# ACTIVATION BY SUXAMETHONIUM OF PRIMARY AND SECONDARY ENDINGS OF THE SAME DE-EFFERENTED MUSCLE SPINDLE DURING STATIC STRETCH

## By H.-U. FEHR

*From the Research Laboratories of the Pharmaceutical Department of CIBA Limited, Basle, Switzerland*

Suxamethonium (succinylcholine, SCh) activates both primary and secondary endings of muscle spindles in the cat and in the rabbit (Granit, Skoglund & Thesleff, 1953; Tokizane, Kusama & Eldred, 1959; Diete-Spiff, 1961; Granit, 1962; Verhey & Voorhoeve, 1963). Statements regarding the extent of activation of the two types of endings in the cat are contradictory: one group of investigators found both types of endings to be strongly activated by SCh (Tokizane *et al.* 1959), another group found primary endings to be activated by SCh to a much greater extent than secondary endings (Verhey & Voorhoeve, 1963). Assumptions regarding the site of action of SCh are also controversial. On the one hand, it has been suggested that SCh acts directly on sensory spindle endings in the cat, frog and rabbit (Granit *et al.* 1953; Henatsch & Schulte, 1958; Diete-Spiff, 1961). On the other hand, indirect evidence has led to the assumption that SCh activates mammalian spindle endings by contracture of the intrafusal muscle fibres (Smith & Eldred, 1961). Others have supposed that intrafusal contracture cannot be the only way of activation (Verhey & Voorhoeve, 1963). The possible sites of action have also been discussed by Brinling & Smith (1960). In the frog, the possibility of SCh exerting a direct excitatory effect on isolated sensory spindle endings has been ruled out with certainty (Ottoson, 1961).

In the present experiments, the effect of SCh on the static activity of primary and secondary endings was studied on endings of the same spindle of the tenuissimus muscle of the cat. Simultaneous recording of the entire time course of activation by SCh of correlated primary and secondary endings revealed aspects of the effect which allowed definite conclusions to be drawn, first, as to the site of action of SCh on mammalian muscle spindles, and, secondly, as to the time course of the response to SCh of the two types of intrafusal muscle fibres.

## METHODS

All experiments were performed on adult cats anaesthetized with sodium pentobarbitone (Nembutal, Abbott). Initially, 40 mg/kg was injected intraperitoneally and during the course of the operation a further 20–30 mg/kg was injected intravenously. A segment including the nerve entry zone was isolated from the tenuissimus muscle and surrounded with a pool of liquid paraffin oil at 37° C. The arteriovenous pedicles and the preserved distal nerve branch to the isolated segment were mobilized so as to prevent mechanical effects on the segment. The ventral roots of L 6–S 2 were cut. Functionally single spindle afferents from the isolated segment were isolated in the dorsal roots of L 7 and S 1. The corresponding endings were localized in the muscle with the technique developed by Bessou & Laporte (1961, 1962). A pair of electrodes with the cathode proximal was applied to the deep surface of the isolated segment and displaced from the distal end up to the entry zone of the preserved nerve branch. Single rectangular shocks of 0·2 msec and of 4 times threshold strength for extrafusal contraction were applied to the muscle at intervals of $\frac{1}{2}$ mm. The first directly evoked response could be recorded from a given afferent fibre once the cathode had reached the region of the corresponding ending. When the electrodes were moved further, up to the nerve branch entry zone, the conduction time decreased in a regular manner, thus excluding the possibility of indirectly evoked responses. The distance between endings of the same spindle was usually 0·5 mm, occasionally 1 mm, whereas that between endings of neighbouring spindles ranged from 4·5 to 7 mm with an average of 6 mm, which compares favourably with the measurements derived from anatomical data given by Boyd (1956, 1962a) (all measurements apply to a length of the isolated segment amounting to 90 % of the maximal physiological length; max. physiol. length = length at maximal extension of the leg). Isolation of afferents from the same spindle was facilitated by the use of a six-channel recording equipment (J. F. Tönnies, Freiburg/Breisgau, Western Germany). Afferents from the same spindle entered the spinal cord through the same or through neighbouring dorsal roots, as already established in a morphological study by Cuajunco (1932). Afferent fibres of successive spindles entered the spinal cord in a random distribution, which is in agreement with similar findings in other muscles (Swett & Eldred, 1959). In order to avoid the study of mechanically damaged spindles and of overlapping spindles in the nerve entry zone (Boyd, 1962a), endings lying at least 7·5 mm proximal to the distal end of the isolated segment and 6 mm distal to the nerve branch entry zone were used. The conduction velocity of the afferent fibres in the nerve was determined in the usual way (Paintal, 1952).

Before the pharmacological experiments, the relation between the frequency of afferent discharge and the extension of the muscle was determined by stretching the isolated segment at 2 min intervals in steps of 5 % from 75 to 105 % of the maximal physiological length. The discharge frequency was measured 1 and 30 sec after phasic stretch. The units ' % of maximal physiological length' were chosen to allow a direct comparison of the results from preparations with isolated segments of different absolute length.

SCh was injected intravenously in doses of 0·03, 0·1, 0·3, and 1 mg/kg. The time allowed to elapse after injection of the various doses was 15, 15, 30, and 60 min, respectively. Since equal doses of SCh elicit quantitatively reproducible responses from muscle spindles, provided that the time interval between the injections is long enough (Brinling & Smith, 1960), the influence of the degree of static stretch of the isolated segment on the effect of SCh could be included in the study. The effect of each dose of SCh was studied, first, at 80 % of the maximal physiological length, corresponding to about the resting length, and, secondly, at maximal physiological length. The desired length was adjusted 5 min before the injections. The fast onset and decline of the effect of SCh required a uniform injection procedure. All doses of SCh were made up in a total volume of 0·5 ml. of 0·9 % NaCl and injected into a cannula of 0·6 ml. inserted into the V. jugularis externa from which the solution was driven out by infusion of 1 ml. of 0·9 % NaCl at a constant rate of 0·5 ml./min.

The whole experimental programme was recorded in four pairs of one primary and one secondary ending from the same spindle and on two secondary endings from the same spindle. In several additional pairs of endings only part of the programme could be accomplished. The condition of the preparations was good throughout the experiment, the discharge frequency at the end being similar to the control value at the beginning in all endings.

### RESULTS

SCh activated both primary and secondary spindle endings, but marked quantitative and qualitative differences existed between the effects on these two types of endings, as has been summarized earlier (Fehr, 1964).

### *Extent of activation*

The first major difference was that primary endings of tenuissimus spindles were activated by SCh to a much greater extent than secondary endings. This finding is illustrated in Fig. 1 for an intravenous dose of
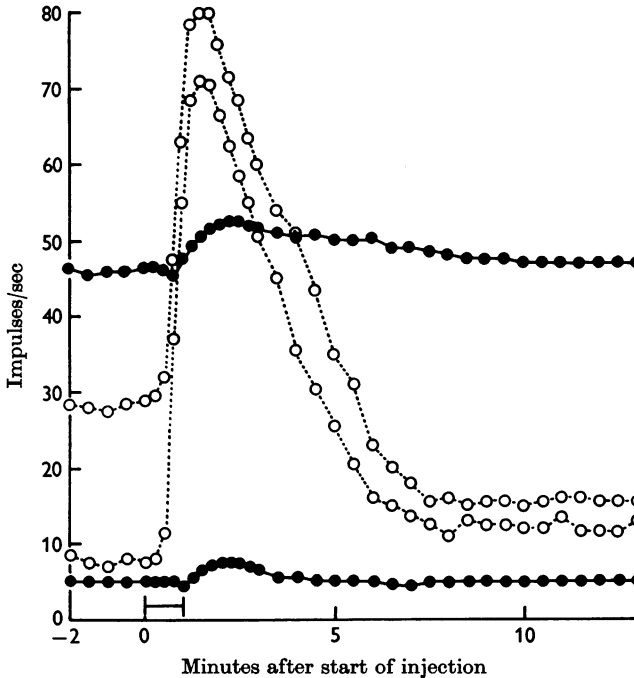


Fig. 1. Cats, sodium pentobarbitone anaesthesia, artificial respiration. Effect of suxamethonium (0·3 mg/kg intravenously ⊢⊣) on the mean frequency of afferent discharge (impulses/sec) in Group IA fibres (open circles) and in Group II fibres (filled circles) at maximal physiological length of the isolated segment of the de-efferented tenuissimus muscle (upper traces) and at 80 % thereof (lower traces). Results compiled from four pairs of one Group IA fibre and one Group II fibre connected to the same muscle spindle. Conduction velocities: Group IA fibres, 104–110 m/sec, Group II fibres, 36–43 m/sec.

0·3 mg/kg, and in Fig. 2 for the whole range of doses administered. Activation of muscle spindles by SCh has been reported to be favoured by increasing the initial static stretch of the muscle (Granit *et al.* 1953). In the present experiments, the effect of each dose of SCh was studied at two different lengths of the isolated segment, namely at maximal physiological length and at 80% thereof. As shown in Figs. 1 and 2, the increase in
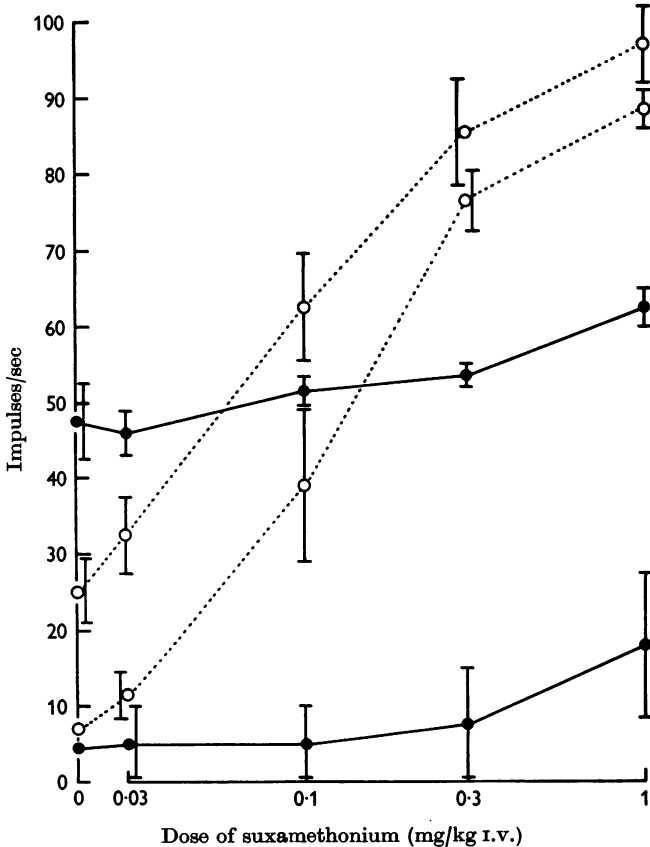


Fig. 2. Cats, sodium pentobarbitone anaesthesia, artificial respiration. Peak of frequency of afferent discharge (impulses/sec, mean and s.E. of mean) in response to increasing intravenous doses of suxamethonium in Group I A fibres (open circles) and in Group II fibres (filled circles) at maximal physiological length of the isolated segment of the de-efferented tenuissimus muscle (upper traces) and at 80% thereof (lower traces). Same fibres as in Fig. 1.

afferent discharge frequency of both primary and secondary endings was not higher at maximal physiological length than at 80% of that length. However, this finding does not necessarily exclude the possibility that spindle activation by SCh is favoured by some intermediate stretch. At

80% of the maximal physiological length, corresponding to about the resting length, SCh in doses of 0·1–1 mg/kg intravenously evoked an almost selective afferent inflow from primary endings (Figs. 1 and 2). At maximal physiological length, activation of secondary endings by SCh in the highest intravenous dose of 1 mg/kg just reached the steady discharges of these endings at 105% of the maximal physiological length, measured 30 sec after phasic stretch (Figs. 2 and 3), but remained below the discharges of these endings at 105%, measured 1 sec after phasic stretch (not shown in Fig. 3). Therefore, the limitation of activation of secondary endings by SCh must be caused by a factor other than a limited capacity of these endings for steady discharges.
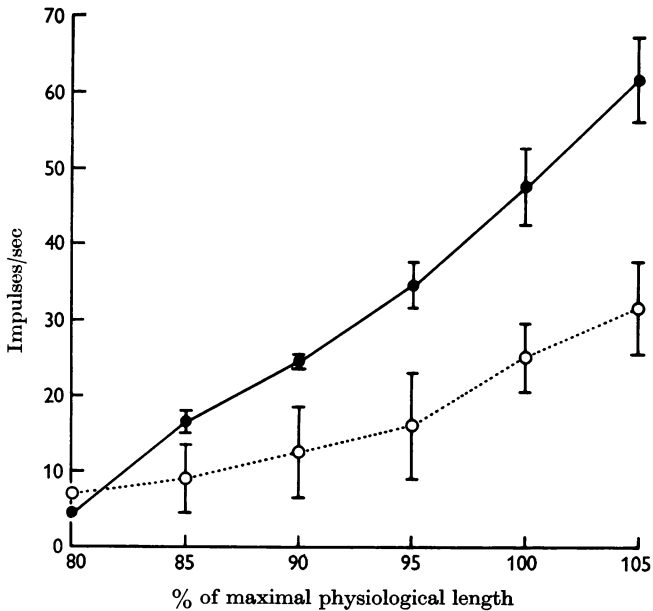


Fig. 3. Cats, sodium pentobarbitone anaesthesia, artificial respiration. Frequency of afferent discharge (impulses/sec, mean and s.E. of mean) in Group IA fibres (open circles) and in Group II fibres (filled circles), measured 30 sec after adjustment of length, plotted against the length of the isolated segment of the deefferented tenuissimus muscle in % of the maximal physiological length. Same fibres as in Figs. 1 and 2.

## Time course of activation

The second difference between the effects of SCh on primary and secondary spindle endings is concerned with the time course of activation. The intervals between commencement of injection of SCh and peak of activation were somewhat shorter in primary endings than in secondary endings. In eleven out of twelve instances, in which both the primary and

the correlated secondary ending were activated by SCh, the peak of activation of the primary ending preceded that of the secondary ending by 15–135 sec (mean 63 sec), and in only one instance was the inverse sequence observed with an interval between the peaks of only 15 sec. Thus, in the individual spindle the peak of activation of the secondary ending coincided with the beginning of the decrease in activity of the primary ending. It should be noted that this finding could only be obtained by simultaneously recording the activity of primary and secondary endings of the same spindle, since statistical treatment of the values revealed that the difference in the time course of primary and secondary activation was not significant. The activation of two secondary endings of the same spindle followed an almost identical time course.

### Recovery from activation

A final difference is concerned with the recovery from activation. In secondary endings the discharge frequency slowly decreased to its initial level (Fig. 1). In primary endings at maximal physiological length, and with intravenous doses from 0·1 mg/kg upwards, the activity frequently decreased gradually to below its initial level and even reached zero in some cases (Fig. 1). At 80 % of the maximal physiological length, the primary activity sometimes remained slightly above its initial level (Fig. 1, and Granit *et al.* 1953). The initial level of activity could be re-established in both conditions by a slight phasic stretch and subsequent elastic shortening of the isolated segment to its original length. However, this test was carried out only at the end of the recovery phase, before the length was adjusted for the next injection of SCh.

### Initial phase of suxamethonium action

An initial decrease in activity to zero has been reported for primary endings in the cat (Brinling & Smith, 1960), for spindle endings in the rabbit (Diete-Spiff, 1961), and for endings in the frog (Henatsch & Schulte, 1958) with the muscle at rest, and it has been assumed to be caused by an unloading of the muscle spindles produced by transient fasciculations of extrafusal muscle fibres (Brinling & Smith, 1960; Diete-Spiff, 1961). With the timing of injection and recording used in the experiments described so far, only slight initial decreases in frequency by up to 4 impulses/sec could be observed. Initial decreases in activity of secondary endings coincided with the beginning of the increase in activity of the correlated primary endings. An initial decrease in primary activity, however, was not necessarily correlated with an increase in secondary activity. In an additional experiment, the activity of the primary and one secondary ending of the same spindle at maximal physiological length was

continuously recorded during intravenous injection of 0·1 mg/kg of SCh. The activity of the primary ending dropped to zero 0·36 sec after the beginning of excitation in the secondary ending and re-appeared 1 sec later with increasing frequency. This finding, too, could only be obtained by recording simultaneously the activity of correlated endings. It provides an important argument for the discussion of the site of action of SCh.

### *Exception from the general pattern of activation*

In three experiments, the activity of three secondary endings of different spindles was recorded simultaneously. The activation by SCh of the various secondary endings of the same isolated segment appeared to be surprisingly uniform, being low in one experiment, somewhat higher in another, and nearly equal to that of primary endings in a third. The last observation forms the only exception from the general pattern of activation by SCh of secondary endings. The exception is confined to the extent of the activation, leaving the usual differences between primary and secondary endings as regards time course of activation and recovery from activation untouched.

It remains to be said that the increased discharges were regular in both types of endings, as already reported for primary endings (Granit *et al.* 1953). Occasionally, slight rhythmic changes in activity synchronous with the arterial pulse were recorded in primary endings owing to their high sensitivity to rapid changes in muscle length (Bessou & Laporte, 1962).

### DISCUSSION

Granit *et al.* (1953), Henatsch & Schulte (1958), Diete-Spiff (1961), and Verhey & Voorhoeve (1963) believe that a direct action of SCh on the sensory endings themselves must be assumed in order to explain the effects of SCh. By contrast, SCh in concentrations below $10^{-5}$ g/ml. was found to have no direct effect on isolated spindle endings of the frog and in higher concentrations to depress spindle activity (Ottoson, 1961), and indirect evidence led to the assumption that SCh excites sensory spindle endings in the cat by causing the intrafusal muscle fibres to contract (Smith & Eldred, 1961). The present results yield additional evidence in favour of the latter assumption. Continuous recording of the onset of effect of SCh revealed a simultaneous transient decrease in activity of the primary ending and an increase in activity of a correlated secondary ending. Similarly, stimulation of a $\gamma$ fibre is reported to have produced on one occasion simultaneously an increase in activity of the primary ending and a decrease in activity of a correlated secondary ending, an effect which has been interpreted as being due to an unloading of the nuclear-chain fibre

system produced by contraction of the correlated nuclear-bag fibre system (Bessou & Laporte, 1962). The opposite change recorded in primary and secondary activity during the onset of SCh action cannot of course be accounted for by an unloading of the whole spindle produced by extra-fusal fasciculations. It can only be explained by assuming that spindle activation by SCh is initiated by contracture of both systems of intrafusal muscle fibres, contracture starting somewhat earlier in the nuclear-chain fibre system than in the nuclear-bag fibre system in this experiment. The small initial decreases in activity in the one type of ending accompanied by an increase in activity in a correlated ending of the other type, described above, are interpreted in a similar way, though unloading of the whole spindle by transient extrafusal fasciculations may also occasionally cause or contribute to the decrease in activity (Brinling & Smith, 1960; Diete-Spiff, 1961). Since initial decreases in activity were recorded in both primary and secondary endings, there seems to be no rule as to the sequence of onset of contracture in the two systems of intrafusal muscle fibres.

On the assumption that SCh acts selectively on the intrafusal muscle fibres, leaving the sensory endings untouched, the difference between primary and secondary endings in the extent of activation by SCh can be explained as follows: if SCh excites sensory spindle endings by stretch produced by reversible contracture of the intrafusal muscle fibres, activa-tion of the various endings depends on the degree of stretch of these endings resulting from the tension developed by the polar regions of the correlated intrafusal muscle fibres, the counteracting tension developed by the underlying regions, the passive mechanical properties of the various regions, and a possible yielding of the attachments of the intrafusal muscle fibres. The tension developed by the various regions can be expected to depend on their myofibril density. Most primary endings ramify both on the almost non-contractile nuclear bags (Barker, 1948; Merrillees, 1960; Cooper & Daniel, 1963) connected to readily contractile polar regions of a relatively high myofibril density (Boyd, 1962*a, b*) and on the not very contractile central region of the nuclear-chain fibres (Cooper & Daniel, 1963) connected to polar regions of a relatively low myofibril density (Boyd, 1962*a, b*). Most secondary endings ramify mainly on readily contractile regions of the nuclear-chain fibres (Barker, 1962; Boyd, 1962*a, b*). This arrangement, illustrated in Fig. 4, should result in rela-tively high stretch of primary ramifications on nuclear bags, lower stretch of primary ramifications on the central region of nuclear-chain fibres, and lowest stretch of the majority of secondary endings. Stretch of the central region of the nuclear-chain fibres may also help to reduce the stretch of the secondary endings. Therefore—on the assumption that SCh acts selectively on the intrafusal muscle fibres along their entire

length and that the tension developed by the various regions depends
on their myofibril density—primary endings are likely to be activated
by SCh to a greater extent than secondary endings, and this indeed
was recorded. The lower extent of activation by SCh of secondary
endings as compared with that of primary endings is exactly opposite
to the higher sensitivity of de-efferented secondary endings to static
stretch (Fig. 3, and Bessou & Laporte, 1962). Thus, stretch of secondary
endings in response to SCh must be extremely small as compared with
that of primary endings. The relatively high activation by SCh of
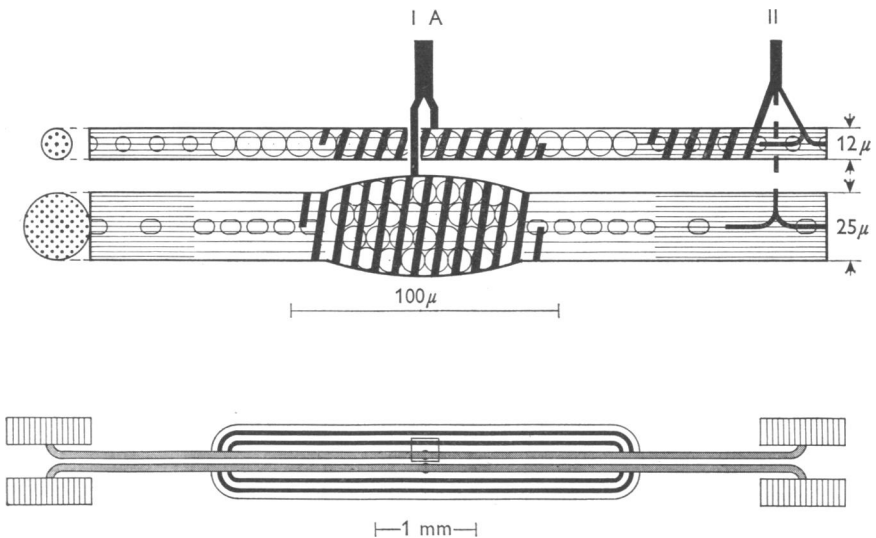


Fig. 4. Schematic representation of cat hindlimb muscle spindle, modified from
Barker & Cope (1962) and Jansen & Matthews (1962). Measurements based on
data of Boyd (1962a, b). Lower diagram: whole spindle. Only the long scale is
accurate. Grey areas: nuclear-bag fibres; black areas: nuclear-chain fibres,
hatched areas: extrafusal muscle fasciculi. Sensory and motor innervation omitted.
Upper diagram: equator region of one nuclear-bag and one nuclear-chain fibre with
sensory innervation and myofibril density. (For further explanation, see text.)

secondary endings observed in one experiment could be explained by a
difference in the localization of these endings, i.e. they may have been
localized rather towards the not very contractile central region of the
nuclear-chain fibres than on readily contractile regions, or alternatively
by having unusually large terminals on the myotubes of the nuclear-bag
fibres. Similar conduction velocities of the secondary afferents in all
experiments, however, point to a similar location of the endings (Boyd,
1962c), thus favouring the latter possibility. A difference between primary
and secondary endings in the extent of activation by SCh, similar to that

observed, is likely to occur also in response to selective contracture of the nuclear-chain fibre system, provided that all primary endings have sufficient ramifications on the central region of these fibres.

However, the difference in the time course of activation by SCh of primary and secondary endings affords another argument in favour of the assumption that both systems of intrafusal muscle fibres are caused to contract by SCh. In addition, the difference in the time course of activation indicates that the two systems of intrafusal muscle fibres respond differently to SCh, contracture and release from contracture proceeding more quickly in the nuclear-bag fibre system than in the nuclear-chain fibre system.

The long-lasting changes in frequency of discharge observed in primary endings during recovery from activation require special attention. A decrease in activity to below its initial level has been assumed to indicate a direct action of SCh on the sensory endings themselves (Diete-Spiff, 1961). This assumption is questionable, since prolonged changes in activity of de-efferented muscle spindles have also been observed in the absence of any drug action, namely after tendon taps (Granit, Homma & Matthews, 1959), after one or several brief twitches from a submaximal shock to the muscle nerve (Granit *et al.* 1959), and after cessation of $\gamma$ fibre stimulation (Kuffler, Hunt & Quilliam, 1951). As pointed out above, the initial activity could be re-established in our experiments by slight phasic stretch of the isolated segment and consequent elastic shortening to its original length. Thus, at the moment when this manipulation of the muscle was carried out (before the length was adjusted for the next injection of SCh), the changes in activity were most likely to be mechanical in origin. On the basis of the present experiments, no conclusion can be drawn as to the origin of the changes in activity in the earlier stages of recovery. In the few instances in which the changed activity was not constant, but tended towards initial levels, additional post-excitatory phenomena in the endings themselves (Matthews, 1964) might have been contributing to the change in activity. If so, the problem would then arise as to why the direction of these phenomena was dependent on the degree of stretch, facilitation occurring at resting length and depression at maximal physiological length, though activation of primary endings by SCh was similar at both lengths. An explanation still has to be found for the dependency of the mechanically caused component in the changes of primary activity on the degree of stretch. The final decrease in activity to below its initial level, observed in many primary endings at maximal physiological length, is tentatively explained as follows: the tension developed by the polar regions of the nuclear-bag fibres of large diameter and relatively high myofibril density (Boyd, 1962*a*, *b*) seems to be strong enough not only to stretch the nuclear bags, but also to bring the opposite insertions of the nuclear-bag fibres closer together. In most instances, this active reduction in length of the nuclear-bag fibres was not fully reversible, leading to the observed final decrease in activity to below its initial level, which could be reversed only by appropriate manipulation of the muscle. At resting length, the insertions of the nuclear-bag fibres seem to be unaffected by the SCh-induced contracture. The incomplete recovery from activation, observed in some primary endings with the muscle at rest, could be due to an incomplete return of the relaxing polar regions of the nuclear-bag fibres to their original configuration at rest and consequent persistent stretch of the nuclear bags. In this condition, too, appropriate manipulation of the muscle re-established the initial discharge frequency. This interpretation of the mechanically caused component in the long-lasting changes in activity observed in primary endings during recovery from activation runs up against one difficulty. Persistent yielding of the insertions of nuclear-bag fibres at maximal physiological length should result in a concomitant

unloading of the nuclear-chain fibres because of their insertion in nuclear-bag fibres (Boyd, 1962a, b). The expected decrease in secondary activity to below its initial level has, however, never been recorded.

In conclusion, the different response to SCh of primary and secondary endings could be satisfactorily explained by an action of SCh on both types of intrafusal muscle fibres along their entire length, by the different localization of the two types of endings, and by the different structural features of the correlated intrafusal muscle fibres.

## SUMMARY

1. The effect of suxamethonium, injected intravenously, on the activity of primary and secondary spindle endings during static stretch was studied on endings of the same muscle spindle of the tenuissimus muscle in the cat, anaesthetized with sodium pentobarbitone.

2. Suxamethonium activated both primary and secondary spindle endings, but marked quantitative and qualitative differences existed between the effects on these two types of endings.

3. Primary endings were activated by suxamethonium to a much greater extent than secondary endings. In both types of endings the maximum increase in discharge rate was similar at resting length and at maximal physiological length of the muscle.

4. The peak of activation was reached earlier in primaries than in secondaries.

5. In primary endings, the recovery from activation depended on the degree of static stretch. At maximal physiological length, the discharge frequency frequently decreased to below its initial level. With the muscle at rest, the activity sometimes remained slightly above its initial level. In secondary endings, the activity decreased continuously to its initial level at both lengths.

6. New arguments support the assumption that suxamethonium excites spindle endings by causing the intrafusal muscle fibres to contract along their entire length. Evidence is presented that both the nuclear-bag and the nuclear-chain fibre system are caused to contract and that the two systems of intrafusal muscle fibres respond differently to suxamethonium, contracture and release from contracture proceeding more quickly in the nuclear-bag fibre system than in the nuclear-chain fibre system.

7. The different response of primary and secondary endings to suxamethonium is explained by the structural features of muscle spindles.

## REFERENCES

BARKER, D. (1948). The innervation of the muscle-spindle. *Quart. J. Micr. Sci.* **89**, 143–186.

BARKER, D. (1962). The structure and distribution of muscle receptors. In *Symposium on Muscle Receptors*, ed. BARKER, D., pp. 227–240. Hong Kong: University Press.

BARKER, D. & COPE, M. (1962). The innervation of individual intrafusal muscle fibres. In *Symposium on Muscle Receptors*, ed. BARKER, D., pp. 263–269. Hong Kong: University Press.

BESSOU, P. & LAPORTE, Y. (1961). Méthode d'observation simultanée des décharges afférentes provenant des terminaisons primaire et secondaire d'un même fuseau neuro-musculaire, chez le Chat. *J. Physiol., Paris*, **53**, 273–274.

BESSOU, P. & LAPORTE, Y. (1962). Responses from primary and secondary endings of the same neuromuscular spindle of the tenuissimus muscle of the cat. In *Symposium on Muscle Receptors*, ed. BARKER, D., pp. 105–119. Hong Kong: University Press.

BOYD, I. A. (1956). The tenuissimus muscle of the cat. *J. Physiol.* **133**, 35–36 P.

BOYD, I. A. (1962 a). The structure and innervation of the nuclear bag muscle fibre system and the nuclear chain muscle fibre system in mammalian muscle spindles. *Phil. Trans.* B, **245**, 81–136.

BOYD, I. A. (1962 b). The nuclear-bag fibre and nuclear-chain fibre systems in the muscle spindles of the cat. In *Symposium on Muscle Receptors*, ed. BARKER, D., pp. 185–190. Hong Kong: University Press.

BOYD, I. A. (1962 c). Discussion remark. In *Symposium on Muscle Receptors*, ed. BARKER, D., p. 281. Hong Kong: University Press.

BRINLING, J. C. & SMITH, C. M. (1960). A characterization of the stimulation of mammalian muscle spindles by succinylcholine. *J. Pharmacol.* **129**, 56–60.

COOPER, S. & DANIEL, P. M. (1963). Muscle spindles in man; their morphology in the lumbricals and the deep muscles of the neck. *Brain*, **86**, 563–586.

CUAJUNCO, F. (1932). The plurisegmental innervation of neuromuscular spindles. *J. comp. Neurol.* **54**, 205–235.

DIETE-SPIFF, K. (1961). The discharge pattern of muscle spindles of the rabbit on activation of intrafusal muscle fibres. *J. Physiol.* **159**, 282–296.

FEHR, H.-U. (1964). Die Wirkung von Suxamethonium (Succinylcholin) auf die statische Aktivität primärer und sekundärer Endigungen derselben de-efferentierten Muskel-spindel. *Helv. physiol. acta*, **22**, 69–70 C.

GRANIT, R. (1962). Discussion remark. In *Symposium on Muscle Receptors*, ed. BARKER, D., p. 15. Hong Kong: University Press.

GRANIT, R., HOMMA, S. & MATTHEWS, P. B. C. (1959). Prolonged changes in the discharge of mammalian muscle spindles following tendon taps or muscle twitches. *Acta physiol. scand.* **46**, 185–193.

GRANIT, R., SKOGLUND, S. & THESLEFF, S. (1953). Activation of muscle spindles by succinylcholine and decamethonium. The effects of curare. *Acta physiol. scand.* **28**, 134–151.

HENATSCH, H.-D. & SCHULTE, F.-J. (1958). Wirkungsmechanismus von Acetylcholin und Succinylcholin auf die Muskelspindeln des Frosches. *Pflüg. Arch. ges. Physiol.* **265**, 440–456.

JANSEN, J. K. S. & MATTHEWS, P. B. C. (1962). The central control of the dynamic response of muscle spindle receptors. *J. Physiol.* **161**, 375–378.

KUFFLER, S. W., HUNT, C. C. & QUILLIAM, J. P. (1951). Function of medullated small-nerve fibres in mammalian ventral roots: efferent muscle spindle innervation. *J. Neurophysiol.* **14**, 29–54.

MATTHEWS, P. B. C. (1964). Muscle spindles and their motor control. *Physiol. Rev.* **44**, 219–288.

MERRILLEES, N. C. R. (1960). The fine structure of muscle spindles in the lumbrical muscles of the rat. *J. biophys. biochem. Cytol.* **7**, 725–742.

OTTOSON, D. (1961). The effect of acetylcholine and related substances on the isolated muscle spindle. *Acta physiol. scand.* **53**, 276–287.

PAINTAL, A. S. (1952). Conduction velocity of single respiratory and cardiovascular afferent fibres in the cervical vagus. *J. Physiol.* **117**, 40–41 P.

SMITH, C. M. & ELDRED, E. (1961). Mode of action of succinylcholine on sensory endings of mammalian muscle spindles. *J. Pharmacol.* **131**, 237–242.

SWETT, J. E. & ELDRED, E. (1959). Relation between spinal level and peripheral location of afferents in calf muscles of the cat. *Amer. J. Physiol.* **196**, 819–823.

TOKIZANE, T., KUSAMA, I. & ELDRED, E. (1959). Unpublished data. In Fujimori, B., Tokizane, T. & Eldred, E. (1959). Effect upon monosynaptic reflexes of decamethonium and succinylcholine. I. Peripheral mechanisms. *J. Neurophysiol.* **22**, 165–176.

VERHEY, B. A. & VOORHOEVE, P. E. (1963). Activation of Group IA and Group II muscle spindle afferents by succinylcholine and other cholinergic drugs. *Acta physiol. pharm. neerl.* **12**, 23–29.