

Original Article

A comparison of a prototype electromyograph vs. a mechanomyograph and an acceleromyograph for assessment of neuromuscular blockade*

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Summary

The extent of neuromuscular blockade during anaesthesia is frequently measured using a train-of-four stimulus. Various monitors have been used to quantify the train-of-four, including mechanomyography, acceleromyography and electromyography. Mechanomyography is often considered to be the laboratory gold standard of measurement, but is not commercially available and has rarely been used in clinical practice. Acceleromyography is currently the most commonly used monitor in the clinical setting, whereas electromyography is not widely available. We compared a prototype electromyograph with a newly constructed mechanomyograph and a commercially available acceleromyograph monitor in 43 anaesthetised patients. The mean difference (bias; 95% limits of agreement) in train-of-four ratios was 4.7 (–25.2 to 34.6) for mechanomyography vs. electromyography; 14.9 (–13.0 to 42.8) for acceleromyography vs. electromyography; and 9.8 (–31.8 to 51.3) for acceleromyography vs. mechanomyography. The mean difference (95% limits of agreement) in train-of-four ratios between opposite arms when using electromyography was –0.7 (–20.7 to 19.3). There were significantly more acceleromyography train-of-four values > 1.0 (23%) compared with electromyography or mechanomyography (2–4%; $p < 0.0001$). Electromyography most closely resembled mechanomyographic assessment of neuromuscular blockade, whereas acceleromyography frequently produced train-of-four ratio values > 1.0, complicating the interpretation of acceleromyography results in the clinical setting.

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Introduction

Non-depolarising neuromuscular blocking drugs are frequently used to facilitate tracheal intubation, as a component of balanced general anaesthesia to provide surgical exposure, or to optimise mechanical ventilation in the intensive care unit. The extent or 'depth' of

neuromuscular blockade has often been measured using an evoked motor response in which the ulnar nerve is stimulated at the wrist, resulting in contraction, or 'twitch', of the adductor pollicis muscle in the hand. Because the intensity of the evoked motor response varies considerably, the twitch response is usually standardised by using a series

of four stimuli spaced 500 ms apart, the so-called 'train-of-four' [1–3]. As depth of neuromuscular block increases, the twitch intensity decreases from the first twitch to the fourth twitch (fade) until the individual twitches disappear completely, starting with the fourth twitch. The evoked motor response can be measured manually by palpating the twitch, or by using monitors that measure the twitch quantitatively. The use of quantitative twitch monitoring is strongly recommended by many authorities because it is considerably more sensitive for detecting the extent of fade than subjective monitoring by palpation [4, 5]. Quantitative monitoring techniques include mechanomyography, acceleromyography and electromyography.

Mechanomyography measures isometric force generated at the thumb by the adductor pollicis muscle. Mechanomyography is often regarded as the gold standard for quantification of twitch, but has seldom been available for routine clinical use in patients, and is currently not readily available even for laboratory use [4, 6]. Fuchs-Buder et al. [7] suggested that mechanomyography should be the comparator when new monitoring techniques are evaluated.

Acceleromyography is the quantitative monitoring technique that is most widely used in clinical practice, and has also been used for studies on neuromuscular blocking drug pharmacology. It measures the evoked movement of the thumb. A major limitation of acceleromyography is that the thumb must be unrestricted and free to move, which generally precludes the use of acceleromyography if the hand is tucked at the patient's side during surgery. Additionally, investigators have consistently reported that acceleromyography often measures a train-of-four ratio larger than either mechanomyography or electromyography [8, 9]. When measured by acceleromyography, baseline train-of-four ratio in the absence of neuromuscular blocking drugs is often greater than 1.0, for reasons that are unclear.

Electromyography measures the electromyogram of the stimulated muscle [10]. Electromyography has the advantage that thumb motion is not required to make the measurement, hence it can be used when thumb movement is restricted or the patient's arm is tucked at their side. Commercial availability of electromyography for clinical monitoring of neuromuscular blockade has been very limited.

The aim of this study was to assess the performance of a prototype electromyograph compared with a widely available acceleromyograph monitor, as well as the standard of mechanomyography. For the latter, we built a mechanomyographic twitch monitor from modern electronic components.

Methods

Our institutional review board approved this study and patients gave written, informed consent. Patients with known neuromuscular abnormalities were not recruited.

The mechanomyograph instrument was built in our laboratory and consisted of a force transducer, signal amplifier and analogue-to-digital converter held in a plastic wrist and hand immobiliser (Fig. 1). The immobiliser was made with a 3D printer. The mechanomyograph force transducer response was linear with precision to 5 g and accuracy to 25 g for measurements examined from 0 to 5 kg, with sensitivity to 10 g within that range (Fig. 2). A preload of 200–300 g was applied to the thumb before measurements. Custom software was created to drive the hardware components, analyse the voltage response after the train-of-four stimulus, and calculate the train-of-four ratio, using the LabVIEW package (National Instruments, Austin, TX, USA).

The electromyograph response measurement was made using a custom-printed electromyograph electrode array (Fig. 3) connected to custom electromyograph signal analysis software (TwitchView Monitor, Blink Device Company, Seattle, WA, USA). For mechanomyograph and electromyograph measurements, a train-of-four stimulus was applied using a TOF Watch S twitch monitor (Organon, Dublin, Ireland) and electrodes (3M Red Dot; 3M Healthcare, St. Paul, MN, USA) applied over the ulnar nerve at the wrist.

For acceleromyography, we used a Stimpod NMS 450 (Xavant Technology, Pretoria, South Africa). The Stimpod was used to both deliver a train-of-four stimulus and record the evoked response with an accelerometer attached to the thumb. The thumb was unrestricted, no artificial preload was added, and hand movement was not restricted. Electrodes were applied over the ulnar nerve at the wrist.

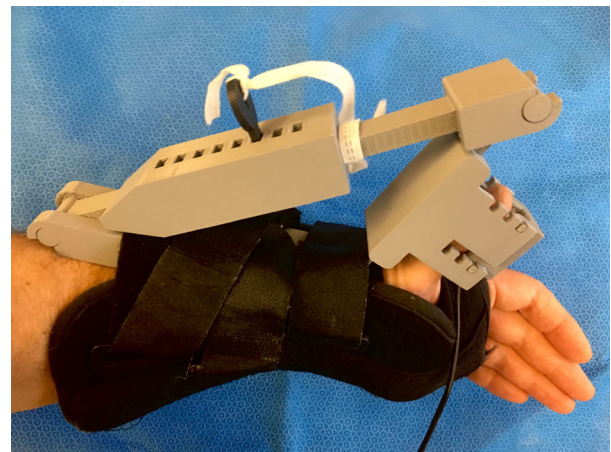


Figure 1 Mechanomyograph.

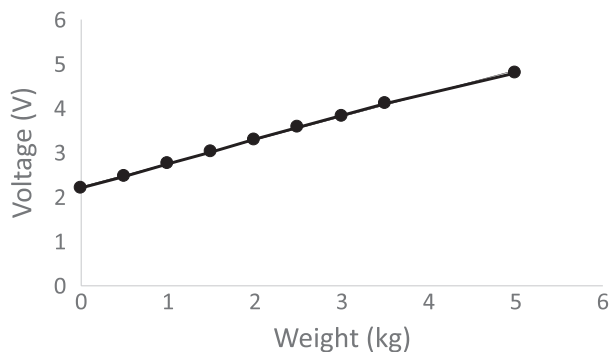


Figure 2 Plot of output voltage of mechanomyograph force transducer with added calibration weights.

The Stimpod sensor was attached to the distal phalanx of the thumb using the plastic circumferential band supplied, reinforced with tape if necessary.

All train-of-four ratio values were unadjusted, and not limited to a maximum value of 1.0. The amplitude of the train-of-four stimulus was set at 60 mA. No skin preparation was performed before attaching the electrodes. Temperature homeostasis was maintained in all patients through the use of active warming. End-tidal CO₂ was maintained between 4.3 kPa and 5.3 kPa. The anaesthetic technique used was at the discretion of the anaesthetist, and included propofol; opioids (fentanyl and hydromorphone); sevoflurane or isoflurane; suxamethonium; and rocuronium or vecuronium.

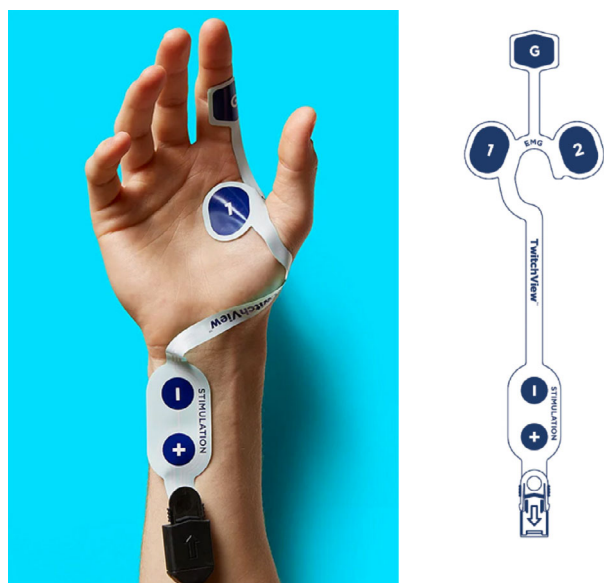


Figure 3 The electrode array of the electromyograph. Sensing electrodes over the adductor pollicis muscle and first dorsal interosseus muscle; reference electrode on the first finger. The stimulating electrodes were not used.

In general, monitors were compared on the same arm, but practical constraints such as wrapping the arm, or the presence of intravenous or arterial catheters, determined the placement of monitors in some patients. The monitors for acceleromyography vs. electromyography comparisons, and electromyography vs. mechanomyography, were applied on the same or opposite arms. However, acceleromyography and mechanomyography were always compared on opposite arms. A comparison of electromyographic responses in both arms was also performed.

For each device, duplicate train-of-four measurements were taken within ≤ 2 min, approximately every 5 min from induction of anaesthesia until just before emergence from anaesthesia. Measurements were not made for 10 min following administration of neuromuscular blocking drugs or reversal agents, in order to avoid periods when the extent of neuromuscular blockade was changing very rapidly. When measurements were made on both arms, the train-of-four twitch stimulus was administered in each arm within 2 min.

Bland–Altman analysis was used for describing the relationship between the difference and the average of the

Table 1 Physical characteristics and intra-operative details of 43 enrolled patients. Values are median (IQR [range]) or number (proportion).

Age; years	62 (47–65 [30–74])
Sex; female	26 (61%)
BMI; kg.m ²	30 (26–33 [21–49])
ASA physical status	
2	15 (35%)
3	25 (58%)
4	3 (7%)
Duration of operation; min	182 (141–318 [23–717])
Types of surgery	
General	33 (77%)
Gynaecological	10 (23%)
Neuromuscular blocking drugs	
Rocuronium	27 (63%)
Vecuronium	11 (26%)
Rocuronium and vecuronium	4 (9%)
Suxamethonium ^a	1 (2%)
Reversal drugs used	
Neostigmine	19 (44%)
Sugammadex	18 (42%)
None	6 (14%)

^a11 values comparing electromyography with acceleromyography, following recovery from suxamethonium given at induction.

train-of-four ratio for pairs of twitch monitoring devices [11]. A test of proportions was used to compare the difference in the proportion of measurements that had a train-of-four ratio > 1.0 between each device. A p value < 0.05 was considered statistically significant. Statistical comparisons were performed using STATA version 11.0 (StataCorp LP, College Station, TX, USA).

Results

Forty-three patients were enrolled. Table 1 gives their physical characteristics. Representative data from a single patient are shown in Fig. 4. We compared train-of-four using mechanomyography vs. electromyography in 25 patients (808 data pairs), acceleromyography vs. electromyography in 31 patients (615 data pairs), acceleromyography vs. mechanomyography in 19 patients (263 data pairs) and bilateral electromyography in 24 patients (325 data pairs). Bland–Altman plots and scatter plots of train-of-four ratios for mechanomyography vs. electromyography, acceleromyography vs. electromyography and acceleromyography vs. mechanomyography are shown in Figs. 5–7. The plots for comparisons between opposite arms using electromyography are shown in Fig. 8. The mean difference (bias) for mechanomyography vs. electromyography was 4.7; for acceleromyography vs. electromyography 14.9; for acceleromyography vs. mechanomyography 9.8; and for electromyography vs. electromyography -0.7 . The proportion of

train-of-four ratio values > 1.0 was significantly greater for acceleromyography (22.7%) than for mechanomyography (2.4%) or electromyography (3.9%; $p < 0.0001$).

Discussion

Mechanomyography, which measures isometric force, has long been considered the gold standard for twitch quantification, but has not been used for routine clinical monitoring [6]. Mechanomyography was previously used in studies of neuromuscular blocking drugs, but is now rarely used because older equipment, such as the Grass force transducer, is obsolete and no longer commercially available. For this reason, we constructed a mechanomyograph that can be used for the validation of acceleromyograph and electromyograph devices.

We confirmed previous studies demonstrating that acceleromyograph monitors frequently produce train-of-four ratios > 1.0, whereas mechanomyography and electromyography seldom produce train-of-four ratios > 1.0 [12–19]. The mechanism that causes baseline (i.e. before drug administration) acceleromyograph train-of-four ratio to be > 1.0 is unknown. From the standpoint of utilising a threshold value of the train-of-four ratio for judging the adequacy of recovery (often cited as 0.9 [20]), the mechanomyograph and electromyograph devices appear to be more reliable and consistent. Some authorities have recommended ‘normalising’ train-of-four ratio values obtained from acceleromyography, by dividing

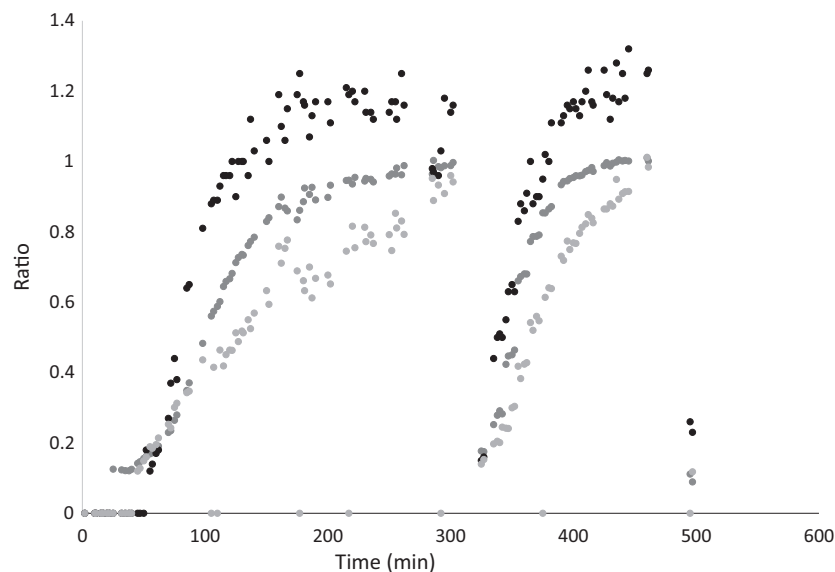


Figure 4 Simultaneous acceleromyograph, electromyograph and mechanomyograph train-of-four values in one patient. Acceleromyograph and electromyograph readings obtained from the same hand, and mechanomyograph readings from the opposite hand. Doses of vecuronium at 0 min (7 mg), 300 min (1 mg), 301 min (1 mg), 467 min (2 mg), 475 min (1 mg). Black – acceleromyograph; dark grey – electromyograph; light grey – mechanomyograph.

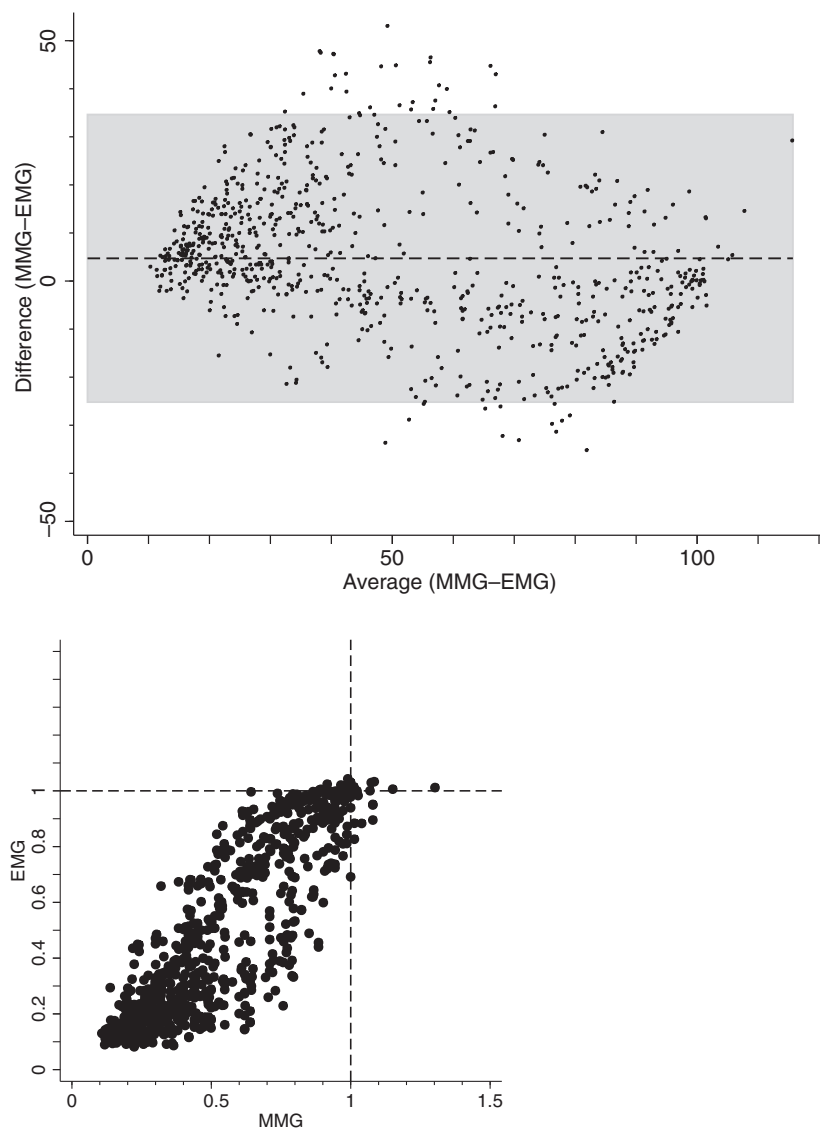


Figure 5 Train-of-four ratios using mechanomyograph vs. electromyograph. Top: Bland–Altman plot. Shaded area represents 95% limits of agreement. Bottom: scatter plot of individual values.

the train-of-four ratio by the baseline train-of-four ratio (e.g. $0.9/1.3 = 0.77$) [16, 21]. Obviously, if a baseline train-of-four ratio value is not obtained before the administration of the neuromuscular blocking drug, as is often the case in routine clinical practice, then normalising the train-of-four ratio values is not possible. If an acceleromyograph ratio of 0.9 is obtained during recovery in a patient with an acceleromyograph train-of-four ratio baseline value > 1.0 , that patient may not have adequately recovered. When mechanomyography or electromyography is used, a train-of-four ratio of ≥ 0.9 may indicate adequate recovery more reliably.

Our results on comparisons of acceleromyography with electromyography or mechanomyography are similar to

those reported previously. Liang et al. compared acceleromyography with electromyography, and found that acceleromyography underestimated the train-of-four ratio by ≥ 0.15 compared with electromyography [17]. They concluded that the difference was not due to imprecision of measurement, but instead represented a fundamental difference between these monitoring modalities. They suggested that a train-of-four ratio of 1.0 using acceleromyography could not be relied on to exclude residual neuromuscular blockade. Kopman et al. compared acceleromyography with electromyography, and found that train-of-four ratio using acceleromyography was 0.1 higher than electromyography on average, with the 95%CI being 0.2 higher [22]. Claudius et al. reviewed the literature on

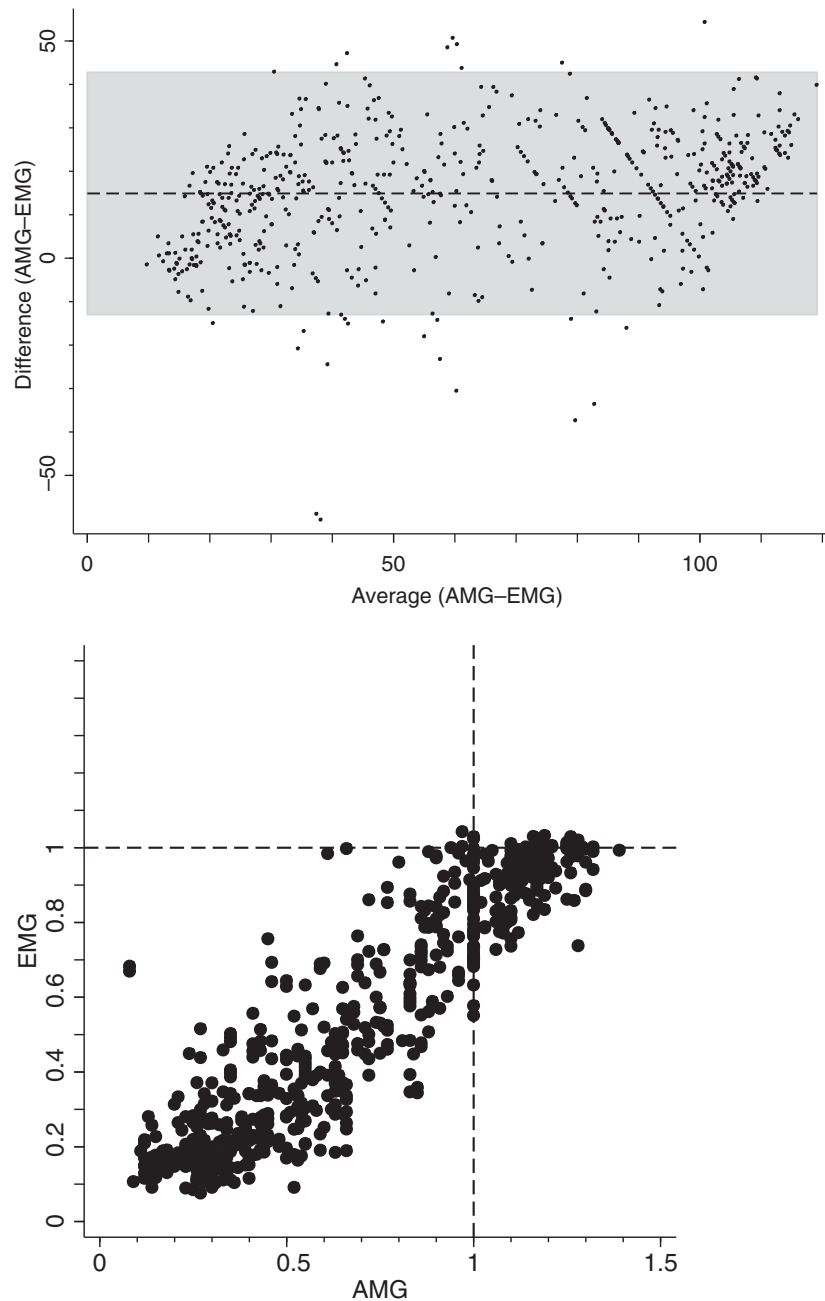


Figure 6 Train-of-four ratios using acceleromyograph (AMG) vs. electromyograph (EMG). Top: Bland–Altman plot. Shaded area represents 95% limits of agreement. Bottom: scatter plot of individual values.

acceleromyography and concluded that there was uncertainty about the threshold train-of-four ratio for recovery from neuromuscular blockade [14]. Suzuki et al. documented that baseline acceleromyography train-of-four ratio varied from 0.95 to 1.47 [18]. Capron et al. compared acceleromyography to mechanomyography and found that acceleromyography overestimated recovery when compared with mechanomyography, such that the train-of-

four ratio with acceleromyography had to be at least 1.0 in order to correspond to a train-of-four ratio of 0.9 with mechanomyography [12].

There are a number of limitations to our study. We aimed to follow good clinical research practice for studies of neuromuscular blocking drugs, as recommended by Fuchs-Buder et al. [7]. However, we deliberately chose not to standardise the anaesthetic care or neuromuscular blocker

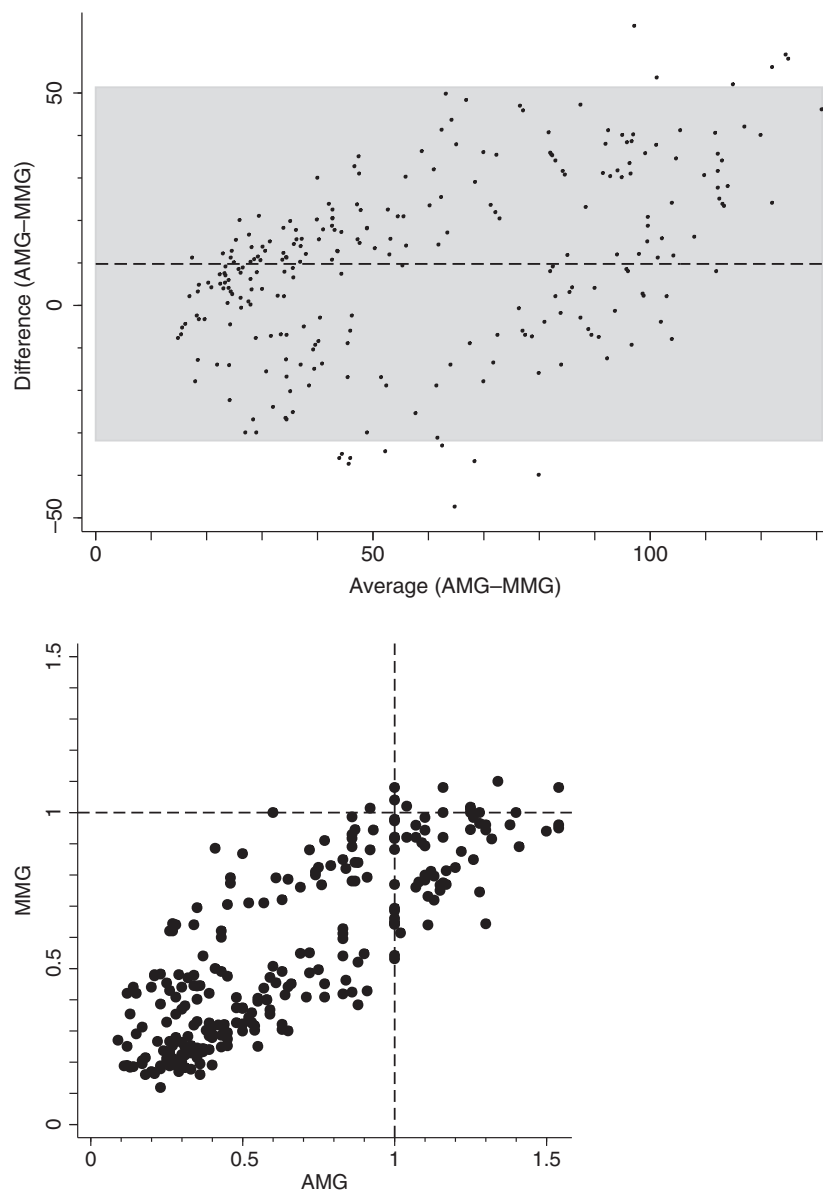


Figure 7 Train-of-four ratios using acceleromyograph (AMG) vs. mechanomyograph (MMG). Top: Bland–Altman plot. Shaded area represents 95% limits of agreement. Bottom: scatter plot of individual values.

administration, in order to obtain results that would be applicable to routine anaesthetic care. One of the disadvantages of this approach was that, in some cases, patients were managed under deep block for most of the surgical procedure, limiting the opportunity to measure train-of-four. Due to this, some patients contributed more data points than others. We deliberately chose not to prepare the skin before applying electrodes; not to apply preload to the thumb during acceleromyograph measurements; not to restrain finger movement; and not to normalise acceleromyograph values, because in our experience these steps are not widely used in anaesthetic practice. We

compared electromyograph signal quality on a number of healthy volunteers before and after skin preparation using either alcohol or mild skin abrasion. Although the skin impedance was reduced with skin preparation, it did not result in an appreciably larger amplitude signal.

Presumably due to the effects of a blood pressure cuff on distribution of neuromuscular blocking drugs in each arm, it is possible for significant arm-to-arm differences in twitch to occur, particularly in the period immediately following administration of a neuromuscular blocking drug. This phenomenon has to be considered when comparing the results from devices placed on opposite arms. Although

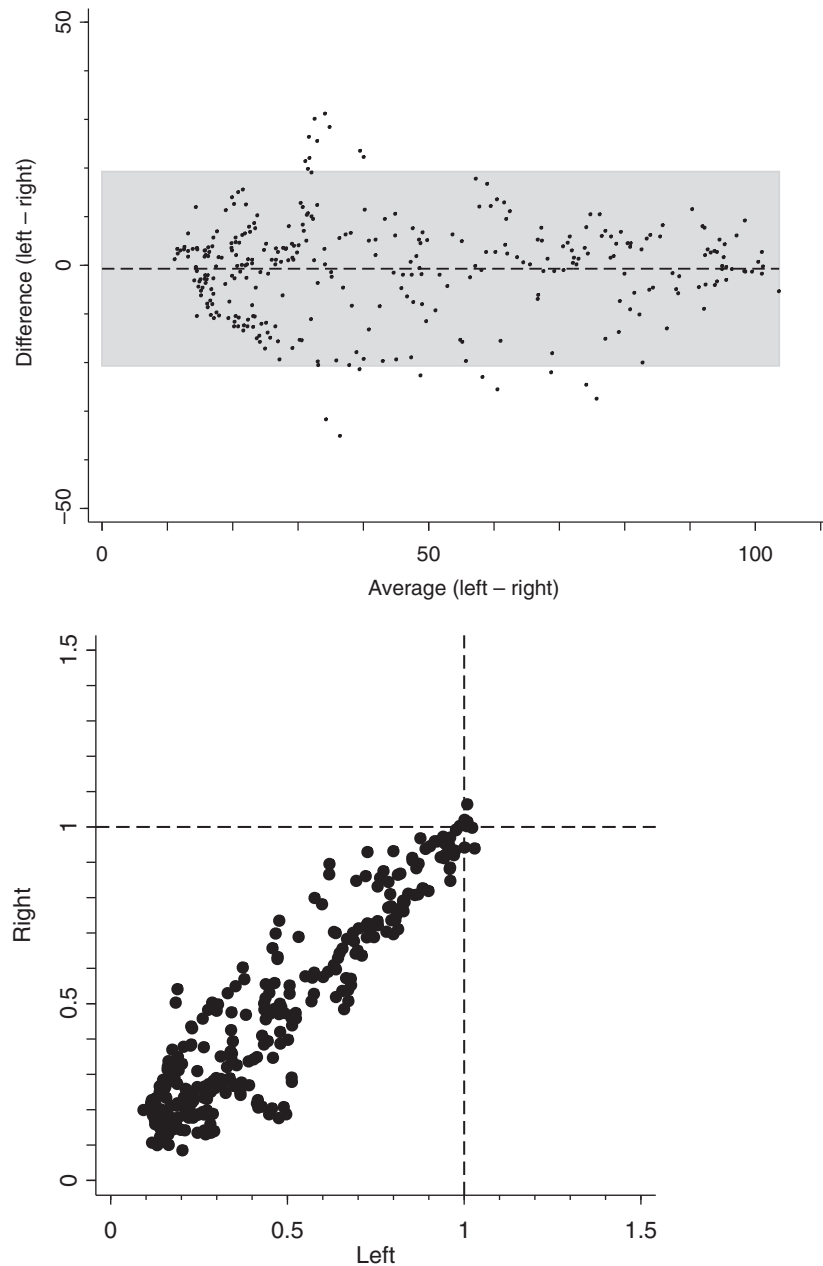


Figure 8 Train-of-four ratios in left arm vs. right arm, using electromyograph. Top: Bland–Altman plot. Shaded area represents 95% limits of agreement. Bottom: scatter plot of individual values.

we did observe some arm-to-arm differences during our study, the excellent agreement between electromyograph monitors placed on opposite arms strongly suggests that when large numbers of data pairs are considered, any differences caused by arm-to-arm differences in neuromuscular blocker distribution must be minor, at least when periods of rapid change after drug administration or reversal are avoided. Our findings concerning arm-to-arm differences agree with that of Claudius et al. [23]. We decided therefore not to restrict comparisons to those

where the devices were on the same arm. In particular, it was not possible to compare mechanomyography and acceleromyography on the same arm, since the mechanomyograph device restrains movement of the thumb. Mechanomyography vs. electromyography and acceleromyography vs. electromyography comparisons were obtained from the same arm whenever possible.

In conclusion, we obtained a wide range of train-of-four ratios from anaesthetised patients using a prototype electromyograph monitor, in comparison with a

mechanomyograph constructed in our laboratory and a commercially available acceleromyograph. The results were consistent with previous comparative studies of neuromuscular monitors, suggesting that mechanomyography is an appropriate gold standard comparator for validating acceleromyography or electromyography devices [7]. We found that the prototype electromyograph, now commercially available as the TwitchView Monitor, resembled mechanomyography more closely than acceleromyography. We confirmed the results of previous studies showing that many baseline acceleromyography train-of-four ratio values exceed 1.0, whereas baseline mechanomyography and electromyography values seldom exceed 1.0, a finding with significant implications for clinical practice.

Acknowledgements

JH is the Chief Executive Officer of, and has shares in, Blink Device Company, which has commercial rights to the prototype TwitchView electromyograph monitor used in this study. JH provided the device and supplied the EMG disposables for the study. No external funding or other competing interests declared.

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