STIMULUS FREQUENCY IN THE DETECTION OF NEUROMUSCULAR BLOCK IN HUMANS

BY

HASSAN H. ALI, J. E. UTTING AND CECIL GRAY

SUMMARY

Study of the literature on the physiology of neuromuscular transmission suggested two new methods of assessing the degree of neuromuscular block in the human subject. These were, first, a comparison of the height of the recorded twitch tensions developed in response to repeated single stimuli applied at differing frequencies and, second, examination of the extent of reduction in amplitude of twitch tensions developed in response to a short train of four stimuli. In assessing the first method the use of three frequencies of stimulation was tried (i.e., 0.1 Hz (c.p.s.), 0.3 Hz and 1.0 Hz). It was found that as the frequency of stimulation was increased there was reduction in the amplitude of the recorded twitch response in curarized subjects, and that this reduction appeared to depend on the degree of curarization. In assessing the second method a short train of four stimuli at 2 Hz was used, and it was found that there was a progressive fade of successive recorded mechanical twitch responses in curarized subjects which again appeared to depend on the degree of curarization. It is suggested that the amplitude of the twitch response at a higher frequency expressed as a percentage of that at the slower rate, and the last response of the train of four expressed as a percentage of the first may be useful in measuring degree of neuromuscular block in man.

It has been found that measurement of the force of an isometric muscle contraction evoked by motor nerve stimulation gives a more accurate index of neuromuscular block than does measurement of the action potential which is associated with the contraction (Botelho, 1955): indeed measurement of the force of contraction in this way has been said to be the best method of assessing neuromuscular block in clinical situations (Katz, 1965).

Study of the twitch response in a variety of conditions has shown that after administration of tubocurarine, and a number of other compounds the faster the rate of stimulation used the greater is the degree of neuromuscular block and the smaller will be the amplitude of the muscle twitch response obtained (Chou, 1947; Guyton and Reeder, 1949; Preston and Van Maanen, 1953; Wislicki, 1958; Blackman, 1963).

The decrease in the size of the muscle twitch which follows an increase in the stimulus frequency is rapid, a steady level usually being reached by the fifth twitch after changing to the faster rate when working in the range from 0.1 Hz to 10 Hz (Rosenblueth and Morison, 1937; Maaske, Boyd and Brosnan, 1938; Blackman, 1963).

Grob, Johns and Harvey (1956) demonstrated the effect of intra-arterial injection of various drugs on the evoked electromyogram in human subjects. They applied a standard pattern of stimulation which consisted of trains of four stimuli at a frequency of 25 Hz, the trains of stimuli being repeated at intervals of 2–10 seconds (i.e., 0.5–0.1 Hz). Before tubocurarine was given each of the four muscle action potentials obtained in this way was of equal height; and when a small dose of the drug (0.15 mg) was administered intra-arterially there was usually no effect on the initial muscle action potential of the train when it was compared with the pre-injection height. In these circumstances, however, there was slight steplike depression of the subsequent second, third and fourth potentials, the fourth being depressed most and the second least. As the dose of tubocurarine

was increased depression of the first potential was also seen, together with increasing steplike depression of the successive three potentials, the fourth again being the most affected.

Roberts and Wilson (1968) have already used a train of four stimuli at 4 Hz to assess the progress and treatment of patients with myasthenia gravis. Evidence obtained in experimental animals and humans indicates that during repetitive nerve stimulation there is a progressive decrease in the amount of acetylcholine released from the motor nerve endings, a decrease reflected in a progressive decrease in the size of the endplate potentials (Liley and North, 1953; Boyd and Martin, 1956; Brooks and Thies, 1962; Elmqvist and Quastel, 1965).

The following investigation was undertaken in an attempt to find a satisfactory objective measure of changes of neuromuscular block based on these phenomena.

METHODS

Stimulation and recording.

The ulnar nerve was stimulated by means of 25-gauge needle electrodes placed subcutaneously at the wrists (Katz and Wolf, 1964). Mechanical twitch responses were elicited with square wave stimuli of 0.3 msec duration, the voltage being adjusted to 10–20 per cent above that required for maximal response. Stimuli were delivered through a stimulus isolation unit (Grass; SIU 478) from a Grass stimulator (model S8). The resulting adduction of the thumb activated a tensile/compressive transducer (Ether UFI ± 32 ounces), assembled in the form of a hand grip (Ali, 1970). This resulted in an almost completely isometric contraction. The output of the transducer was amplified and recorded on a Devices single channel recorder (type R2).

Pattern of nerve stimulation.

Single stimuli of duration 0.3 msec were delivered repetitively at frequencies of 0.1 Hz (one stimulus every 10 sec), 0.3 Hz (one stimulus every 3 sec) and 1 Hz (one stimulus every sec). In addition a train of four stimuli was delivered at a frequency of 2 Hz and a train duration of 2 sec (there was thus an interval of 0.5 sec between each of the four stimuli in the train); this train of four stimuli was repeated every 10 sec (i.e., at a train frequency of 0.1 Hz).

Ratios of twitch height.

Three ratios of twitch heights were selected for particular study. First the amplitude of the twitch at the highest frequency of stimulation (1.0 Hz) was expressed as a percentage of the amplitude obtained at the slowest rate of stimulation (0.1 Hz). Secondly, the percentage of the amplitude of the muscle twitch obtained when the frequency of stimulation was 1.0 Hz compared to the amplitude of the muscle twitch obtained at the frequency of 0.3 Hz. Thirdly, the height of the last of the train of four responses was expressed as a percentage of the height of the first response. These three ratios were considered as possible indices of the degree of recovery from the effect of the curarizing drug during surgery, and of the degree of residual curarization after neostigmine had been given. A group of conscious volunteers was also studied for the purpose of comparison.

Patients and volunteers.

Four groups of experiments were conducted, there being ten individuals in each group; in no case was there any evidence of neuromuscular disease. The age of the volunteers and patients was within the range of 18–65 years; the anaesthetized patients (groups 2–4 inclusive) were all undergoing elective lower abdominal or limb surgery.

Group 1 consisted of conscious volunteers. After a recording of the muscle response to the three different frequencies and to the train of four stimuli had been obtained for control purposes each volunteer was given tubocurarine 5 mg intravenously. The various patterns of stimulation were investigated until there was full recovery of the height of twitch responses to the control levels. The findings were correlated with the response to simple clinical tests for muscle paralysis.

Group 2 consisted of anaesthetized patients to whom a small dose of tubocurarine was administered; pulmonary ventilation was not controlled. Morphine 10 mg and atropine 0.6 mg was given as premedication 1 hour before surgery. Induction of anaesthesia was with thiopentone (200–300 mg) and was maintained with nitrous oxide and oxygen (5 l/min and 2 l/min) together with halothane (0.5–2 per cent). In some cases a face mask was used but in others an endotracheal tube was passed; in the latter case the larynx and trachea
were previously anaesthetized with lignocaine solution (4 per cent). When a clinically steady state of anaesthesia had been achieved, each patient was given tubocurarine 10 mg: 15 min after the drug had been administered atropine 0.6 mg and neostigmine 2.5 mg were given to reverse the neuromuscular block. As in the volunteers in group 1, twitch responses were studied using the pattern described in the section on methods. Control heights of muscle twitch were obtained before the relaxant was given but after the patient had been anaesthetized, and the investigation was continued until full recovery of the twitch heights was achieved as compared to the control. The procedure was regarded as monitoring neuromuscular block and formal permission of the patient was not considered to be required; a full explanation of the procedure, however, was given to each patient.

**Group 3** consisted of a group of anaesthetized patients to whom a larger dose of tubocurarine was administered; pulmonary ventilation had to be controlled. The premedication used was similar to that in the previous group, as was the induction of anaesthesia. The induction dose of thiopentone, however, was followed by tubocurarine 0.6 mg/kg body weight. A cuffed orotracheal tube was passed; anaesthesia was maintained with a mixture of nitrous oxide and oxygen 5 l/min and 2 l/min and IPPV was employed. No other supplement to the anaesthesia was used. At the end of the operation atropine 1.2 mg and neostigmine 5.0 mg were given together intravenously, either as a single dose or in two equal parts. Sometimes control values were obtained before the relaxant was given; in some cases, however, this was not done and the pattern obtained before neostigmine administration was used to compare with that obtained after the drug had been given.

**Group 4** consisted of anaesthetized patients to whom suxamethonium was given. Premedication and the induction and maintenance of anaesthesia was similar to that used in the patients in group 3, and pulmonary ventilation was controlled until adequate spontaneous ventilation returned. The suxamethonium was given in a dose of 20–65 mg soon after the induction of anaesthesia and was used to facilitate endotracheal intubation. The effect of suxamethonium was also tested in patients after prolonged anaesthesia with nitrous oxide/oxygen and halothane (1–2 per cent); again controlled respiration was employed after suxamethonium was given, until adequate spontaneous respiration returned. The twitch response was studied before suxamethonium was given and during and after recovery from the drug.

**RESULTS**

The sections which follow give a qualitative account of the results obtained. A further paper (Ali, Utting and Gray, 1971) gives a quantitative account of the use of the train of four stimuli in assessing degree of residual curarization. It was found that the use of the train of four stimuli had advantages over the use of the simple change of frequency for the quantitative estimation of non-dепolarizing block; for though the two indices ran pari passu the train of four stimuli appeared to be a more sensitive index.

**Control tracings (all groups).**

(a) Change of frequency of stimulation.

Before a muscle relaxant was given there was no diminution of the height of the twitch response following a change from lower to higher frequency (figs. 1, 2, 6, 7): this applied when the stimulus frequency was increased both from 0.1 Hz to 1 Hz and from 0.3 Hz to 1 Hz.

(b) Train of four stimuli.

In every case in which the train of four stimuli was applied before a muscle relaxant was given the twitch responses corresponding to each of the four stimuli were all of equal height (figs. 3, 5, 9, 10).

**Pattern after tubocurarine (groups 1–3).**

The change in the pattern of twitch response seen after tubocurarine was similar in the three groups in which its action was tested. The differences in the three groups were only in the degree of change observed.

(a) Change of frequency of stimulation.

A change in frequency of stimulation from 0.1 Hz to 1 Hz and from 0.3 Hz to 1 Hz caused a diminution of twitch height but the degree of depression was much more marked in the change from 0.1 Hz to 1 Hz; this change of frequency,
therefore, seemed to give a more sensitive index of the degree of curarization. In the figures attention has been concentrated on the change from 0.1 Hz to 1.0 Hz.

(A) Control muscle twitch before tubocurarine is administered shows no difference in twitch heights at the two rates of stimulation used.

(B) During curarization there may be initially no difference in the twitch height at the slower rate of stimulation from that obtained in the control period but a change to the faster frequency results in a sharp decline in twitch height.

(C) As recovery progresses the ratio of the twitch height at the faster to the slower frequency gradually approaches unity.

Diagrammatic illustration of the effect of a small dose of suxamethonium on the twitch response to the train of four stimuli at 2 Hz. A represents the control response (i.e., before the administration of the drug). Under anaesthesia with nitrous oxide and oxygen, suxamethonium reduces the twitch height in each of the four responses equally (B). Under prolonged halothane anaesthesia, however, a degree of fade was sometimes apparent after suxamethonium was given (C).

Therefore, seemed to give a more sensitive index of the degree of curarization. In the figures attention has been concentrated on the change from 0.1 Hz to 1 Hz.

Group 1 illustrates the effect of a small intravenous dose of tubocurarine. In four of the ten volunteers there was no change either in the initial twitch height or after the change of frequency (i.e., no detectable change from control conditions): these volunteers made no complaint of dizziness or diplopia. In two cases there was no change in the twitch height at 0.1 Hz when tubocurarine was given but a change in frequency from 0.1 Hz to 1 Hz caused a diminution of the twitch height (figs. 1, 6). In the case of the other four volunteers there was diminution of the twitch height at 0.1 Hz after tubocurarine was given.
The effect of tubocurarine on the twitch height in a volunteer. There was no change in twitch height when the frequency of stimulation was increased from 0.1 Hz to 1 Hz (A to B) before tubocurarine was administered. After tubocurarine 5 mg was administered, this change in frequency caused a diminution of twitch height (D to E and F to G). Note the slight increase in the height of the muscle twitch after tubocurarine was given.

The effect of tubocurarine on the twitch height in an anaesthetized patient. Change of frequency from 0.1 Hz to 1 Hz before tubocurarine was given caused no change in twitch height (A). Change in frequency from 0.3 Hz to 1 Hz during curarization caused diminution in twitch height (B, C, D, E, F). After neostigmine there is recovery of the twitch and with depression of the twitch height on the change of the frequency from 0.1 Hz to 1 Hz (G, H). Note that the per cent depression of the twitch response at 1 Hz is much less after neostigmine than before.
and a relatively more marked diminution when the frequency of stimulation was increased from 0.1 Hz to 1 Hz (fig. 2). All the volunteers who showed these changes had diplopia, slurred speech and found difficulty in opening the eyes.

The changes observed in the anaesthetized patients in group 2 were qualitatively the same as in group 1 but the quantitative changes were greater (fig. 7). In group 3 the large dose of tubocurarine administered usually resulted in complete ablation of the twitch, but during recovery, both before and after neostigmine, the same pattern of partial curarization seen in groups 1 and 2 was observed.

(b) *Train of four stimuli.*

In group 1 it was found that three of the volunteers showed no change in twitch height in response to the train of four stimuli (i.e., there was no change from control twitch heights) after the tubocurarine was administered. In five of the volunteers there was no change in the first twitch response of the train of four but diminution of the subsequent three twitches (fig. 3b) and in two volunteers there was depression of the first twitch response as well as diminution of the subsequent three twitches (fig. 3c, d). One of the volunteers who showed no diminution of twitch response to the changes of frequency studied showed some diminution in the second to fourth twitch height of the train of four. During recovery from tubocurarine each of the four twitch heights gradually returned to control levels; the first was the most rapid to return and the fourth was the slowest.

The same pattern was seen in the anaesthetized patients in groups 2 and 3; and it was, of course, found that the recovery process was accelerated by neostigmine (figs. 9, 11). When the larger doses of tubocurarine were given (i.e., in group 3), however, there was complete ablation of the twitch.
which reappeared either during spontaneous recovery or when neostigmine was given (fig. 11).

Pattern after suxamethonium (group 4).
Suxamethonium usually abolished the twitch response completely. When recovery was taking place it was found that change of stimulus frequency from slower to faster rate did not result in a change in the slope of the recovery curve (figs. 4, 8). The response to the train of four stimuli was ablated by suxamethonium but on recovery all four twitch responses were of equal height when the twitch response reappeared if halothane was not being used in the anaesthetic (figs. 5B, 12A). In the case of prolonged halothane anaesthesia, however, small doses of suxamethonium led to some degree of "fade" in the responses to the train of four stimuli during both the onset of action and recovery from suxamethonium (figs. 5C, 12B, C).

DISCUSSION
Methods used clinically to assess the degree of neuromuscular block are mostly dependent on the pattern of evoked muscle response to change in stimulus frequency (Churchill-Davidson and Christie, 1959).

(a) Observation of the twitch response to single repeated nerve stimuli.
(As by the Block-Aid Monitor; Burroughs Wellcome Ltd.) This method will only detect
considerable degrees of curarization, but it may be helpful in deciding whether prolonged apnoea after anaesthesia is peripheral or central in origin.

(b) Failure to sustain tetanus (tetanic fade).

The extent of this failure is dependent on the frequency and duration of stimulation (Gissen and Katz, 1969), and furthermore fade may be absent during a 40–50 per cent block following tubocurarine (Katz, 1965). Heisterkamp, Skovsted and Cohen (1969) showed that the mean twitch tension was reduced to 35 per cent of control values after tubocurarine (patients anaesthetized with methoxyflurane); 63 per cent of these patients failed to demonstrate fade when stimulated with a tetanic volley of frequency 30 Hz and duration 3 sec.

Fig. 11

A 50-year-old male patient, 68 kg. Anaesthesia was induced with thiopentone and followed by tubocurarine 45 mg (panel 1), and maintained on nitrous oxide/oxygen and IPPV. Complete ablation of the twitch response at 0.3 Hz was observed after 4 min. Spontaneous recovery of the twitch at the same frequency appeared 70 min later.

Panel 2. Neostigmine 2.5 mg was given 80 min after tubocurarine. Recovery of the twitch response to 0.3 Hz stimuli was monitored for 4 min, after which trains of four stimuli at 2 Hz being repeated every 10 sec; note the appearance of the first response only which progressively increased in amplitude with small subsequent responses to the train of four stimuli. At the end of panel 2 a further dose of neostigmine 2.5 mg was given.

Panel 3 shows the gradual and progressive increase in the four responses 1 minute after the second neostigmine dose.

Panel 4 shows an increase in the twitch height in response to stimuli at 0.3, 0.1 and 1 Hz respectively. Note that the twitch height is higher than the control before tubocurarine, yet there is still some fade in the four responses to the train of four stimuli 10 min after the first neostigmine dose.
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(c) Post-tetanic potentiation (PTP).

This is markedly influenced by the duration and frequency of the preceding tetanus, as well as by the post-tetanic interval (Liley and North, 1953). PTP can occur in the absence of neuromuscular block (Von Euler and Brown, 1938; Botelho and Cander, 1953; Hughes and Morrell, 1957); in this case the phenomenon seems to be explained either by a change in the contractile response of the muscle or by repetitive firing of the nerve or muscle.

Gissen and Katz (1969) investigated the relationship between twitch, tetanus and PTP in an attempt to obtain an adequate index of neuromuscular block in man. They found that the response to tetanic stimulation at various frequencies gave a more sensitive index of neuromuscular block than did study of either twitch response or PTP: during partial neuromuscular block, tetanus is not maintained at higher frequencies of stimulation even though the magnitude of the twitch response to single stimuli may have returned to control level. As a result of their investigations these workers suggested that clinical nerve stimulators be modified to provide tetanic stimulation at several fixed frequencies (i.e., 25, 50, 100 and 200 Hz).

(d) Monitoring the effects of anticholinesterase therapy on the twitch response.

This may be a useful practical guide, but because these drugs have multiple actions, including that of post-junctional block (Roberts, 1963), the results cannot always be relied upon;

Fig. 12

Responses to the train of four stimuli at 2 Hz after initial responses to single stimuli at 0.3 Hz.

(A) Administration of and recovery from suxamethonium; anaesthesia with nitrous oxide and oxygen only.

(B, C) During administration and recovery from suxamethonium; anaesthesia with nitrous oxide, oxygen and halothane. Note the relative depression of the second, third and fourth heights. (S.CH = suxamethonium.)
and they offer neither proof of the presence of neuromuscular block nor a measurement of its degree.

(e) Facilitation.
This has been suggested by Berry (1966) as a possible method of assessing neuromuscular block in the absence of a control response before curarization. He utilized a facilitation phenomenon based on the application of two stimuli to the motor nerve with a very small time interval: this resulted in partial restoration of neuromuscular transmission in the curarized preparation—a phenomenon which he showed to be due to summation of endplate potentials. He compared the twitch tension resulting from a single stimulus and that resulting from a double stimulus with an interval of 1–1.8 msec between the two stimuli. Berry maintained that an increase in the muscle tension in response to the double stimulus may reveal evidence of neuromuscular block and suggested that this might provide a technique which could be applied in the human subject to detect residual curarization.

Ideally the objective measurement of neuromuscular transmission should assess muscle strength as a proportion of fibres functioning at different twitch rates. It might be thought that comparison of isometric twitch heights obtained before a relaxant drug is given and again during recovery should provide a valid comparison, but there are several reasons why this is not so.

Unless monitoring is performed routinely, control levels of twitch tension are not available when postoperative muscle weakness is suspected; moreover, complete stability of recording over a period of hours cannot be guaranteed. Drugs may cause repetitive nerve firing, as, for example, some of the anticholinesterases (Masland and Wigton, 1940; Blaber and Bowman, 1963) or repetitive muscle firing, as, for example, germaine diacetate (Flacke, 1963). Repetitive nerve firing and repetitive muscle firing will both cause twitch heights out of proportion to the number of muscle fibres which are active, and this may result in twitch responses which are greater than normal despite the fact that a substantial number of endplates may remain blocked.

The methods of assessment of neuromuscular block investigated in this paper have several advantages over those in current use. Although they do not give a direct measurement of the proportion of fibres responding to motor nerve stimulation (this in any case will vary with the frequency of stimulation) it can be reasonably postulated that they afford a direct comparison between the degree of neuromuscular block in one patient and in another, and between the degrees of neuromuscular block found in the same patient at different times. These methods, moreover, do not require control levels of developed twitch tensions, which, in any case, can be misleading. They are simple and unlikely to be complicated by pure nerve or muscle effects, and do not cause the same amount of discomfort to the conscious patient recovering from anaesthesia as do tetanic rates of stimulation of 50 Hz or more.

The importance of particular levels of block as measured in this manner remains to be assessed. Tubocurarine 5 mg in conscious volunteers produced results which suggested a variable degree of block, though it might be added that the experimental findings using the two ratios appeared to correlate with the degree of diplopia and weakness as assessed clinically. A variation in response between individuals such as the result suggested could be due to a number of factors—for example, differences in dose/body weight ratio, in distribution, in plasma binding, and in muscle sensitivity.

While the degree of neuromuscular block demonstrated with tubocurarine 5 mg given to conscious volunteers is not associated with morbidity, the same degree of block might possibly be significant if it were present for long periods in a patient in the postoperative period. It is important, therefore, to establish the degree of reversal of neuromuscular block, which is compatible with safe return to the ward, and it seems probable that this can be achieved using the train of four stimuli (Ali, Utting and Gray, 1971). This test may also prove to be useful in assessing sensitivity to relaxants, and the likely dose requirements for particular operations. It could also be used as a tool for investigating the effects on neuromuscular transmission of other drugs and inhalation agents used during anaesthesia.

REFERENCES
STIMULUS FREQUENCY IN DETECTION OF NEUROMUSCULAR BLOCK


FREQUENCE DES STIMULI DANS LA DETECTION DU BLOCK NEUROMUSCULAIRE CHEZ L'HOMME

SOMMAIRE

L'étude de la littérature au sujet de la physiologie de la transmission neuromusculaire a suggéré deux nouvelles méthodes pour évaluer le degré de blocage neuromusculaire chez l'homme. Il y a en premier lieu une comparaison de l'intensité des tensions enregistrées de la convulsion, développée en réaction à des stimulations individuelles répétées appliquées à des fréquences différentes, et en second lieu l'estimation du degré de réduction de l'amplitude des tensions de la convulsion, développée en réaction à une courte série de quatre stimulations. Pour la première méthode, trois fréquences de stimulation ont été essayées (soit 0.1 Hz (CPS), 0.3 Hz et 1.0 Hz). On observa que l'augmentation de la fréquence de stimulation s'accompagne d'une réduction de l'amplitude de la réaction convulsive enregistrée chez les sujets curarisés, et que cette réduction semblait dépendre du degré de curarisation. Pour évaluer la seconde méthode, on utilisla une courte série de 4 stimulations à 2 Hz et on nota qu'il y eut une réduction progressive des réactions convulsives mécaniques successives, qu'on enregistrera chez les sujets curarisés et que cette réduction sembla dépendre du degré de curarisation. Les auteurs croient que l'amplitude de la réaction convulsive à une fréquence plus élevée, exprimée en pourcentage de celle à un taux plus lent, ainsi que la dernière réaction de la série de quatre, exprimée en pourcentage de la première, peuvent servir utilement pour mesurer le degré de blocage neuromusculaire chez l'homme.
REIZFREQUENZ ZUR ERMITTlung EINER NEUROMUSKULÄREN BLOCKADE BEIM MENSCHEN

ZUSAMMENFASSUNG

Das Studium der Literatur über die Physiologie der neuromuskulären Übertragung gab Anlaß, zwei neue Methoden zur Ermittlung des Grades eines neuromuskulären Blockade beim Menschen vorzuschlagen. Diese Methoden waren: (1) ein Vergleich der Höhe der bei Zuckung registrierten Spannungen, wie sie sich als Reaktion auf mit verschiedenen Frequenzen applizierte Einzelreize entwickelten; (2) eine Untersuchung des Ausmaßes der Amplitudenabnahme der bei Zuckung registrierten Spannungen, wie sie sich als Reaktion auf vier in kurzer Folge applizierte Reize entwickelte. Bei der ersten Methode wurden drei verschiedene Reizfrequenzen versucht (d.h. 0,1 Hz (CPS), 0,3 Hz und 1,0 Hz). Es wurde festgestellt, daß mit steigender Reizfrequenz die Amplitude der registrierten Zuckungsreaktion bei Personen unter Curare-Wirkung verringert wurde und daß diese Reduzierung vom Grad der Curarisierung abhängig zu sein schien. Bei der zweiten Methode wurden vier in kurzer Folge applizierte Reize mit 2 Hz angewendet. Es zeigte sich, daß es bei Personen unter Curare-Wirkung zu einer fortschreitenden Abnahme der nachfolgend registrierten mechanischen Zuckungsreaktion kam, was wiederum vom Grad der Curarisierung abhängig zu sein schien. Es wird angenommen, daß (zu 1) die Amplitude der Zuckungsreaktion auf die höhere Frequenz, ausgedrückt als Prozentsatz derjenigen bei der geringeren Frequenz und (zu 2) die letzte Reaktion auf die Folge von vier Reizen, ausgedrückt als Prozentsatz der Reaktion auf den ersten Reiz, möglicherweise nützlich sind, um den Grad einer neuromuskulären Blockade beim Menschen zu messen.