J. Physiol. (1985), **362**, *pp.* 205–213
With 2 text-figures
Printed in Great Britain

INFLUENCE OF HUMAN MUSCLE LENGTH ON FATIGUE

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(*Received 10 August 1984*)

SUMMARY

1. The effect of muscle length on susceptibility to fatigue has been examined in human ankle dorsiflexor muscles. The fatiguing procedure consisted of either indirect tetanic stimulation at 20 Hz or maximal voluntary contraction; each procedure lasted 90 s.

2. The amplitude of the evoked muscle compound action potential (M-wave) increased during the first 30 s or so of the tetanic fatiguing procedure and then decreased. The torque developed by the dorsiflexor muscles declined throughout the period of tetanization.

3. A significantly greater reduction in twitch and tetanic torque was found after the fatiguing procedure had been conducted at the optimum muscle length rather than with the muscle in a shortened position. Relaxation after tetanic stimulation was slower after fatigue had been induced at the optimum muscle length.

4. It is concluded that muscle fatigue is related to the number of actin–myosin cross-bridge interactions and is unlikely to be accounted for solely on the basis of changes in the ionic composition of the transverse tubular fluid.

INTRODUCTION

From the pioneering studies of Merton (1954) it is known that the major site of fatigue during voluntary exertion is situated in the muscle fibre interior. In spite of much subsequent research it is still not clear whether fatigue results from primary dysfunction of excitation–contraction coupling (Edwards, Hill, Jones & Merton, 1977; Hultman & Sjöholm, 1983) or is induced by metabolic events associated with the activation of the contractile filaments (Dawson, Gadian & Wilkie, 1978; Hultman, Sjöholm, Sahlin & Edström, 1981; Hultman & Sjöholm, 1983).

In an attempt to distinguish between these two possibilities we have exploited the length–tension relationship of the human ankle dorsiflexor muscles. It has been shown that torque generated by the fully shortened dorsiflexors is less than half that generated by these muscles at their optimum length (Marsh, Sale, McComas & Quinlan, 1981). By employing an identical fatiguing sequence with the dorsiflexors either at the fully shortened or at the optimum lengths, the above question may be resolved. If excitation–contraction uncoupling is responsible for fatigue, then the amount of fatigue should be independent of muscle length (see, however, Discussion).

Alternatively, if fatigue is dependent on the number of force-producing cross-bridge interactions, then there should be greatest fatigue at the optimum length.

Since these experiments were performed in humans we have been able to study fatigue in the same muscles on different occasions. The general relevance of the experimental results has been increased by investigating the effects of voluntary contraction as well as those of indirect muscle stimulation.

METHODS

Subject

The experiments were performed on ten healthy volunteers whose ages ranged from 23 to 48 years (mean, 31·1 ± 8·5 years). The study received the approval of the Ethics Committee at McMaster University and informed consent was obtained from each of the subjects.

Stimulating and recording arrangements

Surface electrodes were utilized in all experiments. The stimulating electrodes consisted of rectangular pieces of aluminium foil (2 × 4 cm); the cathode was placed directly over the common peronal nerve at the neck of the fibula while the anode was situated over the antero-superior aspect of tibialis anterior. This electrode placement was associated with least discomfort during stimulation and it minimized inadvertent excitation of the plantarflexors. Two silver chloride cups (9 mm in diameter), placed over the belly and tendon of tibialis anterior, served as recording electrodes. A ground electrode was placed over the belly of tibialis anterior between the stimulating and recording electrodes. Rectangular voltage pulses of 50 μs duration were delivered from a stimulator (Devices Ltd., model 3072) which received a triggering pulse from a digital timing device (Devices Ltd., Digitimer, model 3290). The muscle torques and evoked mass potentials (M-waves) were displayed on a variable persistence storage oscilloscope (Hewlett–Packard model 141B). Supramaximal stimulus intensities were utilized in all experiments.

Fatiguing and testing procedures

The experiment embodied a testing sequence which was performed before, and immediately following, a fatiguing procedure. The fatiguing procedure consisted of 90 s of tetanic stimulation at a frequency of 20 Hz and was performed on each subject on two occasions. The dorsiflexor muscles were fatigued at their optimum tension producing length (L_0) on one occasion and at their fully shortened length (L_s) on another occasion. Preliminary studies revealed that L_0 and L_s generally corresponded to 15 deg of plantarflexion and 25 deg of dorsiflexion respectively. At least one week separated the two experiments and the order of testing was randomized.

The testing sequence consisted of two maximal dorsiflexor muscle twitches, separated by a tetanus lasting 2 s. The first twitch served as a control while the second twitch was intended to assess the potentiating effect of the 'test' tetanus. The latter consisted of 1 s of stimulation at 20 Hz followed immediately by 1 s of stimulation at 80 Hz. Irrespective of the muscle length (L_0 or L_s) at which the fatiguing process had been executed, the testing sequence was carried out with the ankle joint plantarflexed to 40 deg.

The rapid changes of ankle position required in this study were achieved using a torque measuring device similar to that described by Marsh *et al.* (1981). Briefly, this device incorporated an isometric foot holder which rotated about an axis coincident with that of the ankle joint. Torque produced by the isometric dorsiflexor contraction was detected by two strain gauges attached to the underside of the footplate. Both testing and fatiguing procedures were performed under ischaemic conditions produced by the application of an inflated pressure cuff around the thigh. In this way recovery of the fatigued muscles during the brief period between the fatiguing and testing procedures was minimized. Preliminary studies revealed that occlusion of the blood supply to the relaxed dorsiflexors for 90 s had a negligible effect on torque production.

To ensure that the results of the tetanic fatiguing procedure were physiologically valid, a second study was performed in which fatigue was induced by maximal voluntary contraction of the ankle dorsiflexors for 90 s in place of electrical stimulation.

The degree of dorsiflexor fatigue induced in each subject was determined by comparing the testing sequence recorded before the fatiguing procedure with that recorded exactly 3 s after the end of

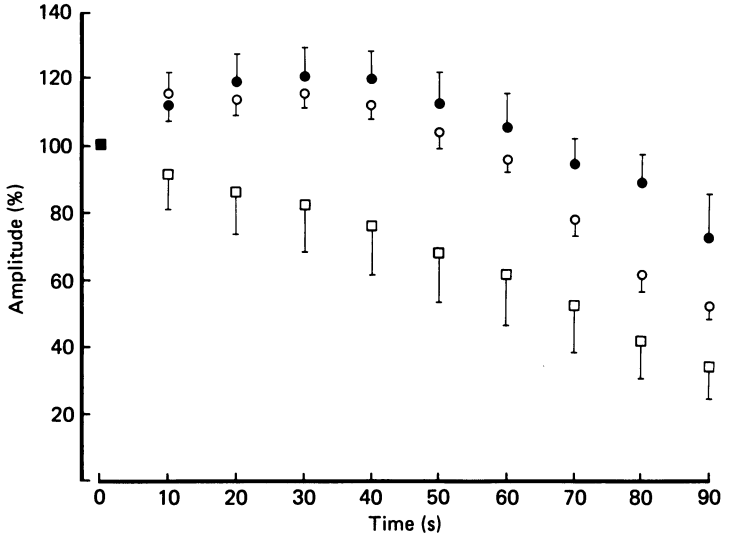

Fig. 1. Changes in amplitude of tibialis anterior compound action potential (M-wave) and in isometric torque developed by ankle dorsiflexors during 90 s of tetanic stimulation at 20 Hz. M-waves were measured with the muscles shortened (●) or at the optimum length (○); torque was measured at the optimum length only (□). Values shown are means ± S.E. of mean.

the fatiguing procedure. A paired Student's *t* test with a significance value of 5 % was used to analyse the data. Throughout the text mean values have been given with their standard deviations but in Fig. 1 the standard errors of the means have been employed instead.

RESULTS

Subject variability

The ten subjects differed considerably in their susceptibility to fatigue, as assessed during the fatiguing procedure or in the subsequent testing sequences. These variations were not significantly correlated with the contraction and half-relaxation times of the dorsiflexor muscles, and were therefore probably independent of the proportions of type I and type II muscle fibres. It is possible, however, that such a correlation might have emerged had the investigation been conducted on individuals of the same sex and of more similar ages.

Observations during the tetanic fatiguing procedure

During 90 s of low frequency stimulation there was a steady decline in tetanic torque which could easily be seen when the muscle was in the optimum position (L_o); by the end of the fatiguing procedure the mean torque output had fallen to $34{\cdot}3 \pm 30{\cdot}1$ % of its initial value. When the muscle was fatigued in the shortened position (L_s), that is, with the ankle completely dorsiflexed, repetitive stimulation of the peroneal nerve often evoked only minor fluctuations in torque output. This behaviour was attributed to contamination of the dorsiflexor responses by those of peroneus longus and brevis; these muscles, which both plantarflex the ankle and evert the foot, are also innervated by the common peroneal nerve. With the ankle

dorsiflexed, the two peronei would have been at more favourable lengths to develop torque than the dorsiflexors; torque developed by the latter muscles was therefore negated by the former. For this reason no comparison could be made of the decline in dorsiflexor torque at L_0 and L_s during the fatiguing procedure itself. Observations were made on the evoked muscle compound action potential (M-wave) and provided evidence of altered excitation of tibialis anterior muscle fibres. At both muscle lengths the M-waves gradually increased in peak-to-peak amplitude, reaching maximal

TABLE 1. Effects of fatigue induced by tetanic stimulation at the optimum and shortened muscle lengths (L_0 and L_s respectively). *CT*, contraction time; $\frac{1}{2}RT$, twitch half-relaxation time; P_t, maximum twitch torque; P_0^{20}, maximum tetanic torque during 20 Hz stimulation; P_0^{80}, maximum tetanic torque during 80 Hz stimulation; $\frac{1}{5}P_0^{80}$, time taken for 80 % relaxation after 80 Hz tetanus

	L_0			L_s		
	Control	Fatigued	*P*	Control	Fatigued	*P*
M-wave (mV)	10·7 ± 4·7	9·1 ± 4·3	N.s.	9·3 ± 2·7	8·6 ± 2·9	N.s.
CT (ms)	114 ± 13	113 ± 10	N.s.	115 ± 16	106 ± 14	N.s.
$\frac{1}{2}RT$ (ms)	100 ± 20	123 ± 30	N.s.	101 ± 17	129 ± 21	< 0·005
P_t (N m)	5·0 ± 2·0	1·5 ± 0·8	< 0·001	4·9 ± 2·1	2·3 ± 1·2	< 0·005
P_0^{20} (N m)	23·4 ± 11·1	10·5 ± 6·3	< 0·01	22·0 ± 9·2	14·8 ± 7·1	N.s.
P_0^{80} (N m)	25·0 ± 13·0	12·4 ± 7·4	< 0·02	26·3 ± 12·7	19·3 ± 10·9	N.s.
P_t/P_0^{20}	0·23 ± 0·05	0·14 ± 0·08	< 0·02	0·22 ± 0·04	0·16 ± 0·04	< 0·005
P_t/P_0^{80}	0·22 ± 0·05	0·14 ± 0·11	< 0·05	0·19 ± 0·04	0·14 ± 0·06	< 0·02
$\frac{1}{5}P_0^{80}RT$ (ms)	168 ± 41	715 ± 210	< 0·001	144 ± 30	418 ± 88	< 0·001

values at approximately 30 s (Fig. 1). The M-waves then declined with the mean amplitudes, expressed in terms of the initial values, falling to 53·1 ± 12·5 % and 76·2 ± 32·5 % at L_0 and L_s respectively.

The behaviour of the M-wave during the fatiguing procedure deserves brief comment, being unrelated to the main discussion. The initial increase in amplitude was most probably a function of the supernormal period of excitability of the muscle fibres (Stalberg, 1966). The subsequent decline in the M-wave amplitude was similar to that described in the human quadriceps femoris by Hultman & Sjöholm (1983), who also employed 20 Hz stimulation but without ischaemia of the limb. Our results do not necessarily conflict with those of Bigland-Ritchie, Kukulka, Lippold & Woods (1982), who were unable to detect a reduction in the M-wave during fatigue; these workers studied voluntary contraction of the intrinsic muscles of the hand, without ischaemia, for a period of 1 min.

Observations after the tetanic fatiguing procedure

As described in Methods, the responses of dorsiflexor muscles were measured before and after the fatiguing procedure using the same testing sequence; the latter consisted of a single shock, 20 Hz stimulation for 1 s, 80 Hz stimulation for a further second and a second shock. This testing sequence was always performed with the ankle plantarflexed to 40 deg, regardless of the position of the joint during the fatiguing procedure. The terminal stimulus was intended to assess the effect of fatigue on the potentiated twitch but measurements of these responses have not been presented since the mean potentiation, even in the control period, amounted to only 10 %.

Table 1 shows the mean twitch torque, tetanic torque and M-wave amplitude after the fatiguing procedure had been performed at L_0 and L_s and also during the two preceding control periods. It can be seen that the control values agreed closely, indicating that the dorsiflexor muscles had fully regained their function during the interval between the two examinations in each subject. The table also shows that

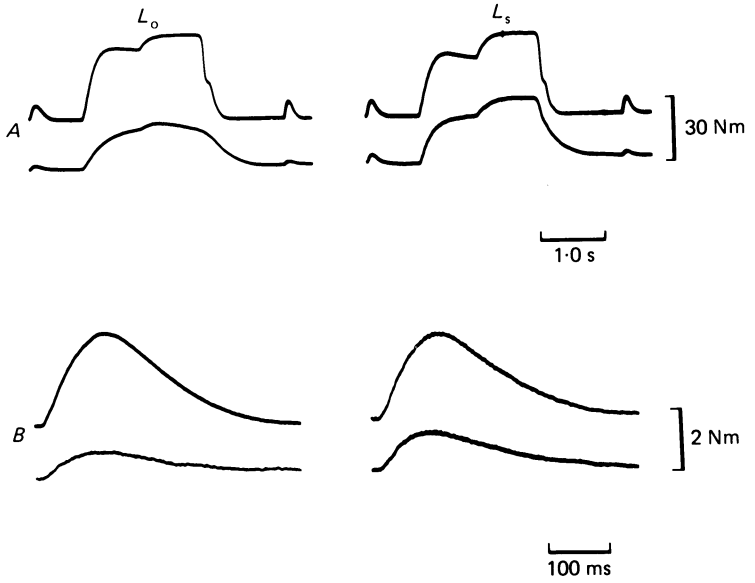

Fig. 2. Changes in twitch and tetanic torque of ankle dorsiflexors following 90 s of indirect stimulation at 20 Hz; muscles were fatigued at either the optimum length (L_0) or in the shortened position (L_s). *A* shows the results of testing the muscles with a single stimulus, followed by tetani at 20 Hz and 80 Hz and a second stimulus; *B* shows the initial twitches only. The upper and lower traces of each pair depict the responses before and after the fatiguing procedure.

the tetanic torques in the control period were only slightly larger when the testing stimulation was carried out at 80 Hz rather than at 20 Hz, reflecting the steep initial portion of the force–frequency curve for the tibialis anterior with the ankle plantarflexed (Marsh *et al.* 1981).

When the testing sequence was repeated after completion of the fatiguing procedure the twitch torque was found to be significantly smaller than in the control period, irrespective of the muscle length at which fatigue had been induced (Fig. 2). Although the tetanic torques were also diminished, the differences between the control and fatigued mean values were only statistically significant when the fatiguing procedure had been performed at L_0. Since the twitch torques were more affected by fatigue than the tetanic torques there were significant reductions in twitch:tetanus torque ratios; this was true for both rates of testing tetanic stimulation (20 Hz and 80 Hz) and for L_0 as well as L_s. In contrast to the mechanical events, the M-waves were found to have recovered their sizes in the 3 s elapsing between the end of the fatiguing procedure and the start of the testing sequence (Table 1). No significant changes were found, as a consequence of fatigue, in the mean

contraction times; however, the twitch half-relaxation times were prolonged and this change was significant for L_s. The most profound alteration in time course involved the relaxation time at the conclusion of the 80 Hz tetanus at both L_0 and L_s; in individual cases the time for 80 % relaxation increased by 2·5–9 times (Table 1).

TABLE 2. Comparison of fatigue effects following tetanic stimulation at L_0 and L_s. Abbreviations as in Table 1

	Fatigue/control (%)		
	L_0	L_s	P
P_t	29·0 ± 13·8	48·3 ± 13·8	< 0·001
M-wave	92·3 ± 14·4	85·4 ± 9·2	N.s.
CT	98·2 ± 15·7	92·7 ± 9·6	N.s.
$\frac{1}{2}RT$	127 ± 35	131 ± 28	N.s.
P_0^{20}	42·3 ± 16·6	65·7 ± 9·2	< 0·01
P_0^{80}	49·2 ± 16·9	72·2 ± 16·9	< 0·001
$\frac{1}{5}P_0^{80}RT$	448 ± 184	297 ± 68	< 0·001

TABLE 3. Comparison of fatigue effects following voluntary contraction. Abbreviations as in Table 1

	Fatigue/control (%)		
	L_0	L_s	P
M-wave	94·1 ± 6·4	96·0 ± 14·1	N.s.
P_t	15·0 ± 10·4	61·4 ± 10·4	< 0·05
P_0^{20}	31·8 ± 23·2	74·2 ± 12·6	< 0·05
P_0^{80}	47·8 ± 14·4	82·3 ± 10·8	< 0·05
$\frac{1}{5}P_0^{80}RT$	487 ± 352	228 ± 83	N.s.

Because of the design of the experiments, it was possible to compare the effects of muscle length on fatigue for each subject, rather than pooling the data as in Table 1. Table 2 displays the 'fatigued' values as percentages of the respective control values for L_0 and L_s; the differences between the mean percentages have been tested statistically for each of the muscle parameters. It was observed that not only the twitch torques, but also the tetanic torques, were smaller when the fatiguing procedure had been performed at L_0 rather than at L_s. Such a difference could be demonstrated for each of the ten subjects as well as for the pooled data; typical examples are displayed in Fig. 2. The rate of relaxation after 80 Hz tetanic stimulation was also affected by the length of the muscle during the fatiguing procedure, being significantly lower for L_0 than for L_s. No effect of length could be demonstrated on the relaxation of the twitch after fatigue (Table 2).

Observations after the volitional fatiguing procedure

Four subjects were examined to determine whether the effects of fatigue after sustained voluntary contraction were similar to those after tetanic stimulation. As

with the tetanic fatiguing procedure, the voluntary contraction was performed for 90 s at L_0 and L_s in each subject, with the same testing sequence being performed at 40 deg of plantarflexion. The results of this part of the study resembled those obtained after tetanically induced fatigue with greater losses of twitch and tetanic torque occurring after fatigue at L_0 than at L_s (Table 3). As only four subjects were examined, however, the levels of statistical significance between results for L_0 and L_s were less pronounced than after tetanically induced fatigue.

DISCUSSION

In keeping with other results (Hultman & Sjöholm, 1983) the present study has shown that the muscle fatigue which follows a period of low-frequency stimulation is not due to impaired excitation of muscle fibres but must instead involve excitation–contraction coupling or the contractile machinery. The bulk of the published evidence suggests that, of the two latter possibilities, a failure of excitation–contraction coupling is the more important. For example, when frog muscle is completely fatigued by tetanic stimulation the fibres can still develop further tension by undergoing contractures in response to caffeine (Eberstein & Sandow, 1963). Similarly, after an episode of low-frequency stimulation or voluntary contraction, significantly more fatigue can be demonstrated when the testing procedure involves low-frequency, rather than high-frequency, stimulation (Edwards *et al.* 1977). This disparity suggests that it is not the contractile machinery, but the activation of the latter, which is defective.

Jones (1981) has suggested that a breakdown in excitation–contraction coupling could result from ionic imbalance across the T-tubular membrane. Repeated excitation would cause sodium ions to enter the fibres and potassium ions to leave; because of the small sizes of the T-tubules relatively large changes in ionic concentration would be expected and could lead to failure of inwardly propagated action potentials. The present experiments have addressed this possibility. If fatigue depends solely on the number of excitations of the T-tubules, as predicted by the ionic hypothesis of fatigue (see above), then the muscle length at which the contractions were performed should be unimportant. In this study, however, a definite effect of length on susceptibility to fatigue has been demonstrated. Thus, the twitch and tetanic torques in test contractions were significantly smaller when tetanic or voluntary activation leading to fatigue had been performed at the optimum length rather than in the shortened position. Our results are similar to those of Aljure & Borrero (1968) who studied toad sartorius muscles *in vitro*: no other investigation of muscle length on fatigue appears to have been performed.

Our interpretation of the present results is that fatigue is related to the number of effective cross-bridge interactions during excitation of the muscle fibres. At the optimum length there is sufficient overlap of the actin and myosin filaments for all cross-bridges to be engaged (Gordon, Huxley & Julian, 1966). At short sarcomere lengths, however, opposing actin filaments overlap with each other and presumably interfere with cross-bridge attachment, since active tension is reduced. The alternative possibility, that all the cross-bridges are activated and that an 'internal' opposing force prevents the development of 'external' tension, appears less likely on the basis

of the recent study by Julian & Morgan (1981). A third explanation is that there is a failure of inwardly-propagating action potentials in the T-tubules at short fibre lengths (Taylor & Rüdel, 1970). Such a possibility would not only account for the reduced torque found at short muscle lengths but would be expected to diminish changes in cation concentration across the T-tubules during muscle activity (see above). Reliable measurements of T-tubular action potentials have yet to be made (Adrian, 1982) but there is indirect evidence to suggest that inward propagation does occur at short lengths. Thus the intracellular calcium ion transients following single stimuli are only slightly smaller at short fibre lengths than at the optimum length (Blinks, Rüdel & Taylor, 1978). Although the rise in intracellular calcium ions is reduced at short lengths during tetanic stimulation (Blinks *et al.* 1978) it is probable that the calcium binding sites on the myofilaments are saturated at concentrations well below those usually achieved in tetanic contractions (Blinks *et al.* 1978). The results of Julian & Morgan (1981), made with potentiating substances, have also been interpreted as indicative of maximal inward activation of fibres at short lengths.

If a reduced number of cross-bridge attachments is indeed responsible for decreased tension development at short lengths, as suggested by Julian & Morgan (1981), it follows that there would be less consumption of ATP and precursors, and also less accumulation of hydrogen ions and other products of contraction. Now that nuclear magnetic resonance spectrometry has been successfully applied to muscle (Dawson *et al.* 1978) it should be possible to determine which of the metabolic changes during fatigue are dependent on muscle length. It would still be necessary to establish which, if any, of these events was responsible for the increased sensitivity of lengthened muscle to fatigue. The results of the present study do not exclude the possibility that a failure of excitation–contraction coupling may be secondary to such a metabolic change. The results do, however, make it appear unlikely that only ionic mechanisms are involved in a failure of excitation–contraction coupling.

We are indebted to Glen Shine and Nancy Kowalchuk for technical assistance and to Angelika Opic for secretarial services. Financial assistance was given by the Muscular Dystrophy Association of Canada; Sara Fitch was the recipient of a Caltex (W. Australia) scholarship.

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