Comparison of tactile and mechanomyographical assessment of response to double burst and train-of-four stimulation during moderate and profound neuromuscular blockade

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It is common clinical practice to estimate the degree of neuromuscular blockade by tactile evaluation of twitch responses. The aim of the present study was to evaluate the use of tactile responses of adductor pollicis to double-burst stimulation (DBS) and train-of-four (TOF) peripheral nerve stimulation for monitoring moderate and profound levels of neuromuscular blockade. The study comprised 44 women scheduled for gynaecological laparotomy and anaesthetised with midazolam, fentanyl, thiopentone, halothane, nitrous oxide and atracurium. The tactile responses of the adductor pollicis were compared with mechanomyographical measurements in the contra lateral arm during recovery from neuromuscular blockade. The observers (anaesthetic nurses) of the tactile responses were blinded with regard to the stimulation pattern and the mechanomyographical measurements. The time from injection of the initial dose of atracurium until tactile reappearance of the first twitch in DBS (D_1), was 24.6 (0–39.8) min, median (range). This was more rapid than the time until tactile reappearance of the first twitch in TOF (T_1) 32.8 (18.2–43.4) min ($P < 0.05$). The median time from tactile reappearance of D_1 until T_1 recovered to 15% of the control twitch height was longer than the median time from tactile reappearance of T_1 (14.6 versus 10.5 min) ($P < 0.05$). One or two responses to DBS or TOF were often felt before any responses had been detected mechanomyographically in the contralateral arm. When three or four responses to TOF were felt, responses were always detected mechanomyographically. It is concluded that tactile evaluation of responses to DBS stimulation can estimate deeper levels of blockade than tactile evaluation of responses to TOF.

En pratique, on détermine le degré curarisation par l'appréciation tactile du twitch. Cette étude vise à évaluer l'utilisation de la réponse tactile de l'adducteur du pouce à la stimulation d'un nerf périphérique au double burst (DBS) et au train de quatre (TOF) pour le monitorage des niveaux profonds et modérés de bloc neuromusculaire. Quarante-quatre femmes programmées pour une laparoscopie gynécologique et anesthésiées au midazolam, fentanyl, thiopentone, halothane, protoxyde d'azote et atracurium sont incluses dans l'étude. La réponse tactile de l'adducteur du pouce est comparée avec la réponse mécanomyographique du côté contralatéral pendant la récupération du bloc. Les observatrices (infirmières anesthésistes) ne sont pas au courant du mode de stimulation, ni des mesures mécanomyographiques. L'intervalle entre la dose initiale d'atracurium et la réapparition tactile du premier twitch sur le DBS (D_1) est pour la médiane (étendue des valeurs) de 24,6 (0–39,8) min. Cet intervalle est plus court que celui mesuré entre la réapparition tactile du premier twitch au TOF (T_1) 32,8 (18,2–43,4) min ($P < 0,05$). La médiane de l'intervalle entre la réapparition tactile de D_1 et la récupération de T_1 à 15% du contrôle est plus grande que celle de l'intervalle

Key words
MEASUREMENT TECHNIQUES: neuromuscular blockade, mechanomyography, double-burst stimulation, train-of-four;
NEUROMUSCULAR RELAXANTS: atracurium.

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Accepted for publication 8th September, 1994.

qui s'étend jusqu'à la réapparition de T_1 (14,6 vs 10,5) min ($P < 0,05$). Une ou deux réponses au DBS ou au TOF sont souvent perçues avant qu'une réponse mécanomyographique ne soit enregistrée du côté controlatéral. Quand trois ou quatre réponses au TOF sont décelées, ces réponses sont toujours enregistrables par mécanomyographie. Pour conclure, l'évaluation tactile des réponses aux DBS peut déceler des niveaux de curarisation plus profonds que l'appréciation tactile des réponses au TOF.

The degree of moderate and profound levels of neuromuscular blockade may be estimated manually by counting the number of responses to train-of-four (TOF) stimulation[1-4] or by counting the number of post-tetanic twitches.[5] Tactile estimation of more superficial levels of block is possible by evaluating the fade of the four successive responses to TOF.[6] Absence of manually detectable fade in TOF, however, does not exclude residual neuromuscular blockade.[7]

A new stimulation pattern, double-burst stimulation (DBS), is more sensitive than TOF in the manual detection of residual blockade.[8-12] However, DBS may also be used for monitoring moderate and profound degrees of blockade,[13-15] and it is capable of detecting more intense levels of blockade than TOF.[13,15]

Despite the availability of monitoring devices with automatic quantification of the TOF ratio, it is still widespread clinical practice to estimate the level of neuromuscular blockade by tactile or visual evaluation of the responses to peripheral nerve stimulation. The aim of the present study was to evaluate the use of tactile responses to TOF and DBS peripheral nerve stimulation for monitoring moderate and profound levels of neuromuscular blockade.

Methods

Patients

The study comprised 44 healthy women between 18 and 60 yr scheduled for gynaecological laparotomy. Patients suffering from neuromuscular disease or patients under treatment with drugs that might interfere with neuromuscular transmission were excluded. The study was approved by the local Ethics Committee, and written informed consent was obtained from each patient.

Anaesthesia

The patients were premedicated with lormetazepam 2 mg *po* in the morning before surgery. Anaesthesia was induced with midazolam 0.04 $mg \cdot kg^{-1}$, fentanyl 3 $\mu g \cdot kg^{-1}$ followed by thiopentone 5 $mg \cdot kg^{-1}$ and maintained with halothane 0.4–0.6% end tidal concentration (Normac®, Datex, Finland), 65–70% nitrous oxide in oxygen and supplemental doses of fentanyl 50 μg as required. Ventilation was controlled and adjusted to maintain the end tidal carbon dioxide pressure between 4.9 and 5.7 kPa (Normocap®, Datex, Finland).

Neuromuscular blockade

Neuromuscular blockade was induced with a bolus injection of atracurium 0.5 $mg \cdot kg^{-1}$ and maintained with atracurium 0.15 $mg \cdot kg^{-1}$ given every time the height of the first twitch in TOF (T_1) recovered to 15% of the control twitch height obtained before induction of neuromuscular blockade (T_1 control).

Nerve stimulation

Two Myotest DBS® nerve stimulators (Biometer, Denmark) were used for stimulation of the ulnar nerves via surface electrodes at the wrist at both arms. Three different patterns of 0.2 or 0.3 ms square wave stimuli were used: (1) single twitch stimulation at 1 Hz (STS), (2) train-of-four stimulation (TOF), and (3) double-burst stimulation (DBS). Train-of-four consists of four stimuli at 2 Hz repeated every 12 sec. Double-burst stimulation consists of two bursts of three stimuli at 50 Hz separated by a time interval of 750 msec and repeated every 20 sec.[16]

Both arms were used for neuromuscular monitoring: one for tactile evaluation, the other for mechanomyographical measurements. Following identical time of stabilisation of response to 1 Hz STS stimulation, supramaximal stimulation was secured in both arms. In the arm used for tactile evaluation, this was done by securing manual detectable response to 10 mA, 1 Hz, STS and subsequently by using 60 mA as stimulating current.[17] In the arm used for Mechanomyographical measurement, supramaximal stimulation was obtained by ensuring that a stable neuromuscular response was maintained when the stimulation current was reduced from 60 mA to 45 mA and by subsequently using 60 mA as stimulating current.

The nerve stimulation pattern in the arm used for mechanomyographical measurements was identical in all patients. When supramaximal stimulation was ensured, the stimulation mode was switched to TOF, and the responses were allowed to stabilise. The height of the first twitch in TOF (T_1) was then recorded as the control twitch height (T_1 control = 100%). When the responses to TOF stimulation had disappeared following injection of the initial dose of atracurium, the stimulation mode was switched to DBS. When the height of the first twitch in DBS (D_1) had recovered to 5% of T_1 control (both D_1 and T_1 twitch responses were measured as percent of T_1 control), the stimulation mode was switched to TOF and again switched back to DBS after injection of each supplemental dose of atracurium. We used the DBS stimulation mode for mechanomyographic measurement during profound blockade because no response to TOF stimulation was detectable at that level of blockade.

In the arm used for tactile evaluation, the stimulation pattern was switched to DBS in half of the patients and to TOF in the remaining patients after supramaximal stimulation had been ensured. A cross-over design was used implying that the stimulation pattern was switched from DBS to TOF or vice versa after injection of each supplemental dose of atracurium.

In order to account for possible differences in muscle strength between the dominant and non-dominant arm, the dominant arm was used for tactile evaluation in half of the patients and the non-dominant arm in the remaining patients.

Accordingly the patients were randomised into four groups of 11 patients each.

A1: Tactile evaluation of response to DBS at the dominant hand followed by tactile evaluation of response to TOF after injection of the first supplement.

A2: Tactile evaluation of response to DBS at the non-dominant hand followed by tactile evaluation of response to TOF after injection of the first supplement.

B1: Tactile evaluation of response to TOF at the dominant hand followed by tactile evaluation of response to DBS after injection of the first supplement.

B2: Tactile evaluation of response to TOF at the non-dominant hand followed by tactile evaluation of response to DBS after injection of the first supplement.

Tactile evaluation

An anaesthetic nurse evaluated the contractions of the adductor pollicis during 25 sec periods every two minutes. The observer was instructed not to look at the arm used for tactile monitoring and to add a little preload to the thumb with the finger. The nurse asked the question: "Do you feel any contractions in the thumb?" and if the answer was yes: "How many contractions do you feel?" The nurse was blinded with regard to the stimulation pattern and to the mechanomyographical measurements in the contra lateral arm.

Mechanomyographical measurements

The contractions in the adductor pollicis were measured using a force displacement transducer with a preload of 300 g (Myograph 2000®, Biometer, Denmark). Twitch heights at 4% or greater were recorded from the digital display on the Myograph. Owing to the noise-suppressing method used in the analogue to digital converter in the Myograph, the minimum detectable level on the digital display is about 3 to 4% of T_1 control. Accordingly twitch heights less than 4% do not appear on the digital display. Twitch heights less than 4% identified on the recording paper but not appearing on the display were all given the value 2%.

The duration of action of the initial and supplemental doses of atracurium was defined as the time from injection of atracurium until T_1 recovered to 15% of T_1 control.

Temperatures were monitored continuously in the nasopharynx or oesophagus and at both hands (TR9®, Ellab, Denmark). Drugs and fluids were administered via an intravenous line in the leg. Blood pressure was measured oscillometrically in the thigh. In order to preserve heat the patients were covered with warm blankets, intravenous fluids were warmed and the temperature in the operating theatre was kept high.

TABLE I Demographic data and duration of action (time from administration of atracurium until mechanomyographically measured T_1 responses reached 15% of T_1 control) of initial and first and second supplementary doses of atracurium

	Group A	*Group B*
Weight, kg	60.5 (49–74)	64.0 (50–78)
Age, yr	46.0 (28–60)	45.0 (29–51)
Initial dose, min	44.4 (30.3–54.4)	42.4 (32.0–56.9)
First supplement, min	25.1 (18.9–37.4)	25.1 (16.7–34.6)
Second supplement, min	27.0 (19.0–29.8)	28.8 (22.4–29.9)

Values are median and (range).

Statistics

Mann-Whitney U-test and Wilcoxon's signed rank test were used. A P value <0.05 was considered statistically significant.

Results

The patients in Groups A and B were comparable with regard to weight, age and duration of action of the initial and supplemental doses of atracurium (Table I). While the tactile responses to TOF stimulation disappeared in all patients following injection of atracurium, the tactile response to DBS persisted in one patient following the initial dose and in five patients following the supplemental dose. The time from injection of atracurium to tactile reappearance of D_1 was recorded as zero in these patients. One patient was withdrawn from the study because of non-adherence to the protocol.

The time from injection of the initial or supplementary doses of atracurium to tactile reappearance of D1 was less than the time to tactile reappearance of T_1 ($P < 0.05$) (Table II). It was not possible to calculate the time from injection of atracurium until tactile reappearance of the second twitch in DBS (D_2) or TOF (T_2). The second twitch in DBS was felt in only 65% of the patients

TABLE II Time (min) from injection of the initial and first and second supplementary doses of atracurium until tactile reappearance of the first twitch in DBS (D_1) and first twitch in TOF (T_1)

Atracurium	Time (min) to tactile reappearance of D_1	n	Time (min) to tactile reappearance of T_1	n
Initial dose	24.6 (0–39.8)	19	32.8 (18.2–43.4)*	20
First supplement	10.1 (0–20.2)	21	16.4 (6.0–28.6)*	21
Second supplement	13.1 (0–20.3)	12	17.3 (12.2–23.4)*	9

Values are median and (range).
*$P < 0.05$ (between groups).

TABLE III Time (min) from tactile reappearance of the first twitch in DBS (D_1) and tactile reappearance of the first twitch in TOF (T_1) following the initial and first and second supplementary doses of atracurium until the mechanomyographical measured T_1 recovered to 15% of T_1 control.

Atracurium	Time (min) from tactile reappearance of D_1 to $T_1 = 15\%$	n	Time (min) from tactile reappearance of T_1 to $T_1 = 15\%$	n
Initial dose	14.6 (7.1–44.6)	19	10.5 (1.8–19.0)*	20
First supplement	16.5 (5.7–27.7)	19	8.7 (3.7–15.1)*	21
Second supplement	12.4 (7.5–25.1)	9	10.6 (5.5–17.6)	8

Values are median and (range).
*$P < 0.05$ (between groups).

and T_2 in only 75% of the patients at the time when the atracurium supplemental dose was given. The time until mechanomyographically measured T_1 recovered to 15% was longer from tactile reappearance of D_1 than from tactile reappearance of T_1 ($P < 0.05$) (Table III).

The relationship between the percentage of patients in whom one or two responses to DBS were felt after initial and supplementary doses of atracurium and the mechanomyographical measurements of D_1 and T_1 is shown in Figure 1. Tactile response to D_1 reappeared in almost half of the patients before any response was detected by the mechomyograph and the D_1 response could be felt in all patients when the mechanomyographically measured T_1 was 5% or greater (Figure 1). The relationship between the myographical measurements and the percentage of patients with one, two, three or four tactile responses to TOF is shown in Figure 2.

The mechanomyographical response at tactile reappearance of D_2 was greater than the mechanomyographical response at tactile reappearance of D_1 ($P < 0.05$). Likewise the mechanomyographical response at tactile reappearance of T_2 was greater than the mechanomyographical response at tactile reappearance of T_1 ($P < 0.05$).

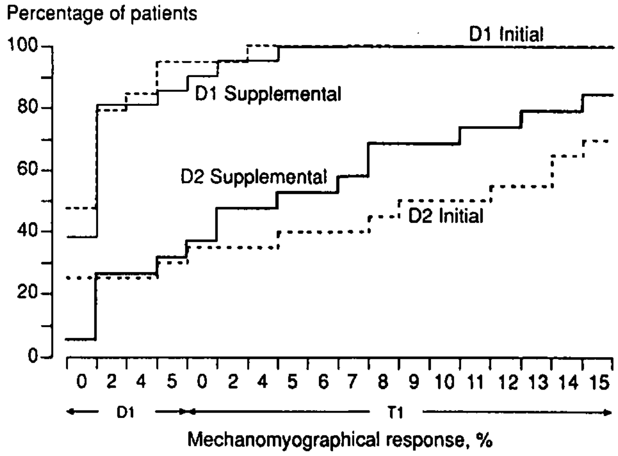

FIGURE 1 Percentage of patients with tactile responses to D_1 or D_2 (Y axis) plotted against D_1 and T_1 measured mechanomyographically in percentage of the T_1 control twitch height (X axis). The thin broken line represents D_1 after initial dose, the thin solid line D_1 after 1st supplementary dose, the thick broken line D_2 after initial dose, and the thick solid line D_2 after 1st supplementary dose.

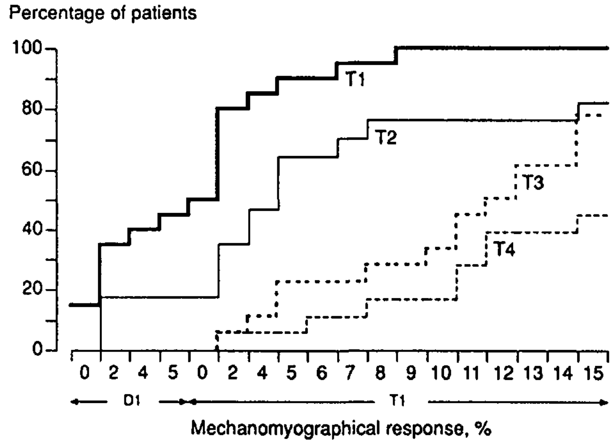

FIGURE 2 Percentage of patients with tactile responses to T_1, T_2, T_3 or T_4 (Y axis) plotted against D_1 and T_1 measured mechanomyographically in percentage of the T_1 control twitch height (X axis). The thick solid line represents T_1, the thin solid line T_2, the thick broken line T_3 and the thin broken line T_4 after initial dose.

The relationship between the tactile and mechanomyographical responses is illustrated in Figures 1 and 2. Furthermore the mechanomyographical response at tactile reappearance of T_1 was greater than the mechanomyographical response at tactile reappearance of D_1 ($P < 0.05$). The relationship between the tactile D_1 and T_1 responses and mechanomyographical responses is illustrated in Figure 3. There were no differences between the mechanomyographical measured twitch heights recorded when the first tactile responses to D_2 and T_2 reap-

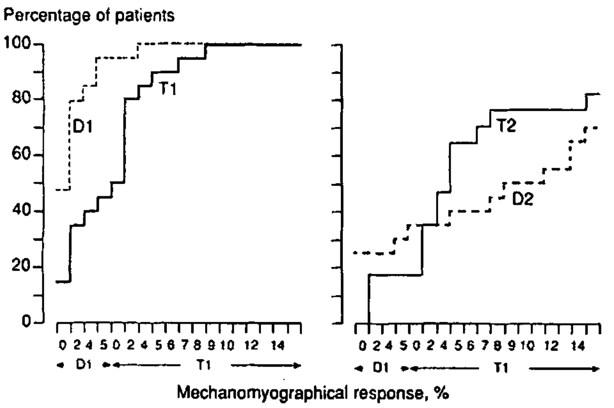

FIGURE 3 Percentage of patients with tactile responses to D_1, D_2, T_1 or T_2 (Y axis) plotted against D_1 and T_1 measured mechanomyographically in percentage of the T_1 control twitch height (X axis). The thin broken line represents D_1 and the thick solid line T_1 after initial dose. The thick broken line represents D_2 and the thin solid line T_2 after initial dose.

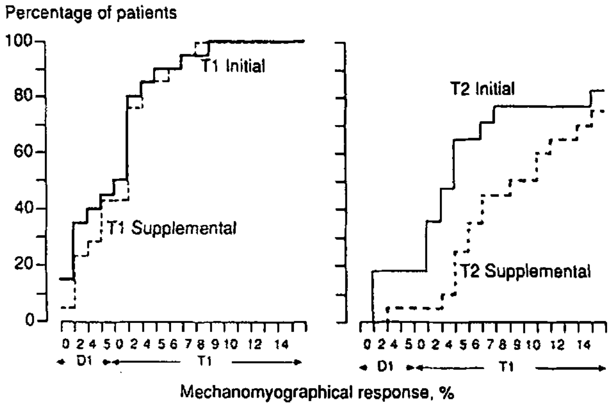

FIGURE 4 Percentage of patients with tactile responses to T_1 or T_2 (Y axis) plotted against D_1 and T_1 measured mechanomyographically in percentage of the T_1 control twitch height (X axis). The thick solid line represents T_1 after initial dose and the thin broken line T_1 after first supplementary dose. The thin solid line represents T_2 after initial dose and the thick broken line T_2 after first supplementary dose.

TABLE IV Mechanomyographical measurements of T_1 at reappearance of one or more tactile responses to DBS or TOF following initial and supplementary atracurium dose, values are median and (range). Differences between the mechanomyographical measured T_1 values at reappearance of tactile response D_1 (or one of the other responses) after initial and supplemental atracurium dose was tested with a Mann-Whitney U-test

	Mechanomyographical T_1 measurements after	
Tactile evaluation	*Initial dose*	*First supplement*
Reappearance of:		
D_1	0 (0–4)%	0 (0–5)%†
D_2	9 (0–>15)%	5 (0–>15)%†
T_1	0 (0–9)%	2 (0–8)%†
T_2	5 (0–>15)%	9 (0–>15)%*
T_3	12 (2–>15)%	>15 (2–>15)%*
T_4	>15 (2–>15)%	>15 (6–>15)%*

*Indicate $P < 0.05$.
†Indicate $P > 0.05$.

peared neither after initial dose nor after 1st supplemental dose (NS). The relationship between tactile reappearance of one or more twitches in DBS or TOF and the mechanomyographical measured T_1 is shown in Table IV. There was no difference in the mechanomyographical measured twitch heights recorded when the first tactile responses to T_1 reappears after initial and supplementary doses respectively (NS), but there was a difference between the mechanomyographical measured twitch heights recorded when the first tactile responses to T_2 reappeared after initial and supplementary doses respectively ($P < 0.05$). The relationship between the tactile T_2 responses and mechanomyographical responses is illustrated in Figure 4. The thenar eminence temperature was >32.0°C and the central temperature >36.0°C at all times. There was no difference in any of the measured variables between the dominant and non-dominant hand (NS).

Discussion

There were three major findings in the study. First, tactile evaluation of response to DBS detected more intense levels of neuromuscular blockade than tactile evaluation of response to TOF stimulation. Second, tactile response to both bursts in DBS reappeared in some of the patients before responses to D_1 or T_1 were detected mechanomyographically in the contralateral arm. Third, when three or four twitches in TOF were felt, T_1 responses were always detected mechanomyographically.

The study design was based on monitoring the evoked neuromuscular responses simultaneously at both hands. The tactile and mechanomyographical measurements were not performed in the same arm for two reasons: (1) The precision of the Myograph measurements is dependent upon stable fixation of the arm. If tactile evaluations are interspersed between the mechanomyographical measurements this stable suspension is disturbed. (2) Simultaneous TOF and DBS measurements cannot be performed in the same arm. The neuromuscular response needs time for stabilisation following changes in stimulation mode. When switching from TOF to DBS mode and vice versa the twitch height responses are not stable until after the third stimulation after the change.[18] In the present study, the tactile responses were evaluated by anaesthetic nurses. The nurses were trained in evaluating the tactile response to nerve stimulation and to give supplemental doses of neuromuscular blocking agents.

Tactile responses often reappeared before responses were detected by the Myograph in the contralateral arm (Figures 1 and 2). There may be several reasons for this. (1) The equipment may be inaccurate or unreliable. (2) The study design may have introduced a systematic error, such as a larger initial delivery of drug to the monitored arm because of the high stimulation rate to obtain a baseline. (3) The nurse may not have made a proper tactile assessment of the adductor pollicis. However, the Myograph was tested immediately before the start of the study, and the bias against known forces was found negligible. Measurements were performed by doctors with long experience in the use of neuromuscular monitoring equipment. A systematic error was minimised by the use of a cross-over design and by randomisation with regard to the use of the dominant or non-dominant hand and with regard to the initial stimulation mode (TOF or DBS). Studies[19] and unpublished observations made by our group have revealed only minor differences in measured neuromuscular blockade between the two arms of a patient monitored with a Myograph 2000 on each arm. In our opinion most of the observed differences between the two monitoring techniques are due to variation within the tactile monitoring technique. The preload at the thumb, the position of the hand as well as the attention of the observer vary with time. The observer may falsely register a movement caused by the surgeon as a twitch response and furthermore the observer is influenced by the previous responses.

Tactile response to D_1 reappeared 8.2 min earlier than the tactile response to T_1 (Table II and Figure 3, $P < 0.05$). Tactile response to DBS can therefore detect more intense levels of blockade than tactile response to TOF. The ability of tactile evaluation of response to DBS to monitor deeper levels of blockade has also been reported in other studies. Braude *et al.* found that the mechanomyographically measured T_1 response was always <20% if only one response to DBS was felt.[15] Unfortunately Braude *et al.* excluded all mechanomyographically measured values where T_1 was <3% of T_1 control. It is therefore not possible from the data of Braude to state how often tactile reappearance of D_1 occurred before tactile or mechanomyographical reappearance of T_1 This may explain why Braude only found one patient with tactile double response to DBS when T_1 was <5% of T_1 control, while the present study found tactile response to both D_1 and D_2 in several of the patients before any mechanomyographical response could be detected.

Mechanomyographical studies[9,13,15] have shown that responses to D_1 reappear before responses to T_1 during recovery from deep neuromuscular blockade. Thus, it was expected that tactile responses to D_1 would be felt before responses to TOF stimulation were measured by the force displacement transducer and also before tactile responses to T_1 were felt (Figure 3). During anaesthesia for neurosurgery or eye surgery, where it might be important to guarantee profound levels of blockade, tactile evaluation of the response to DBS is superior to tactile evaluation of the response to TOF stimulation. Reappearance of the tactile response to DBS gives the anaesthetist an early warning that the neuromuscular blockade is changing from profound to moderate levels.

In about one-third of patients it was possible to feel two responses to DBS stimulation before any response to TOF stimulation was detectable by the Myograph (Figure 1), and tactile responses to both T_1 and T_2 reappeared in some of the patients before any response to TOF stimulation was detectable by the Myograph (Figure 4). We did not study reversal time, but as reversal is not recommended during profound neuromuscular blockade,[20,21] reversal cannot be recommended at tactile reappearance of D_1, D_2, T_1 or T_2 until the safety of such a technique has been verified in clinical studies. Accordingly Haraldsted *et al.*[22] found that when two responses to TOF were palpable, a period of 25.9 min elapsed before a TOF ratio of 0.70 was reached after neostigmine 2.5 mg, a reversal time that indicates that the neuromuscular blockade at the time of reversal was too deep.

Mechanomyographical responses were detected in all patients at tactile reappearance of T_3 and T_4. Even though we did not study reversal time, it is our opinion that this indicates that reappearance of the third or fourth tactile response to TOF stimulation may be used as an indicator for the time of administration of the reversal agent. Further clinical reversal studies are needed to confirm this statement. In a study by Kopman, edrophonium 0.3 $mg \cdot kg^{-1}$, given when the fourth tactile response to TOF stimulation reappeared, antagonised the blockade within ten minutes.[23] Thus, in this study, tactile evaluation of the T_4 response was a reliable indicator for safe administration of reversal agent. However, in a study by Pedersen *et al.* the use of a nerve stimulator was found to have no effect on the dose of relaxant given during anaesthesia, on the need for supplementary doses of anticholinesterase in the recovery room, or on the incidence of postoperative residual neuromuscular blockade evaluated clinically.[24]

In conclusion, we have found that by using tactile evaluation of responses to DBS, it is possible to monitor deeper levels of neuromuscular blockade than by tactile evaluation of responses to TOF stimulation.

References

1 *Ali HH, Utting JE, Gray C.* Stimulus frequency in the detection of neuromuscular block in humans. Br J Anaesth 1970; 42: 967–77.

2 *Lee C-M.* Train-of-4 quantitation of competitive neuromuscular block. Anesth Analg 1975; 54: 649–53.
3 *O'Hara DA, Fragen RJ, Shanks CA.* Comparison of visual and measured train-of-four recovery after vecuronium-induced neuromuscular blockade using two anaesthetic techniques. Br J Anaesth 1986; 58: 1300–2.
4 *O'Hara DA, Fragen RJ, Shanks CA.* Reappearance of the train-of-four after neuromuscular blockade induced with tubocurarine, vecuronium or atracurium. Br J Anaesth 1986; 58: 1296–9.
5 *Viby-Mogensen J, Howardy-Hansen P, Chraemmer-Jørgensen B, Ørding H, Engbaek J, Nielsen A.* Posttetanic Count (PTC): a new method of evaluating an intense non-depolarizing neuromuscular blockade. Anesthesiology 1981; 55: 458–61.
6 *Viby-Mogensen J.* Clinical assessment of neuromuscular transmission. Br J Anaesth 1982; 54: 209–22.
7 *Viby-Mogensen J, Jensen NH, Engbaek J, Ørding H, Skovgaard LT, Chraemmer-Jørgensen B.* Tactile and visual evaluation of the response to train-of-four nerve stimulation. Anesthesiology 1985; 63: 440–3.
8 *Drenck NE, Ueda N, Olsen NV, et al.* Manual evaluation of residual curarization using double burst stimulation: a comparison with train-of-four. Anesthesiology 1989; 70: 578–81.
9 *Gill SS, Donati F, Bevan DR.* Clinical evaluation of double-burst stimulation. Its relationship to train-of-four stimulation. Anaesthesia 1990: 45: 543–8.
10 *Ueda N, Muteki T, Tsuda H, Inoue S, Nishina H.* Is the diagnosis of significant residual neuromuscular blockade improved by using double-burst nerve stimulation? Eur J Anaesthesiol 1991; 8: 213–8.
11 *Saddler JM, Bevan JC, Donati F, Bevan DR, Pinto SR.* Comparison of double-burst and train-of-four stimulation to assess neuromuscular blockade in children. Anesthesiology 1990; 73: 401–3.
12 *Brull SJ, Silverman DG.* Visual and tactile assessment of neuromuscular fade. Anesth Analg 1993; 77: 352–5.
13 *Kirkegaard-Nielsen H, May O.* Double burst stimulation for monitoring profound neuromuscular blockade: a comparison with posttetanic count and train-of-four. Acta Anesthesiol Belg 1992; 43: 253–7.
14 *Kirkegaard-Nielsen H, May O.* The influence of the double burst stimulation (DBS) pattern on the DBS-train-of-four ratio relationship. Anästhesiol Intensivmed Notfallmed Schmerzther (in press).
15 *Braude N, Vyvyan HAL, Jordan MJ.* Intraoperative assessment of atracurium-induced neuromuscular block using double burst stimulation. Br J Anaesth 1991; 67: 574–8.
16 *Engbaek J, Østergaard D, Viby-Mogensen J.* Double burst stimulation (DBS): a new pattern of nerve stimulation to identify residual neuromuscular block. Br J Anaesth 1989; 62: 274–8.
17 *Helbo-Hansen HS, Bang U, Kirkegaard-Nielsen H, Skovgaard LT.* The accuracy of train-of-four monitoring at varying stimulation current. Anesthesiology 1992; 76: 199–203.
18 *Kirkegaard-Nielsen H, Severinsen IK, Lindholm P, Bülow C, Helbo-Hansen HS.* Comparison of response to double burst stimulation (DBS) and TOF nerve stimulation: a methodological study. Acta Anaesthesiol Scand Suppl 1993; 37: 227, 036.
19 *Jensen E, Werner M, Viby-Mogensen J.* Bilateral measurement of neuromuscular blockade using mechanomyography. Anesthesiology 1989; 71: A823.
20 *Engbaek J, Østergaard D, Skovgaard LT, Viby-Mogensen J.* Reversal of intense neuromuscular blockade following infusion of atracurium. Anesthesiology 1990; 72: 803–6.
21 *Magorian TT, Lynam DP, Caldwell JE, Miller RD.* Can early administration of neostigmine, in single or repeated doses, alter the course of neuromuscular recovery from a vecuronium-induced neuromuscular blockade? Anesthesiology 1990; 73: 410–4.
22 *Haraldsted VY, Nielsen JW, Joensen F, Dilling-Hansen B, Hasselstrøm L.* Infusion of vecuronium assessed by tactile evaluation of evoked thumb twitch. Br J Anaesth 1988; 61: 479–81.
23 *Kopman AF.* Tactile evaluation of train-of-four count as an indicator of reliability of antagonism of vecuronium- or atracurium-induced neuromuscular blockade. Anesthesiology 1991; 75: 588–93.
24 *Pedersen T, Viby-Mogensen J, Bang U, Olsen NV, Jensen E, Engbaek J.* Does perioperative tactile evalutaion of the train-of-four response influence the frequency of postoperative residual neuromuscular blockade? Anesthesiology 1990; 73: 835–9.