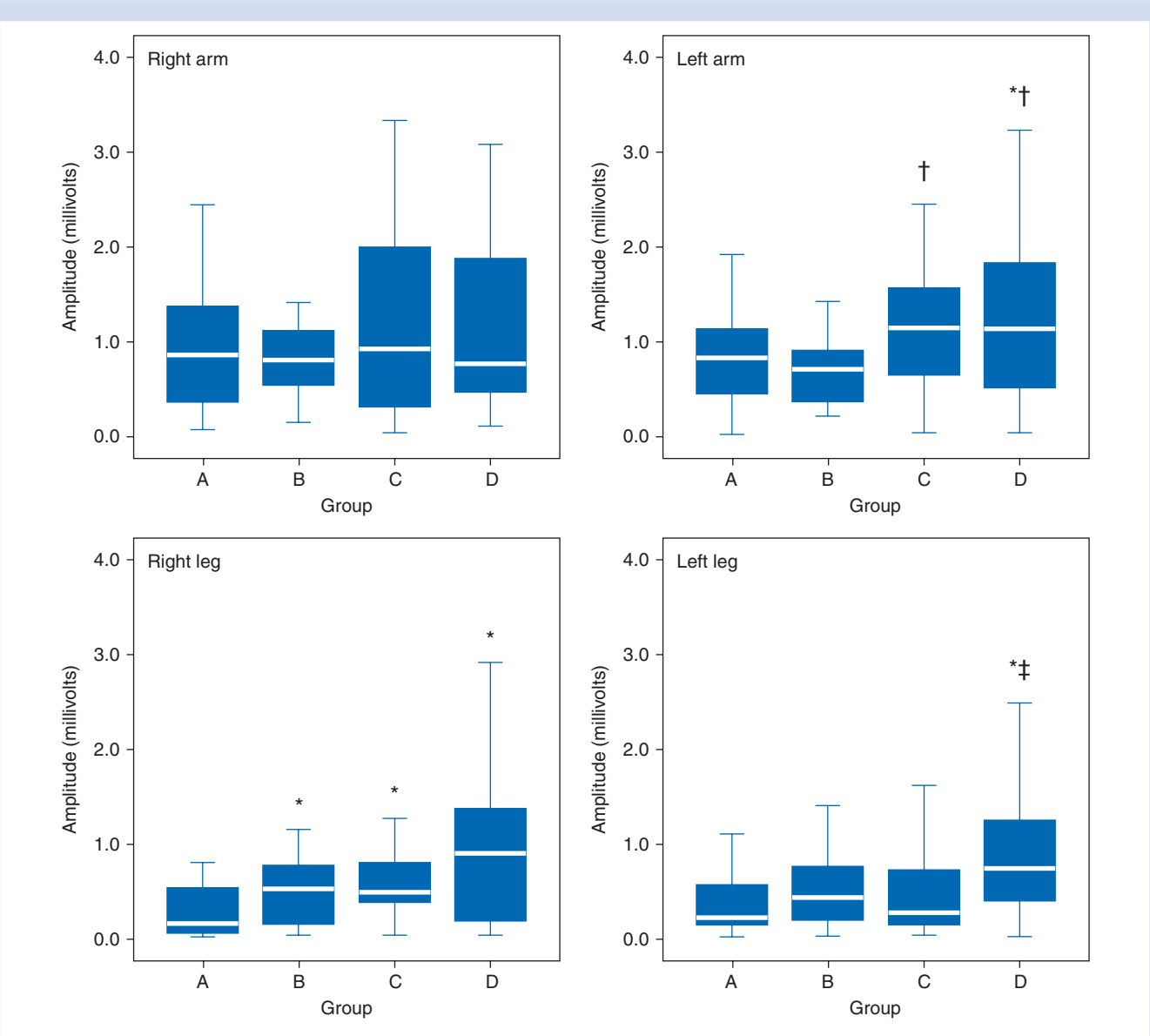

Fig 3 Box plots of transcranial electrical MEP amplitude from both arms and legs obtained after train-of-five pulse transcranial electrical stimulation were shown. Each group aimed at the targets of a TOF of 2 (Group A), a T_1/Tc of 0.5 (Group B), a T_2/Tc of 0.5 (Group C), and no NMB (Group D). Tc is the control twitch response obtained before the administration of the neuromuscular blocking agent. T_1 and T_2 are the first and second twitch responses of the TOF stimulation of the ulnar nerve, respectively. Horizontal bars represent the 90th, 75th, median, 25th, and 10th percentile. *$P<0.05$ compared with Group A; †$P<0.05$ compared with Group B; ‡$P<0.05$ compared with Group C.

needle electrodes inserted into the bilateral tibialis anterior, the abductor hallucis muscles in the lower extremities, the bilateral abductor pollicis brevis, and the adductor digitorum quint muscles in the upper extremities. The optimal baseline amplitude was obtained by adjusting the MEP stimulus intensity in intervals of 50 V from a starting value of 400 V, and lower stimulus intensity was chosen if adequate amplitude is obtained. This stimulus intensity was determined at the beginning of MEP monitoring and was kept constant. Neurophysiological signals were recorded using a commercially available neuromonitoring system (Xltek EP Works, Optima Medical Ltd).

Statistical analysis

The sample size was determined after our pilot study to obtain the SD of the MEP amplitude. A power analysis was performed ($\alpha=0.05$, $\beta=0.20$), indicating that at least 28 patients should be recruited for each group. For this calculation, we assumed the MEP amplitude of the non-paralysed group to be greater than those of the paralysed groups by more than 50%. To compensate for potential dropouts, 30 patients were assigned to each group.

All statistical analyses were performed using SPSS software (SPSS 20.0, Chicago, IL, USA). Measured continuous

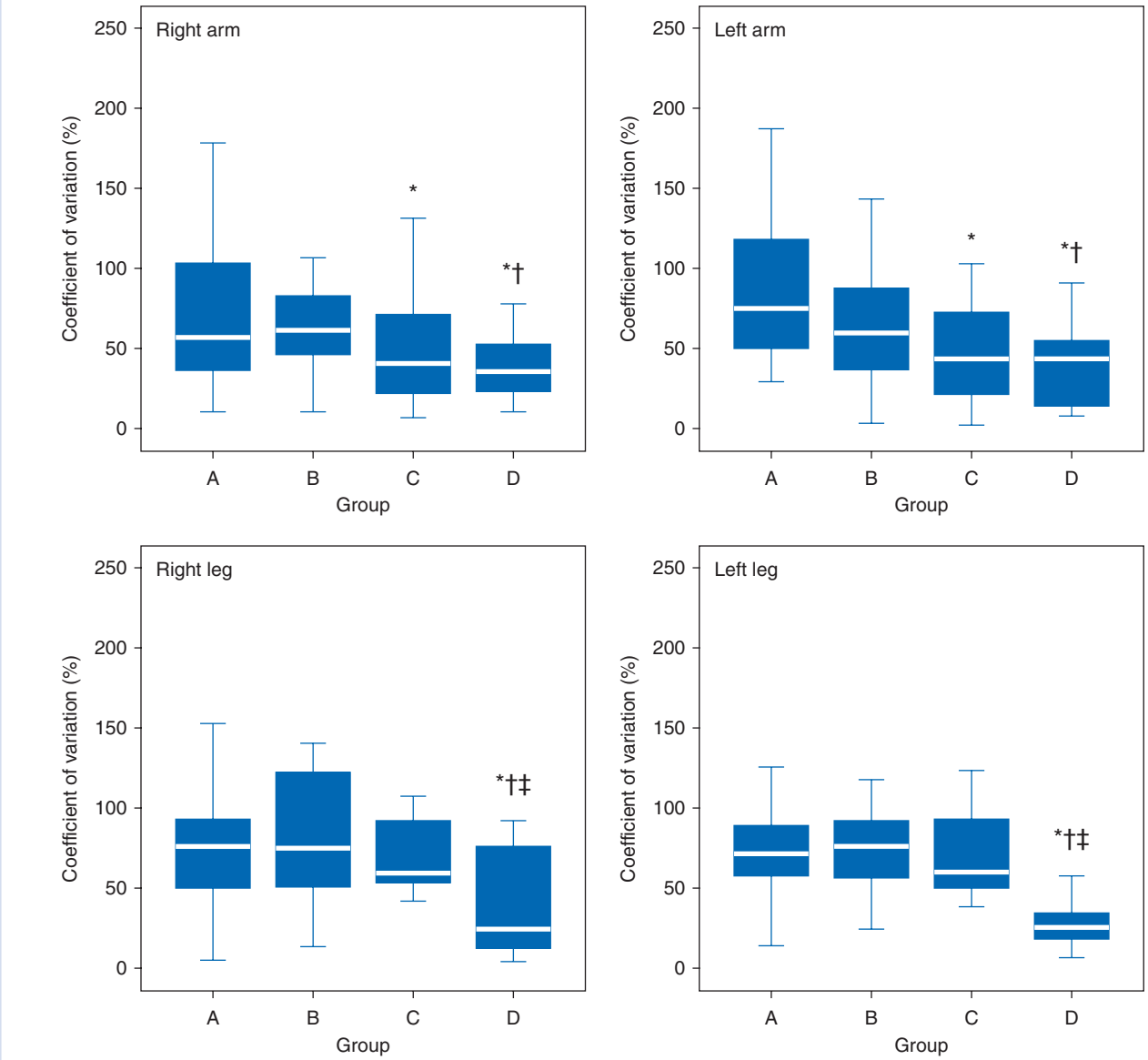

Fig 4 Box plots of the CV (%) of transcranial electrical MEP amplitudes from both arms and legs of all groups. Horizontal bars represent the 90th, 75th, median, 25th, and 10th percentile. The CV of the MEP amplitude (%) was calculated as the SD of the MEP amplitude divided by the mean MEP amplitude value. *$P<0.05$ compared with Group A; †$P<0.05$ compared with Group B; ‡$P<0.05$ compared with Group C.

variables are summarized as mean (SD) or median (interquartile range, IQR). The data distributions were tested for normality with the Kolmogorov–Smirnov test with the Lilliefors correction and visual inspection of *Q–Q* plots. Continuous variables were compared with one-way analysis of variance or the Kruskal–Wallis test with *post hoc* analysis as appropriate. As the amplitudes and CV (%) values were non-normally distributed, the Kruskal–Wallis test with least significant difference (LSD) test as a *post hoc* analysis was performed to compare among the four groups. Incidence data were compared using the χ^2 test or Fisher's exact test according to the expected counts. The statistical tests for individual outcome variables were presented again in detail in the tables. In all cases, a *P*-value of <0.05 was considered significant.

Results

From 125 patients assessed for eligibility, five patients were excluded by the history of cardiac problem ($n=2$) or chronic obstructive pulmonary disease ($n=3$). The remaining 120 patients were randomly assigned and completed the study according to the protocol and were included in the analysis (Fig. 2). Patient characteristic and perioperative data are shown in Table 1. Patients' heights were significantly lower in Group C, but there was no difference in BMI among

Table 3 Comparison of haemodynamic parameters during MEP monitoring. Values are mean (SD), median (IQR), or number. [a]Significantly different from that of Group A; [b]significantly different from that of Group B; [c]significantly different from that of Group C; [d]significantly different from that of Group D. Ephedrine and atropine total dose are the mean of cumulative dose, only when it used. *P*-values are results of one-way analysis of variance or the Kruskal–Wallis test according to the normality of the data for continuous variables, and Fisher's exact test for incidence variables

	Group A	Group B	Group C	Group D	*P*-value
Mean arterial pressure (mm Hg)	79 (5)	82 (7)[d]	82 (6)[d]	77 (7)[b,c]	0.003
Lowest mean arterial pressure (mm Hg)	63 (8)[c]	67 (6)	70 (9)[a,d]	64 (5)[c]	0.003
Mean heart rate (beats min^{-1})	68 (8)	68 (17)	64 (9)	64 (6)	0.269
Lowest heart rate (beats min^{-1})	58 (6)	59 (14)	56 (9)	54 (5)	0.149
Incidence of hypotension (*n*)	4	3	3	3	0.999
Incidence of bradycardia (*n*)	2	2	4	3	0.900
Vasopressor use (*n*)	3	2	2	3	0.999
Ephedrine total dose (mg)	10 (6–10)	10 (5–10)	10 (5–10)	10 (10–10)	0.761
Atropine total dose (mg)	0.5 (0.5–0.5)	0.5 (0.5–0.5)	0.5 (0.5–0.9)	0.5 (0.5–0.5)	0.719

groups. The mean remifentanil infusion dose of Group D was higher than that of Group A or C. There was a significant difference in the end-tidal CO_2 between Groups C and D. The mean infusion dose of vecuronium was significantly lower in Group C than Group A or B. There was no incidence of hypercapnia.

The MEP parameters are shown in Table 2. The mean stimulus intensity did not differ between the groups. The mean MEP amplitudes and CVs of all groups were compared in Figures 3 and 4. The median (IQR) amplitudes of the left leg were 0.23 (0.15–0.57), 0.44 (0.19–0.79), 0.28 (0.15–0.75), and 0.75 (0.39–1.35) mV in Groups A, B, C, and D, respectively. The median (IQR) CVs of the left leg were 71.1 (56.9–88.8), 76.1 (54.2–93.1), 59.8 (48.6–95.6), and 25.2 (17.3–35.0) in Groups A, B, C, and D, respectively. The differences among groups of the MEP amplitudes of the left arm and both legs were statistically significant (Kruskal–Wallis test, $P=0.011$ for the left leg). Also significant were the differences among groups of the CVs of all limbs ($P<0.001$, for the left leg). A *post hoc analysis* indicated that the mean MEP amplitudes of the left arm and both legs were significantly higher in Group D than Group A, B, or C. The mean amplitude of the left arm and right leg was significantly higher in Group C than Group A or B. The CVs of the four limbs were significantly smaller in Group D compared with Group A, B, or C. The CVs of both arms were significantly smaller in Group C compared with Group A.

Nine patients showed abnormal changes in intraoperative MEP (Table 2). There was one case of a patient receiving spine surgery who developed newly onset postoperative neurological dysfunction that was correlated with positive intraoperative MEP monitoring (true positive). There were three cases of patients exhibiting spontaneous movements during surgical field dissection that were associated with MEP stimulus (Table 2), although movement never occurred during microscopic surgery. There were six cases of spontaneous respiration, although its incidence did not differ between the groups (Table 2). The comparison of haemodynamic parameters and drug use is shown in Table 3. The mean arterial pressure of Group D was significantly lower than that of Group B or C. The lowest arterial pressure of Group A and D was lower than that of Group C. Neither the mean nor the lowest heart rate was different between the groups. The incidence of hypotension and bradycardia and also the use of vasopressor, ephedrine, and atropine did not differ.

Discussion

In this study, we compared the effects of varying levels of NMB along with no NMB on anaesthesia and MEP monitoring during neurosurgery. The mean amplitude values were largest and the CV was smallest during MEP monitoring under no NMB. Incidents of spontaneous movement or respiration were not higher under no NMB compared with those observed while maintaining partial NMB. Although the incidence of newly onset postoperative neurological dysfunction was low and the comparison of MEP monitoring efficacy was limited in the present study, we confirmed that not maintaining NMB led to better MEP monitoring parameters without an increased incidence of hypotension or spontaneous movement and respiration.

Questions regarding the necessity of NMB have not been systemically studied but are important to all neurosurgical anaesthesiologists. Although most institutions do not use partial NMB, there are those who insist that not maintaining NMB could result in problems in exposing the surgical field during spine surgery, and also a heightened risk of spontaneous patient movement.[2 5 6] Indeed, there were three cases of spontaneous movement in the present study that were associated with MEP electrical stimulation (Table 2). However, these movements may have resulted from an inadequately low depth of anaesthesia, and there were no cases of movement during the main surgical procedure with the microscope. Moreover, these incidences did not differ among the three groups. As long as an adequate depth of

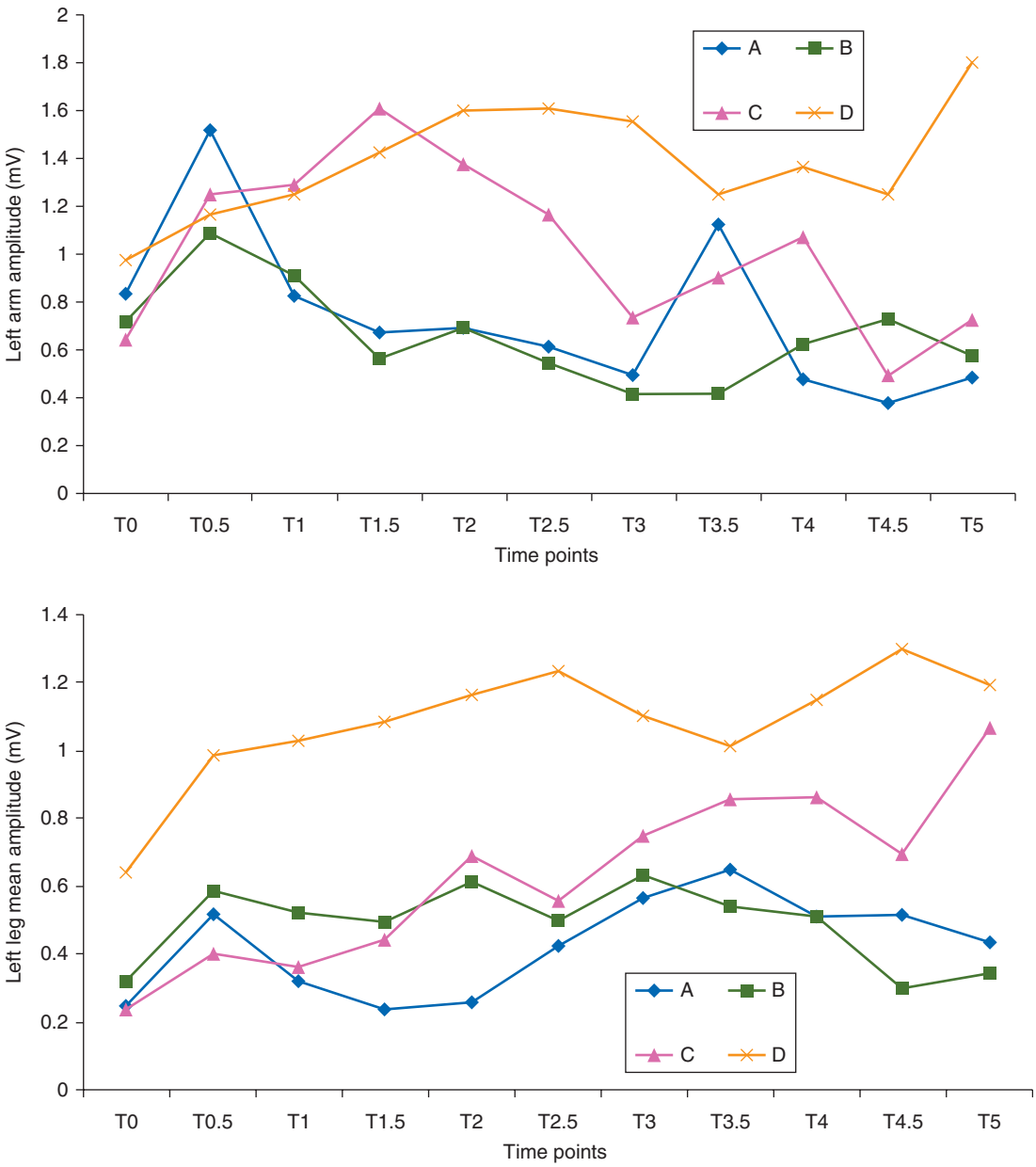

Fig 5 MEP monitoring amplitude of the left arm and the left leg in 30 min intervals for 5 h after the baseline set-up. T0: the MEP monitoring baseline; T0.5, 30 min; T1, 1 h; T1.5, 1.5 h; T2, 2 h; T2.5, 2.5 h; T3, 3 h; T3.5, 3.5 h; T4, 4 h; T4.5, 4.5 h; T5, 5 h after the MEP baseline.

anaesthesia was maintained, the risk of patient movement was not different among the three different levels of NMB and in the group not maintaining NMB.

Proponents of partial NMB also insist that the increasing depths of anaesthesia/opioid use needed to avoid movement in the non-paralysed patient may cause hypotension and result in the need for vasopressors.[8] Although the remifentanil requirements and mean arterial pressure were lower in Group D, the lowest mean level was acceptable clinically, and there was no increased incidence of hypotension, bradycardia, or vasopressor demand. Hypotension could be avoided with close attention to volume status.

Even though partial NMB minimally reduced the MEP amplitudes of both the upper extremities in Group C, the amplitudes of both legs were decreased in all groups maintaining partial NMB, possibly due to the different sensitivities of muscle groups to NMB drugs.[21] The lower extremity signals generally required higher stimulus intensity than those of the upper extremities. Muscle relaxation would increase the risk of monitoring failure or result in increased difficulty in obtaining lower extremity signals. Furthermore, with no NMB, MEP amplitude variability (measured by CV) decreased significantly compared with those observed with partial NMB. The increased CV may increase the incidence of false-positive

or -negative MEP results, and thus result in poor efficacy of MEP monitoring. The decreased amplitude may also increase the incidence of false-positive MEP results, suggesting a neurological deficit even though no dysfunction is present. As the purpose of MEP monitoring is to detect neurological injury by monitoring the changes of MEP amplitude, CV and amplitude of MEP were the primary endpoint of the present study.

MEP monitoring is sensitive to both the anaesthetic agent[22 23] and the NMB.[2 6] Maintaining a constant degree of NMB and levels of anaesthetic was suggested as a strategy to minimize the amplitude fluctuation.[12 13] There was no single ideal vecuronium infusion dose for MEP monitoring as there are many factors that influence the pharmacokinetics or pharmacodynamics of vecuronium in each subject.[24] Even though we tried to fix the vecuronium infusion dose after an adequate degree of NMB was achieved according to the target of each group, a significant degree of fluctuation developed (Fig. 5). We had to change the infusion dose nearly every 15 min to maintain a constant degree of NMB. If other neuromuscular blocking agents such as rocuronium, atracurium,[7] or cisatracurium[25] were used, the degree of fluctuation might have been different.

The degree of NMB can be evaluated not only by the amplitude of single-twitch-evoked electromyography, but also using the TOF count.[4 6 12–14] The first method quantifies the amplitude of the compound muscle action potentials produced by supramaximal stimulation of a peripheral motor nerve and compares this with a reference value obtained before adding the neuromuscular blocking agent.[2 6] Sloan and Heyer[6 14] reported that successful monitoring was accomplished at T_1 between 5% and 50% of baseline.[15–17] A second technique is the TOF response. Previously, it was reported that MEP monitoring was possible with one or two of four twitches remaining.[5 6] We determined the target TOF response of NMB to be count of 2, 0.5 for T_1/Tc or T_2/Tc considering these two methods. With any of these degrees of partial NMB, the MEP amplitudes were smaller and more variable compared with those obtained with no NMB. We also found the degree of partial NMB in Group C more desirable than previously recommended levels of partial NMB in terms of its amplitude and variability. Therefore, if partial NMB is used for MEP monitoring, a target T_2/Tc of 0.5 is recommended over a T_1/Tc of 0.5 or a TOF count of 2.

The present study has several limitations. First, we did not monitor the EEG-based depth of anaesthesia, although the mean infusion dose of propofol was not different among the groups (Table 1). Furthermore, as previous studies have reported confounding results regarding the dose-dependent MEP suppression of propofol[26–30] and this kind of monitoring is partly dependent upon electromyography, it would not help in comparing the depth of anaesthesia between the paralysed and non-paralysed groups. Secondly, this study included three types of surgery, each of which could necessitate different NMB strategies. Muscle relaxation is likely needed to facilitate exposure for major spine surgery, but it is not necessary during craniotomies for tumour resection or aneurysm clipping. However, as the incidence of surgery type was not different among the groups, comparing the MEP parameters was possible. Thirdly, the present study was not powered for the secondary outcomes of MEP monitoring. The comparison of MEP monitoring efficacy[31 32] among the groups is limited as there was only one true-positive MEP in Group A.

In conclusion, different levels of muscle relaxation affected the MEP parameters in the expected direction. If NMB is used during MEP monitoring, a target T_2/Tc of 0.5 is recommended. However, the MEP amplitude was largest and least variable in the group with no NMB compared with any level of partial NMB used. Incidences of spontaneous movement or increased vasopressor requirements did not increase with no NMB. Therefore, no muscle relaxation is strongly recommended over partial NMB during MEP monitoring in neurosurgery.

Declaration of interest

None declared.

References

1 Lang EW, Beutler AS, Chesnut RM, *et al.* Myogenic motor-evoked potential monitoring using partial neuromuscular blockade in surgery of the spine. *Spine* 1996; **21**: 1676–86

2 Mendiratta A, Emerson RG. Neurophysiologic intraoperative monitoring of scoliosis surgery. *J Clin Neurophysiol* 2009; **26**: 62–9

3 Minahan RE, Riley LH III, Lukaczyk T, Cohen DB, Kostuik JP. The effect of neuromuscular blockade on pedicle screw stimulation thresholds. *Spine* 2000; **25**: 2526–30

4 Adams DC, Emerson RG, Heyer EJ, *et al.* Monitoring of intraoperative motor-evoked potentials under conditions of controlled neuromuscular blockade. *Anesth Analg* 1993; **77**: 913–8

5 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**: 584–9

6 Sloan TB, Heyer EJ. Anesthesia for intraoperative neurophysiologic monitoring of the spinal cord. *J Clin Neurophysiol* 2002; **19**: 430–43

7 van Dongen EP, ter Beek HT, Schepens MA, *et al.* Effect of nitrous oxide on myogenic motor potentials evoked by a six pulse train of transcranial electrical stimuli: a possible monitor for aortic surgery. *Br J Anaesth* 1999; **82**: 323–8

8 Pajewski TN, Arlet V, Phillips LH. Current approach on spinal cord monitoring: the point of view of the neurologist, the anesthesiologist and the spine surgeon. *Eur Spine J* 2007; **16** (Suppl. 2): S115–29

9 Kothbauer K. Motor evoked potential monitoring for intramedullary spinal cord tumor surgery. In: Deletis V, Shils J, eds. *Neurophysiology in Neurosurgery: A Modern Intraoperative Approach*. San Diego: Academic Press, 2002: 73–92

10 MacDonald DB, Janusz M. An approach to intraoperative neurophysiologic monitoring of thoracoabdominal aneurysm surgery. *J Clin Neurophysiol* 2002; **19**: 43–54

11 Wang AC, Than KD, Etame AB, La Marca F, Park P. Impact of anesthesia on transcranial electric motor evoked potential monitoring during spine surgery: a review of the literature. *Neurosurg Focus* 2009; **27**: E7

12 Sloan TB, Erian R. Effect of vecuronium-induced neuromuscular blockade on cortical motor evoked potentials. *Anesthesiology* 1993; **78**: 966–73

13 Sloan TB, Erian R. Effect of atracurium-induced neuromuscular block on cortical motor-evoked potentials. *Anesth Analg* 1993; **76**: 979–84

14 Sloan TB. Anesthesia and motor evoked-potentials monitoring. In: Deletis V, Shils J, eds. *Neurophysiology in Neurosurgery: A Modern Intraoperative Approach*. San Diego: Academic Press, 2002: 175–81

15 Gugino LD, Aglio LS, Segal NE, Gonzalez AA, Kraus KH, Woodard EJ. Use of transcranial magnetic stimulation for monitoring spinal cord motor paths. *Semin Spine Surg* 1997; **9**: 315–36

16 Lee WY, Hou WY, Yang LH, Lin SM. Intraoperative monitoring of motor function by magnetic motor evoked potentials. *Neurosurgery* 1995; **36**: 493–500

17 Yang LH, Lin SM, Lee WY, Liu CC. Intraoperative transcranial electrical motor evoked potential monitoring during spinal surgery under intravenous ketamine or etomidate anaesthesia. *Acta Neurochir (Wien)* 1994; **127**: 191–8

18 American Electroencephalographic Society. Guideline nine: guidelines on evoked potentials. *J Clin Neurophysiol* 1994; **11**: 40–73

19 American Electroencephalographic Society. Guideline thirteen: guidelines for standard electrode position nomenclature. *J Clin Neurophysiol* 1994; **11**: 111–3

20 American Electroencephalographic Society. Guideline fourteen: guidelines for recording clinical EEG on digital media. *J Clin Neurophysiol* 1994; **11**: 114–5

21 Abdulatif M, el-Sanabary M. Blood flow and mivacurium-induced neuromuscular block at the orbicularis oculi and adductor pollicis muscles. *Br J Anaesth* 1997; **79**: 24–8

22 Calancie B, Harris W, Broton JG, Alexeeva N, Green BA. 'Threshold-level' multipulse transcranial electrical stimulation of motor cortex for intraoperative monitoring of spinal motor tracts: description of method and comparison to somatosensory evoked potential monitoring. *J Neurosurg* 1998; **88**: 457–70

23 Pechstein U, Nadstawek J, Zentner J, Schramm J. Isoflurane plus nitrous oxide versus propofol for recording of motor evoked potentials after high frequency repetitive electrical stimulation. *Electroencephalogr Clin Neurophysiol* 1998; **108**: 175–81

24 Sloan TB. Anesthetic effects on electrophysiologic recordings. *J Clin Neurophysiol* 1998; **15**: 217–26

25 Dahaba AA, Suljevic I, Bornemann H, Wu XM, Metzler H. No regional difference in cisatracurium dose–response and time-course-of-action between patients in China and Bosnia. *Br J Anaesth* 2011; **106**: 331–5

26 Chen Z. The effects of isoflurane and propofol on intraoperative neurophysiological monitoring during spinal surgery. *J Clin Monit Comput* 2004; **18**: 303–8

27 Kalkman CJ, Drummond JC, Ribberink AA, Patel PM, Sano T, Bickford RG. Effects of propofol, etomidate, midazolam, and fentanyl on motor evoked responses to transcranial electrical or magnetic stimulation in humans. *Anesthesiology* 1992; **76**: 502–9

28 Scheufler KM, Zentner J. Total intravenous anesthesia for intraoperative monitoring of the motor pathways: an integral view combining clinical and experimental data. *J Neurosurg* 2002; **96**: 571–9

29 Nathan N, Tabaraud F, Lacroix F, *et al.* Influence of propofol concentrations on multipulse transcranial motor evoked potentials. *Br J Anaesth* 2003; **91**: 493–7

30 Ubags LH, Kalkman CJ, Been HD, Drummond JC. Differential effects of nitrous oxide and propofol on myogenic transcranial motor evoked responses during sufentanil anaesthesia. *Br J Anaesth* 1997; **79**: 590–4

31 Irie T, Yoshitani K, Ohnishi Y, *et al.* The efficacy of motor-evoked potentials on cerebral aneurysm surgery and new-onset postoperative motor deficits. *J Neurosurg Anesthesiol* 2010; **22**: 247–51

32 Guo L, Gelb AW. False negatives, muscle relaxants, and motor-evoked potentials. *J Neurosurg Anesthesiol* 2011; **23**: 64

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