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CHANGES AT THE NEUROMUSCULAR JUNCTION OF RED AND WHITE MUSCLE FIBRES IN THE CAT INDUCED BY DISUSE ATROPHY AND BY HYPERTROPHY

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In the preceding paper (Jewell & Zaimis, 1954) it was demonstrated that red and white muscle in the cat show sharp contrasts in their response to neuromuscular blocking agents. In particular, a single substance, decamethonium, blocks transmission in tibialis by producing a persistent depolarization, but blocks soleus by a dual mode of action which has both depolarizing and competitive phases. An attempt has been made in the present investigation to elucidate some of the factors which contribute to this difference between the muscles.

Red and white muscle subserve different functions in the limb and show corresponding divergences in their physiological properties. The 'redness' of a muscle, that is the myoglobin content, has been shown to be associated with the amount of exercise to which a muscle is subjected (McClintock, Hines & Jordan, 1939; Lawrie, 1953), and it seemed possible that by altering the state of activity of the muscles, changes might be brought about in the two types of fibres which would include alterations in response to neuromuscular blocking agents.

One of the factors which maintains muscle in a normal functional state is the constraint and tension to which it is subjected by its attachments and by exercise (Young, 1946). Experiments have been performed in which this factor has been modified. If the tendon of insertion of a muscle is cut an atrophy of disuse sets in, which may be as profound as the atrophy initiated by denervation (Ricker, 1901; Lipschütz & Audova, 1921). Such disuse atrophy was effected on both soleus and tibialis. In addition, operations were undertaken in which the tendons of muscles synergistic with soleus, that is gastrocnemius and plantaris, were cut, thus giving soleus the work of these fast muscles to perform. In this way an hypertrophy of soleus was brought about.

A brief communication of these results has already appeared (Jewell & Zaimis, 1953).

METHODS

Twenty-seven animals were used in these experiments; twenty-two were adult cats of varying ages, and five were kittens which were between 14 and 20 weeks old at the time of operation. Operations were performed under Nembutal (sodium pentobarbitone) anaesthesia with full aseptic precautions. *Tenotomy of the soleus muscle* was effected through a vertical skin incision along the back of the leg. The tendon of insertion of soleus was cut, and the muscle separated from gastrocnemius and plantaris. A cone made of fine polythene sheet was slipped over the soleus muscle to prevent adhesions forming. *Tenotomy of gastrocnemius and plantaris* was performed in a similar way, the tendons being drawn up towards the popliteal region and sewn to the skin to prevent the formation of adhesions to soleus. *Tenotomy of tibialis* was performed through a skin incision on the anterior aspect of the ankle and the muscle was drawn out of the annular ligament.

For the acute experiments the procedure adopted was identical to that described in the previous paper (Jewell & Zaimis, 1954). Both hind limbs were pinned, and set up on the Brown-Schuster myograph stand. From the operated limb the contractions of both soleus and tibialis were recorded and from the normal limb the contraction of either muscle depending which was needed as a control. Shielded silver electrodes were placed on the sciatic nerve of each side and the nerves stimulated from the same output channel of the stimulator. At the end of the experiment the muscles were dissected out and weighed. Solutions of drugs were made in 0·9% saline and injected into the jugular vein.

RESULTS

When the three muscles of an animal had been set up for recording a few preliminary observations of their physiological characteristics were made. The time course of the twitch was recorded on a fast drum; the frequency of stimulation necessary to produce complete tetanic fusion was determined for each muscle, and the tetanus to twitch ratio measured. The preparation was found to remain in good condition for several hours allowing a number of doses of neuromuscular blocking substances to be given. In the following description the '% block' of a muscle refers to the reduction in twitch height which a drug brings about, measured at the greatest depth of block and taken as a percentage of the pre-injection twitch height. It is a rough measure which is useful for comparative purposes, but does not take account of the time course of paralysis.

The atrophied soleus muscle

Experiments have been performed on fifteen animals, three of them kittens, in which the soleus of one side had been allowed to atrophy for varying period from 6 to 36 days. The animals recovered quickly after the operations, and no difficulties in walking were observed. In one animal the weight of the atrophied muscle (6 days) was only 9% less than the normal control. In the other animals the atrophied muscle weighed between 17 and 55% less, there being no direct correlation between loss of weight and period of atrophy.

When set up on the myograph the atrophied muscles naturally proved

weaker than the normal ones, but the maximal twitch tension which they developed was well maintained throughout an experiment and indeed sometimes improved during the course of the experiment. In the first few experiments springs appropriate to the strength of the atrophied muscles were not available and the recorded twitch height was small (see Fig. 3); later, weaker springs were used which gave a record more readily comparable with the normal muscle.

Physiological characteristics

The atrophied soleus muscle was found to retain the contraction characteristics of the normal soleus. The single twitch has a relatively long time-course, both in respect of contraction and of relaxation, although some of the atrophied muscles relaxed a little more quickly than the normal ones; tetanic fusion occurred at low frequencies of stimulation, usually between 9/sec and 12/sec, and in only two was a higher frequency of stimulation necessary to produce fusion. One of these was a cat (36 days atrophy) in which the normal muscle showed tetanic fusion at 12/sec, whereas the atrophied muscle had not quite fused at 18/sec; in the other case (24 days atrophy) the frequencies required were 9/sec and 16/sec respectively. The atrophied muscles all maintained a tetanus well, and showed a higher tetanus to twitch ratio than tibialis, though not exhibiting such extreme ratios as the normal soleus.

Brown & Euler (1938) have shown that a difference between the normal tibialis and soleus muscles can be detected by observing the effects of tetanic stimulation interpolated in a series of single maximal twitches. The normal tibialis shows a marked post-tetanic potentiation of the single maximal twitch tension, irrespective of the duration of tetanus or frequency of stimulation, but the effects on the soleus are quite different and depend on the duration of the tetanus. When a tetanus of short duration (2–4 sec) was intercalated between single maximal twitches a depression of the tension of the first few succeeding twitches resulted. Tetani of long duration (20 sec), however, were followed by a potentiation of the succeeding twitches.

In our experiments the muscles were subjected to tetani of varying duration (from 2 to 20 sec, at a frequency of 50/sec) interpolated in a sequence of single maximal twitches. The twitch tension of the normal soleus was depressed after brief tetani, but potentiated after tetani of longer duration, results which are in complete conformity with the findings of Brown & Euler. However, in the atrophied soleus, the phenomenon of post-tetanic depression was not readily elicited. In only one experiment, after a brief tetanus, did such a depression appear. In all the other experiments either no change, or a slight potentiation, of twitch tension was seen to follow a tetanus to the atrophied muscle.

These deviations of the atrophied soleus from the normal would appear to be slight compared with the differences between soleus and tibialis, and these

observations show that the atrophied soleus retains almost unaltered the distinguishing characteristics of slow muscle.

Characteristics of a decamethonium block

Sensitivity to decamethonium. In every animal the atrophied soleus was found to have developed an increased sensitivity to decamethonium, and sometimes proved more sensitive than tibialis. In one cat, for example, in response to 30μg/kg decamethonium, the tibialis was 85% blocked and the

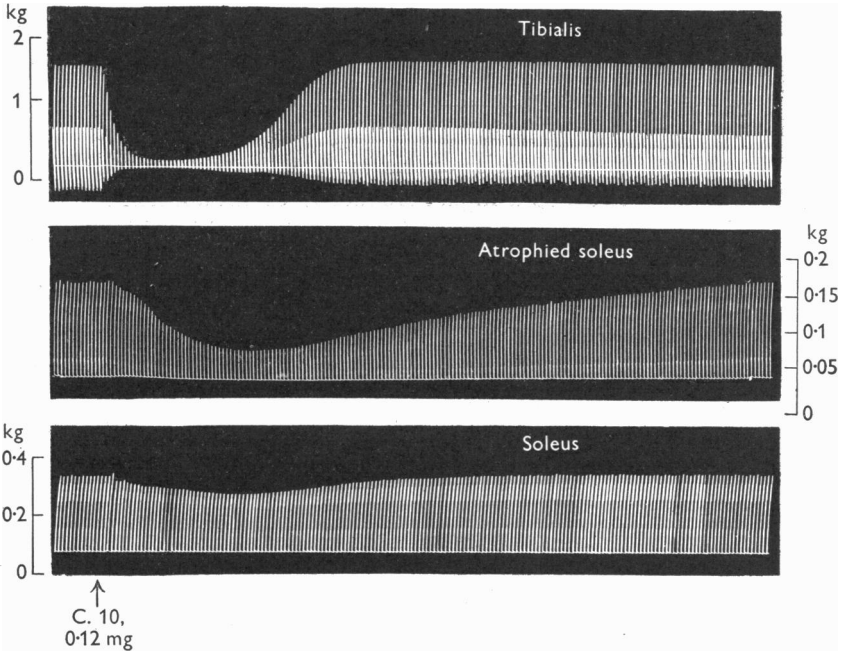

Fig. 1. Sensitivity to decamethonium. Cat, 3·8 kg. Atrophy of one soleus muscle for 11 days. At arrow 0·12 mg decamethonium injected intravenously. In this, and all the following figures, the tracings are of maximal twitches of normal and tenotomized muscles simultaneously recorded in response to indirect stimulation delivered once every 10 sec, and recorded with flat-spring myographs. The tracings have been aligned vertically.

atrophied soleus 78% blocked, whilst the normal soleus was unaffected. In another animal, following 40μg/kg decamethonium, tibialis was 84% blocked, the atrophied soleus was completely blocked, but the normal soleus was only 16% blocked. Fig. 1 illustrates another example of the increased sensitivity of the atrophied muscle.

Two other features of the block should be noted. First the atrophied muscle shows the usual potentiation of the twitch preceding the block, and secondly the block is slower in onset and of longer duration in the atrophied muscle than in either of the normal ones. This is seen in Fig. 1 and may be illustrated

from another experiment in which, after a dose of decamethonium of 30 μg/kg, full recovery of the twitch tension was complete for tibialis and the normal soleus in 15 min, but took twice as long for the atrophied muscle. This extended time-course may in part be accounted for by a diminished blood-flow through the atrophied muscle, but measurements of blood-flow have not been attempted in the present investigation.

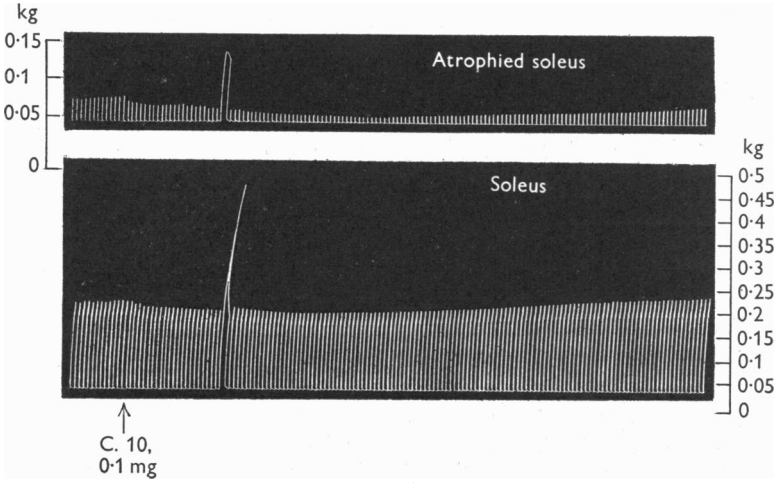

Fig. 2. Tetanus during a decamethonium block. Cat, 4·5 kg. Atrophy of one soleus for 36 days. At arrow 0·1 mg decamethonium injected intravenously. A tetanus given 3·5 min after the injection is well sustained by the atrophied muscle but not by the normal muscle.

Tetanus during a decamethonium block. When tetanic stimulation is applied to the nerve during a decamethonium block it is found that the atrophied soleus usually maintains the tetanus well. This is a characteristic not normally shown by soleus but it is usual for tibialis. Again a tetanus delivered to the atrophied soleus does not antagonize the decamethonium block, a feature which may be said to parallel tibialis and contrast with the normal soleus muscle. These phenomena are illustrated in Fig. 2. In this cat the soleus had been atrophied for 36 days. It will be seen that the atrophied muscle is much more sensitive to decamethonium than the normal one; further, a tetanus is well sustained by the atrophied muscle and no post-tetanic potentiation of the twitch occurs, whereas in the normal muscle the tetanus rapidly falls from its peak to a tension a little less than the twitch tension. The normal muscle shows only a slight post-tetanic antagonism of the block because of the small effect that this dose of decamethonium is having upon it. The effect on the atrophied soleus should, however, also be compared with Fig. 1 in the previous paper (Jewell & Zaimis, 1954) in which a tetanus is given during a 40% block of normal soleus, and in which the poorly sustained tetanus and post-tetanic potentiation are better seen.

Neostigmine during a decamethonium block. As has been shown, neostigmine is always a powerful antagonist of a decamethonium block in the soleus muscle, whilst it has little or no effect upon the course of the paralysis of tibialis. The atrophied soleus is found to imitate the latter muscle. This is illustrated in Fig. 3 which is taken from an experiment in which the soleus had been

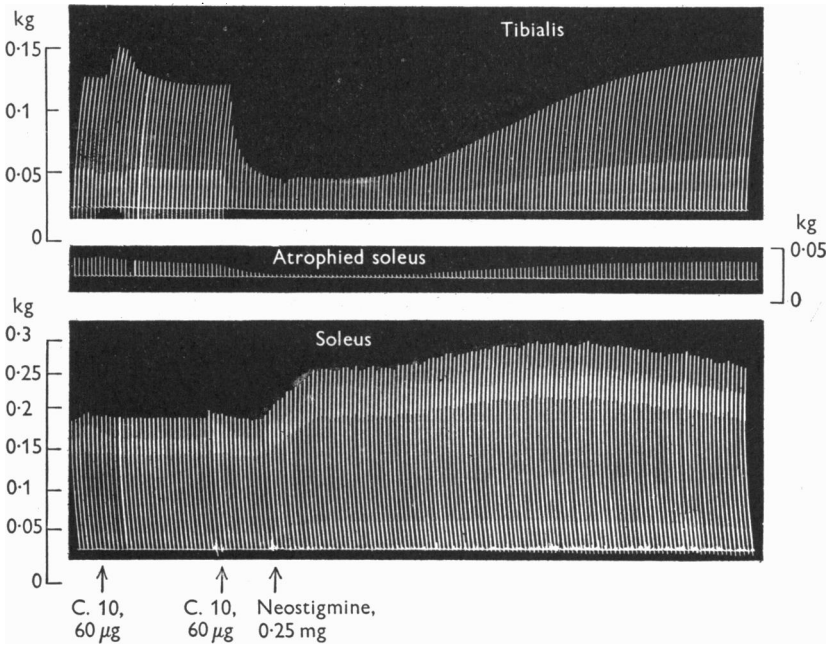

Fig. 3. The effect of neostigmine on a decamethonium block. Cat, 2·1 kg. Atrophy of one soleus for 14 days. Two doses of decamethonium 60 μg intravenously were required to produce block. At the third arrow 0·25 mg neostigmine intravenously.

atrophied for 14 days. Two doses of decamethonium (60 μg) in quick succession were necessary to produce an effective block of tibialis and the atrophied soleus. A dose of 0·25 mg neostigmine, given when the block had reached its greatest depth on both muscles, had no effect on either of them. The normal soleus was not paralysed by this dose of decamethonium but a powerful potentiation of the twitch resulted from the injection of neostigmine. The atrophied soleus in this figure should be compared with the normal soleus in Fig. 2 of the previous paper (Jewell & Zaimis, 1954) in which 0·24 mg of neostigmine produced a marked antagonism of decamethonium in an 80% blocked muscle.

Tubocurarine during a decamethonium block. Convincing evidence that decamethonium blocks normal soleus by competition is seen from the observation that tubocurarine always deepens a decamethonium block, the two drugs

summating in their effect. In the atrophied muscle, on the other hand, not only does tubocurarine never deepen a decamethonium block but it may antagonize it. In Fig. 4 the twitches of a pair of soleus muscles are shown, one of which had been atrophied for 20 days. The injection of 0·2 mg of decamethonium rapidly produced a partial paralysis of the normal muscle and began to reduce the twitch of the atrophied one, which characteristically reacted more slowly. 0·5 mg of tubocurarine given 1 min after the decamethonium reduced the surviving twitch of normal soleus still further. This

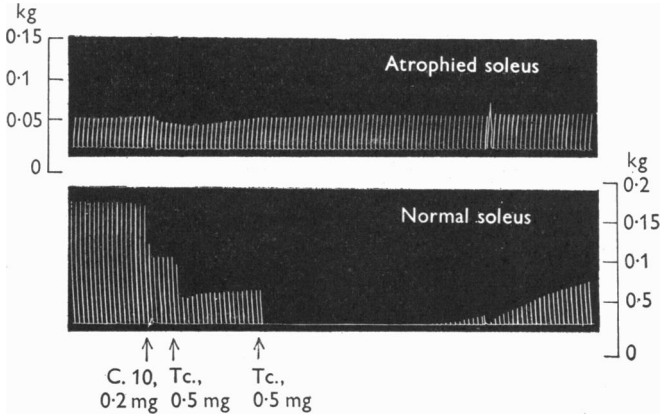

Fig. 4. The effect of tubocurarine on a decamethonium block. Cat, 1·45 kg. Atrophy of one soleus for 20 days. At the first arrow 0·2 mg decamethonium, and at the second and third arrows 0·5 mg tubocurarine intravenously. A brief tetanus is given later during the record.

did not occur in the atrophied soleus, but on the contrary, 2 min after the injection of tubocurarine it had recovered to the full twitch tension. Recovery from previous doses of decamethonium of only 70 μg had taken at least 20 min, so that it is clear that tubocurarine has antagonized decamethonium in the atrophied muscle. A further dose of 0·5 mg tubocurarine brought the block of the normal muscle to completion, but had an insignificant effect on the atrophied muscle. This drug antagonism seen in the atrophied soleus is less spectacular than the antagonism in tibialis, but the two responses are similar.

Sensitivity to tubocurarine

The relative insensitivity of the atrophied muscles to tubocurarine was a feature of all these experiments. The tibialis is usually less sensitive than the normal soleus but the atrophied soleus was found to be less sensitive than tibialis. About twice the dose of tubocurarine necessary to block a normal muscle was required to produce a comparable block of the atrophied muscle. In a typical example of a cat given 0·25 mg/kg tubocurarine the tibialis was 66% blocked, the normal soleus 83% blocked, but the atrophied soleus only

18% blocked. This is illustrated in Fig. 5. In another animal, in which tibialis proved unusually sensitive to tubocurarine, two doses of 0·13 mg/kg given in quick succession, and before any other drugs had been administered, reduced the twitch of tibialis by 57% and of soleus by 44%, but the twitch of the atrophied soleus was reduced to the extent of only 17%.

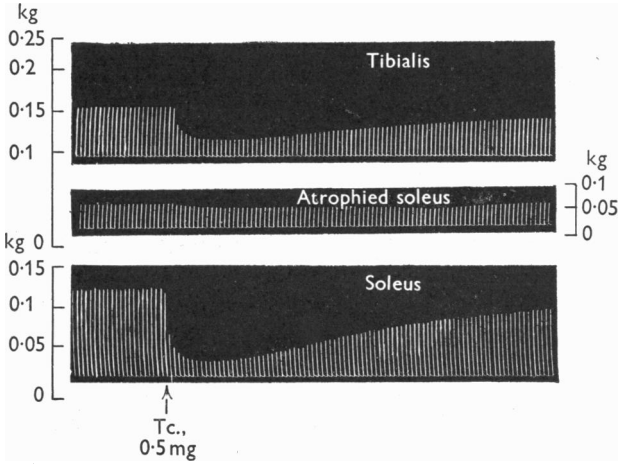

Fig. 5. Sensitivity to tubocurarine. Cat, 2·0 kg. Atrophy of one soleus for 14 days. At arrow 0·5 mg tubocurarine injected intravenously.

Apart from exhibiting this decreased sensitivity the behaviour of the atrophied muscle towards tubocurarine was similar to that of normal muscle. Neostigmine antagonized the tubocurarine block and, after a tetanus given during a partial block, the succeeding twitch tension was temporarily augmented.

The hypertrophied soleus muscle

The operation designed to cause hypertrophy of the soleus was performed on six animals including a kitten. The animals were allowed to survive for 19, 22, 28, 38, 86, and 180 days respectively after the operation. In one of the cats (180 days hypertrophy), which was allowed to run free in the cat room, recovery of gait had proceeded so far that it was impossible to tell which leg had been operated upon. In the other animals, all of which, excepting the kitten, had been housed in individual cages, a weakness of the operated leg was apparent up to the time of acute experiment. In five of the animals the hypertrophied muscles weighed between 32 and 48% more than the normal controls. In the sixth cat, which for several reasons may be considered exceptional, the increase in weight of the muscle was only 8%—this animal will be referred to separately. The tenotomized gastrocnemius and plantaris were examined at the acute experiment and were found to have atrophied

and shortened considerably; in no case had they formed adhesions to the soleus.

Physiological characteristics. The hypertrophied muscle shows the physiological characteristics of red muscle to an exaggerated degree. The twitch is exceptionally slow and the fusion frequency tended to be lower than on the normal side. Thus in one cat the normal soleus gave tetanic fusion when stimulated at 12/sec, whilst the hypertrophied muscle fused at 9/sec; in another cat the rates were 9/sec and 7/sec, respectively, and in the kitten they were 7/sec and 6/sec. Tetanus to twitch ratio was higher for the hypertrophied muscle and it developed a greater maximal twitch tension than the normal one.

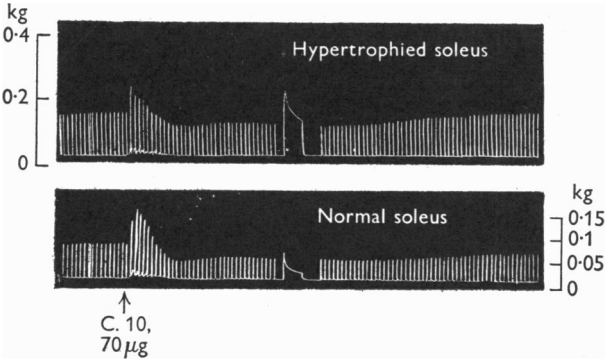

Fig. 6. The action of decamethonium on the hypertrophied (19 days) soleus muscle. Cat, 2·0 kg. At arrow 70 μg decamethonium injected intravenously. A tetanus of 10 sec duration (drum running faster) is given during the partial block. A strong spring was used for the hypertrophied muscle.

Characteristics of a decamethonium block. In two cats no significant difference in the sensitivity of the two soleus muscles to decamethonium was observed, but in the other three the hypertrophied muscles proved to be the less sensitive. Thus in one cat (180-day hypertrophy) a first dose of decamethonium (50 μg/kg) produced a 50 % block of normal soleus and a 34 % block of the hypertrophied soleus; in another animal (38 days hypertrophy) a dose of decamethonium which produced an incomplete block of the normal muscle left the hypertrophied muscle unaffected. Fig. 6 shows tracings of a normal and a hypertrophied (19 days) muscle. The greater resistance of the hypertrophied muscle to decamethonium is evident, it is blocked to a lesser degree and for a shorter period of time, and a tetanus given during the block is better sustained. Apart from these differences the characteristics of the decamethonium block were identical with those in the normal muscle.

Tubocurarine paralysis. The responses of the hypertrophied muscle to this substance differed in no way from normal.

In general, so far as these experiments show, the effect of hypertrophy on the soleus muscle is to accentuate the physiological and pharmacological properties which characterize red muscle, and distinguish it from white muscle.

Brief mention should now be made of the experiment which proved an exception. In this cat, 86 days had elapsed between operation and acute experiment, but the hypertrophied muscle weighed only 8% more than the normal one. When set up on the myograph the 'hypertrophied' muscle proved weaker than the normal one, developing a lower maximal twitch tension, and, whilst the contractions of the normal muscle fused at a tetanic stimulation of 9/sec, the contractions of the hypertrophied muscle had not quite fused at this frequency. In addition, this muscle proved more sensitive to decamethonium than the normal one. Indeed, the muscle behaved as if it were atrophied rather than hypertrophied. The most likely explanation is that atrophic changes had in fact set in, the animal having led an inactive existence in its cage and having used the operated leg but little.

The atrophied tibialis muscle

The tibialis muscle was caused to atrophy in six animals, one of which was a kitten. The animals were allowed to survive for between 13 and 28 days after the operation. The atrophied muscles were found to weigh between 16 and 18% less than their normal controls.

Physiological characteristics. The atrophied tibialis was naturally weaker than the normal muscle, but was found to have retained the properties of fast muscle. Thus the frequency of stimulation necessary to produce tetanic fusion was high; a tetanus was well sustained; marked post-tetanic potentiation of the maximal twitch occurred, and the tetanus to twitch ratio was low, being about 3 : 1.

Characteristics of a decamethonium block. The two tibialis muscles which had been allowed to atrophy for the shorter periods (13 and 15 days) had become slightly less sensitive to decamethonium. However, the four muscles whose atrophy had occurred during longer periods (17, 26, 27 and 28 days) were all more sensitive to the drug than the normal controls. Apart from this increase in sensitivity the atrophied tibialis behaved in no way differently from the normal muscle. A decamethonium block is illustrated in the first part of Fig. 7. The first dose of 25μg/kg produced only a potentiation of the twitch of the normal muscle, but a potentiation followed by a slight depression in the atrophied muscle. A second dose of decamethonium brought the block of both muscles to completion, but the atrophied muscle recovered later than the normal one. The interaction of decamethonium and tubocurarine can be seen in the second part of the figure, where the antagonism was just as marked in both muscles.

Neostigmine (0·25 mg) injected during a decamethonium block may produce a slight deepening of the paralysis of the atrophied muscle. The effect is similar to that sometimes seen with the normal muscle.

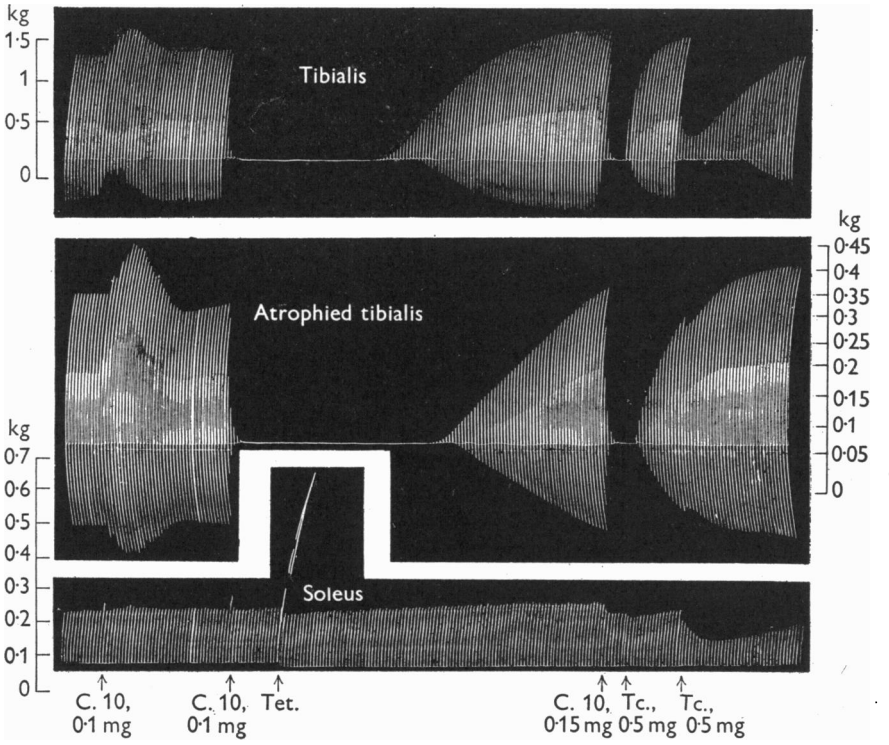

Fig. 7. The atrophied tibialis muscle. Cat, 4·0 kg. Atrophy of one tibialis muscle for 26 days. Injection of decamethonium and tubocurarine intravenously. A weak spring was used for the atrophied muscle.

Tubocurarine paralysis. The atrophied muscle is less sensitive to tubocurarine than the normal. A typical example may be taken from one animal in which a dose of 0·3 mg/kg produced an 88% block of the normal muscle, but only a 66% block of the atrophied one. Another example is given in Fig. 7 in which the second dose of tubocurarine markedly reduced the height of the twitch of the normal muscle but had hardly any effect on the atrophied muscle.

DISCUSSION

The outstanding feature of these experiments is the manner in which red muscle, when atrophied, comes to resemble white muscle in its response to decamethonium. The dual mode of action of decamethonium, which characterizes the response of normal soleus, is no longer seen, for the competitive

phase of its action has disappeared. As a result neuromuscular transmission in the atrophied soleus is apparently interrupted solely by a persistent depolarization of the fibre membranes. Furthermore, not only is the character of the response altered, but, in addition, the red fibres become much more sensitive to decamethonium and less sensitive to tubocurarine.

However, effects of disuse are not confined to the red fibres, for atrophied white muscle shows similar, though smaller changes in sensitivity. These may be due to a lowering of the threshold of the fibre membrane to acetylcholine, an hypothesis which would also explain the qualitative change in the response of soleus. Where decamethonium mimics acetylcholine and acts by depolarization alone, as in tibialis, such a lowering of the threshold would not be expected to produce any change in its mode of action; but, where it shows both depolarizing and competitive propensities, as in soleus, some qualitative change might be expected. A lowering of threshold to acetylcholine renders the manifestation of a competitive action more difficult, and as our experiments have shown, this quality fails to appear in the action of decamethonium on the atrophied soleus. The suggestion that such a change in sensitivity to acetylcholine occurs in tenotomized muscles would concur with the observations of Solandt & Magladery (1942) on the rat. These authors showed that disuse atrophy, produced by upper motor neurone lesion, increased the sensitivity of the limb muscles to acetylcholine.

Our results offer evidence that the changes in the atrophied muscle are in the muscle fibre membrane, since the time course of the twitch, and the development of tetanus, which are presumably properties of the contractile elements, appear to remain unaltered. The atrophied tibialis retains the contraction characteristics of fast white muscle and the atrophied soleus those of slow red muscle. These findings are in accord with those of Eccles (1941) who showed that in disuse atrophy of the tibialis and soleus of the cat, produced by spinal cord section and dorsal-root ganglionectomy, the physiological characteristics of the twitch are unaltered.

The changes in response to neuromuscular blocking agents which occur with disuse would appear, then, to be primarily referable to changes in the membrane, and the experiments reveal an interesting relationship between the two types of fibre. The fact that the red muscle when atrophied loses its dual mode of response to depolarizing agents and comes to resemble white muscle suggests that the white fibre membrane possesses the less differentiated structure. The red fibre reverts to this state with disuse. It would be interesting to know at what stage in development the properties of the fibres diverge, and whether the red fibres develop their more specialized membrane from a structure similar to that which persists in the white fibres. The kittens used in the present experiments were evidently too old to show any differences from the adult animals.

It might have been expected that the hypertrophied soleus, when it took over the work of the two fast muscles, gastrocnemius and plantaris, would show changes by which it approached these muscles in its properties. With regard to the responses studied, however, the reverse proved to be the case, both with respect to pharmacological and physiological characteristics. This failure of the slow muscle to change its characteristics in response to functional demands artificially placed upon it is in contrast to the results reported by Bach (1948). This author cut the tendons of insertion of soleus and tibialis posterior in the rabbit, and sutured soleus to the site of insertion of tibialis. The transplanted soleus was claimed to acquire characteristics resembling those of the white tibialis, and its myoglobin content fell to a level comparable with the white muscle. These changes were supposed to be due to the imposed alteration in the function performed in the limb by the muscle. From our results it would appear much more likely that such changes as were observed were due to a disuse atrophy of the soleus. A particularly relevant observation amongst our experiments was that in which aberrant results were obtained in an animal with an 'hypertrophied' soleus. It seems that inactivity of the animal, or the avoidance of use of the operated limb, had led to changes which would usually be expected from disuse. It is evident that caution is needed in the interpretation of such experiments, and there is no justification for assuming, that, after an operation on a limb, an animal will automatically use its altered musculature efficiently whatever its environment.

Finally, some reference should be made to the use of the terms 'red' and 'white' muscle. The association of 'redness' with particular responses to neuromuscular blocking agents would appear to be applicable to muscles of altered activity, since such muscles do show changes in myoglobin content (McClintock *et al.* 1939; Lawrie, 1950, 1953) which could be said to parallel their changes in sensitivity. Atrophied muscles show a fall in myoglobin content, and hypertrophied muscles an increase, which compare with their respective decrease and increase in resistance to decamethonium. It is not possible to say, however, whether this parallelism is more than merely fortuitous, both effects being independent results of disuse or hypertrophy. The distinction we have drawn between red and white muscle may not necessarily obtain over the whole of the body musculature, and it should be emphasized that 'red fibre' and 'white fibre' have been used simply as convenient descriptive terms for the two types of fibre with which we have been dealing. Future work may show that the association of particular properties of the neuromuscular junction with a high myoglobin content of the muscle fibre prevails only under special circumstances of muscle function.

SUMMARY

1. In cats the tibialis and soleus muscles have been tenotomized in order to cause a disuse atrophy, and muscles synergistic with soleus have been cut to cause soleus to hypertrophy. The responses of these muscles to neuromuscular blocking agents have been examined.

2. In contrast to its action on the normal soleus, decamethonium blocks the atrophied soleus by depolarization, the competitive phase of its action having disappeared. This change in mode of action is accompanied by a marked increase in the sensitivity of the atrophied muscle to the drug. The atrophied soleus thus comes to resemble normal tibialis in its responses.

3. The hypertrophied soleus muscle shows no changes in its response but displays an accentuation of the characteristics of normal red muscle.

4. The atrophied tibialis shows no change in response to decamethonium except for a small increase in sensitivity. The drug continues to effect a neuromuscular block by depolarization.

5. The possibility that the red muscle fibre possesses the more specialized membrane is discussed.

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