The metabolic costs of different types of contractile activity of the human adductor pollicis muscle

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1. The metabolic costs and physiological consequences of shortening contractions of a human muscle working *in situ* have been compared with those of the muscle maintaining a continuous isometric contraction and when performing repeated brief isometric contractions.

2. After a total of 10 s stimulation, the shortening and intermittent brief isometric protocols had very similar effects, causing a 30% loss of force and a threefold increase in the half-time of relaxation. This was in contrast to the continuous isometric contraction protocol where there was less than 10% loss of force or slowing of relaxation.

3. The ATP cost over the first 5 s of the continuous isometric protocol was 27 mmol (l intracellular water)$^{-1}$ while for the shortening and repeated brief isometric protocols the costs were 48 and 46 mmol (l intracellular water)$^{-1}$, respectively.

4. The results show that shortening and repeated brief isometric contractions are considerably more energetically demanding, and hence more fatiguing, than sustained isometric contractions.

Skeletal muscle is used in many different ways, each of which could have different metabolic costs. Knowing these costs would be an important advance in understanding the patterns of fatigue in different forms of exercise. The possibility of differing energy costs is suggested by the fact that the metabolic changes resulting from a 30 s isometric contraction of the quadriceps (Hultman & Sjöholm, 1983) are similar to those of a 30 s maximal sprint (Bogdanis, Nevill, Boobis, Lakomy & Nevill, 1995). During an isometric contraction the muscle is continually active but when sprinting the quadriceps muscle is used only for a limited period during each stride, so the total duration of muscle contraction during a 30 s sprint can only be a fraction of the overall duration of the exercise. The metabolic cost of the dynamic exercise per unit time of muscle activity therefore must be higher than for isometric contractions. In addition, during a sprint the muscle can be reperfused with blood and there is the opportunity for some recovery to take place between each stride. Thus the circumstantial evidence would suggest that the metabolic costs of dynamic exercise are higher than those of isometric contractions.

There is a substantial amount of literature on the metabolic changes during exercise of human (mainly quadriceps) muscle obtained by biopsy measurement (e.g. Edwards, Hill & Jones, 1975; Hultman & Sjöholm, 1983; Greenhaff, Söderlund, Ren & Hultman, 1993; Bogdanis *et al.* 1995) and this has been supplemented by magnetic resonance spectroscopy (e.g. Taylor *et al.* 1986; Cady, Jones, Lynn & Newham, 1989). However, in no case is it possible to identify the specific energy costs of different types of activity such as isometric or shortening contractions.

Direct chemical measurements and inferences drawn from observations of heat production have shown that for amphibian muscle there is an energy cost specifically associated with shortening (see Woledge, Curtin & Homsher, 1985, for review). More recently this type of work has been extended to mouse fast and slow muscles (Barclay, Constable & Gibbs, 1993). For the fast muscle there was only a small increase in energy costs of the shortening contraction when compared with an isometric contraction, while for the slow soleus the difference was between four- and fivefold. With such large possible differences between the various types of contraction and

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between fibre types it is clearly important to have direct measurements of human muscle working *in situ*. We have examined these questions in the adductor pollicis muscle, which has a predominance of slow fibres (Round, Jones, Chapman, Edwards, Ward & Fodden, 1984).

METHODS

Subjects

Five normal healthy subjects (three male and two female, aged 25–45 years) participated in the study after being informed of the nature and risks of the procedures and giving their informed consent. The procedures were approved by the University College London Ethical Committee.

Muscle contraction

The adductor pollicis of the left hand was stimulated via the ulnar nerve at the wrist with the hand held in a hand rig described by Edwards, Young, Hosking & Jones (1977). A band around the second metacarpal of the thumb was attached to a light chain which was either attached to an isometric force transducer or, via a pulley, to a light tin can containing weights. In this way the adductor pollicis was stimulated to contract isometrically or allowed to shorten against the fixed load. The ulnar nerve was supramaximally stimulated with square wave pulses of 50 μs duration at a frequency of 50 Hz. Muscle function and the extent of fatigue were assessed by measuring the force and relaxation of 1 s isometric test tetani (see Fig. 1). Relaxation was measured as the half-time ($RT_{\frac{1}{2}}$) of the exponential portion of the force trace, usually the time taken to fall from 50 to 25% of the maximum force.

Muscle metabolite measurements

^{31}P magnetic resonance spectroscopy (MRS) spectra were collected before and after ischaemic activity using methods similar to those previously described by Cady *et al.* (1989). Each composite spectrum comprised 128 free induction decays (total collection time, 4·8 min) which were subjected to Fourier transformation, phasing, baseline correction and fitting to Gaussian curves. The areas for the resonance peaks of phosphomonoester (PM), inorganic phosphate (P_i), phosphocreatine (PC), phosphodiester (PD) and βATP were calculated by integration of the area between preselected gates. The total MRS-visible phosphorus was taken to be the sum of $PM + P_i + PD + PC + (3 \times \beta ATP)$ and the individual compounds were expressed as a fraction of the total. βATP/total P for the resting muscles was $0{\cdot}109 \pm 0{\cdot}002$ (mean ± S.E.M.). Metabolite concentrations were calculated assuming a constant total P and an [ATP] of 8·2 mM in the intracellular water of the fresh muscle (Cady *et al.* 1989).

The change in intracellular lactate concentration was assumed to be equivalent to the protons required to produce the observed change in pH, making assumptions about the concentrations and dissociation constants of the intracellular buffers. These buffers were: (a) protein-bound histidine, 56 mM, pK (−log of dissociation constant) = 6·8 (Fürst, Josephson & Vinnars, 1970); (b) bicarbonate, 10 mM, pK = 6·1 (Sahlin, Alvestrand, Brandt & Hultman, 1978); (c) carnosine, 7 mM, pK = 6·8 (Mannion, Jakeman, Dunnett, Harris & Willan, 1992); and (d) phosphate – this was added to the computation according to the phosphate measured by MRS (pK = 6·73). The non-phosphate buffer capacity came to 34·5 Slykes, and the total buffer capacity increased to approximately 50 Slykes when P_i reached its highest levels.

ATP cost was estimated from changes in PC, βATP and lactate (LA) concentrations assuming an ATP yield of 1·5 for every LA formed (Δ is post − pre):

$$\text{ATP cost} = (1{\cdot}5 \times \text{LA}) - (\Delta\text{PC}) - (\Delta\beta\text{ATP}).$$

Metabolite concentrations and ATP costs are given as millimoles per litre intracellular water, or millimolar.

Experimental protocols

Before the experiment the hand and forearm were placed in hot water (45 °C) to cause vasodilatation and perfuse the hand with blood at core temperature. Two series of experiments were then carried out.

The first series was concerned with the fatiguing effects of different protocols. Three maximal 1 s tetanic contractions were elicited. After 5 min recovery a cuff was inflated around the upper arm to 200 mmHg and one of three stimulation protocols commenced. After the equivalent of 5 s stimulation, with the muscle still ischaemic, a 1 s test tetanus was elicited and the stimulation protocol repeated. After the equivalent of another 5 s stimulation a second test tetanus was elicited. The cuff was released and the muscle allowed to recover for 10–15 min before repeating the process with a different stimulation protocol.

The second series of experiments was concerned with measuring the metabolic cost of the first 5 s period of stimulation. After warming, the hand was placed in the MR spectrometer and resting muscle metabolite concentrations estimated with an intact circulation. The hand was removed from the magnet, warmed and placed in the hand rig and stimulated with one of the three protocols (see below). After the first period of stimulation, and with the circulation still occluded, the subject's hand was placed back in the MR spectrometer and the muscle metabolites measured again, after which the cuff was released and the muscle allowed to recover as described above.

The subjects repeated each protocol two or three times. The mean was taken of the results for each subject and used to generate the mean values presented here; values are given ± S.E.M.; differences between means were assessed with Student's t test and values of $P < 0{\cdot}05$ were taken as significant.

Stimulation protocols

(1) Continuous isometric. The muscle was stimulated for 5 s at 50 Hz with the thumb attached to the isometric force transducer.

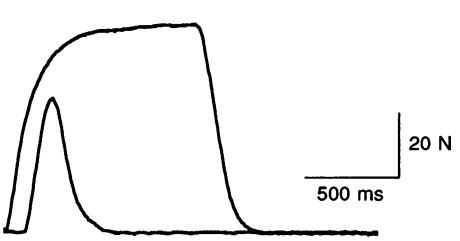

Figure 1. Force traces from 1 and 0·1 s isometric tetani of the fresh adductor pollicis

The trace for the shorter contraction has been displaced 0·1 s to the right.

Table 1. Force and relaxation measurements

Stimulation protocol	Force (%)	Relaxation (%)
(1), 5 s isometric	93 ± 3	109 ± 9
(1), 10 s isometric	92 ± 4	107 ± 8
(2), 50 × 0·1 s shortening	84 ± 1	167 ± 9
(2), 100 × 0·1 s shortening	71 ± 2	335 ± 15
(3), 50 × 0·1 s isometric	85 ± 3	169 ± 6
(3), 100 × 0·1 s isometric	73 ± 3	305 ± 8

Measurements made after the equivalent of 5 and 10 s stimulation using the three protocols: (1) continuous isometric; (2) 0·1 s stimulation with the muscle shortening against a load; (3) 0·1 s stimulation with the muscle held isometric. Force and relaxation half-time ($RT_{½}$) are expressed as a percentage of the values measured from a test tetani of the fresh muscle.

(2) Dynamic. Weights were added to the tin can to give an external load of 30% of the maximal isometric tetanic force. The thumb was attached to the external load and stimulated for 0·1 s every second for a total of 50 s. The 0·1 s contraction was sufficient to adduct the thumb fully and lift the load through approximately 3 cm. At the end of stimulation the external load re-extended the thumb.

(3) Intermittent isometric. The thumb was attached to the isometric force transducer and the muscle stimulated for 0·1 s every second for 50 s, as in protocol (2), the difference being that no external work was done.

Figure 1 shows force traces from a 1 s test tetanus and a 0·1 s tetanus, as used in protocol (3).

RESULTS

Mechanical changes

The force generated by a 1 s test tetanus of the fresh muscle and after the first and second periods of stimulation are shown in Fig. 2 and the values for changes in force and relaxation rate are given in Table 1. The force of the fresh muscles varied from 50 to 100 N between the subjects but all had very similar rates of relaxation, with a mean $RT_{½}$ value of 43 ms. There was little evidence of fatigue as a result of 5 and 10 s isometric contraction (Fig. 2*A*), either in tetanic force or $RT_{½}$. This contrasts with the behaviour of the muscle when allowed to shorten and perform external work (Fig. 2*B*). As a result of this protocol, force fell

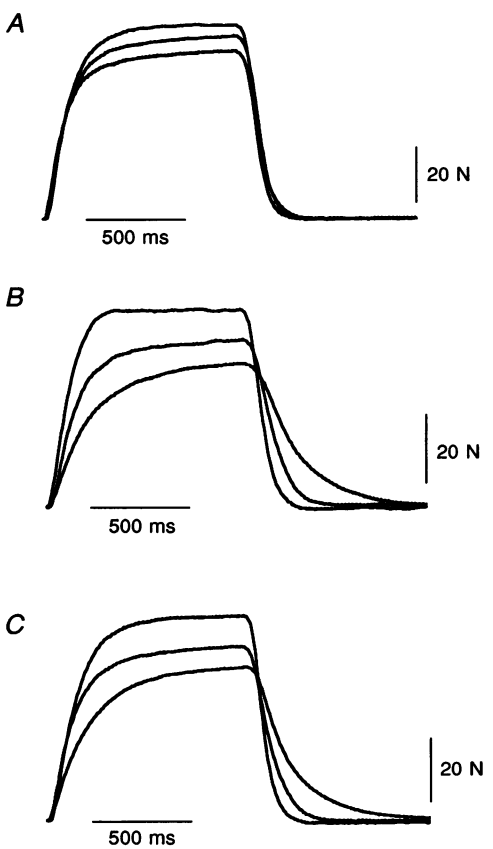

Figure 2. Force traces showing loss of force and slowing of relaxation with the onset of fatigue

Traces recorded from fresh muscle and after the equivalent of 5 and 10 s stimulation using the three protocols. *A*, protocol (1), continuous isometric stimulation; *B*, protocol (2), 0·1 s stimulation with muscle shortening against a load; *C*, protocol (3), 0·1 s stimulation with muscle held isometric.

Table 2. Resting muscle metabolite concentrations and changes as a result of the equivalent of 5 s contractile activity with three different contraction protocols (see Table 1) of the adductor pollicis

	βATP	PC	P_i	LA	pH	
Resting levels	8·2	33·5 ± 3·1	8·5 ± 0·7	—	7·2 ± 0·01	
Contraction protocol	ΔβATP	ΔPC	ΔP_i	ΔLA	ΔpH	ATP turnover
1 × 5 s isometric	0·01 ± 0·02	−14·5 ± 1·5	12·5 ± 1·0	8·3 ± 0·4	−0·12 ± 0·08	26·9 ± 0·7
50 × 0·1 s shortening	−0·7 ± 0·2	−16·4 ± 0·6	16·8 ± 0·8	20·6 ± 1·6	−0·32 ± 0·02	48·0 ± 1·0
50 × 0·1 s isometric	−1·3 ± 0·19	−17·0 ± 0·9	19·0 ± 1·0	18·6 ± 1·3	−0·28 ± 0·02	46·2 ± 0·9

All concentrations are given as mM in the intracellular water.

significantly more and this was accompanied by marked slowing of relaxation, becoming over three times slower than in the fresh muscle after 100 contractions. The intermittent isometric stimulation (protocol (3)) yielded results (Fig. 2*C*) which were very similar to those obtained with the dynamic protocol (2) (Fig. 2*B*), both in terms of the loss of force and the slowing of relaxation.

Metabolic changes

Table 2 shows metabolite concentrations for the resting muscles together with the changes that occurred as a result of the three exercise protocols.

As a result of protocol (1) there was no change in ATP and just under half the muscle PC was split. There was a significant decrease in intracellular pH, calculated to be due to a rise of approximately 8 mM in muscle lactic acid. The total ATP turnover was 27 mM, of which 49% was attributable to glycolysis.

Protocol (2), in which the muscle performed work against an external load, entailed a much greater turnover of ATP, 48 mM, nearly twice that of protocol (1). There was a marginally greater splitting of PC but the most noticeable difference was in the calculated extent of glycolysis where the accumulation of lactic acid was more than twice that seen in protocol (1); the contribution of glycolysis to the ATP turnover was approximately 66%.

No external work was performed in protocol (3) but the pattern of stimulation was the same as that used in the dynamic protocol (2). The metabolic changes were very similar to those seen in protocol (2), with the ATP turnover calculated to be 46 mM, with glycolysis contributing 64% of the total.

DISCUSSION

The results clearly show that a muscle which shortens and performs work fatigues more rapidly than a muscle contracting for an equivalent length of time under isometric conditions. The fatigue is evident not only in the loss of force but also in the characteristic slowing of relaxation. The reason for the more rapid fatigue is the higher energy requirement of this type of exercise, shown by the MRS measurements to be almost twice as high as during continuous isometric contractions. Metabolite measurements were restricted to the first period of stimulation (Table 2) to minimize any effects of fatigue, as it is likely that the ATP turnover will decline as the force falls (Hultman & Sjöholm, 1983). Thus the initial ATP turnover rates may have been higher than measured here when averaged over 5 s, and the difference between the isometric and intermittent protocols even greater than estimated here. The twofold difference between the isometric protocol (1) and the shortening protocol (2) suggests that the contractile properties of this human muscle fall somewhere between those of the mouse fast and slow muscles studied by Barclay *et al.* (1993) and emphasizes the danger of extrapolating data obtained for isometric contractions to situations involving dynamic exercise.

The surprising result was obtained with the intermittent pattern of isometric contractions (protocol (3)). Although the total duration of stimulation with the muscle under isometric conditions was the same as for the continuous pattern of stimulation (protocol (1)), the pattern of fatigue and the energy cost were very similar to those of the dynamic pattern of activity.

Protocol (3) was introduced as a control in the expectation that a series of short isometric contractions would have the same consequences for the muscle in terms of fatigue and metabolic costs as a single isometric contraction of the same total duration. In fact, the intermittent protocol (3) had an energy cost that was nearly double that of the longer contraction in protocol (1) and was very similar to that of the series of shortening contractions in protocol (2). Bergstrom & Hultman (1991) found somewhat higher energy costs when comparing short (0·8 s) and longer (1·6 s) isometric contractions

There are a number of possible explanations for the higher costs of the intermittent isometric protocol. One factor is the likelihood that there will be cross-bridge cycling for longer than the 0·1 s tetanic train. At the end of stimulation there is a short delay before force decays away (Fig. 1). In the case of the adductor pollicis the decay of force has a half-time of about 45 ms so that as a consequence of 0·1 s stimulation there will be some contractile activity occurring over at least 0·2 s. Although isometric force records may be a poor indicator of cross-

bridge turnover, it is notable that the impulse of the short tetanus was 12·6% that of the test contraction lasting ten times longer (Fig. 1). This prolongation might account for a 25% greater energy cost of the intermittent protocol but would not explain the near doubling of the rate actually seen.

The second explanation for the unexpectedly high energy costs of the intermittent isometric protocol is that even under supposedly isometric conditions the muscle shortens against compliant tendons, performing work external to the muscle fibres but within the whole muscle–tendon complex. For a continuous tetanus the muscle will shorten once at the start of the contraction so that any external work will be a small proportion of the total energy turnover; however, if this is repeated with short periods of stimulation, as with protocol (3), then the external work will become an important component. It is unlikely, however, that the internal work performed by the muscle stretching the tendon could be comparable, energetically, to the external work performed lifting a load. The external load was equivalent to 30% of the maximum tetanic force and was raised through approximately 3 cm; for a comparable amount of work during the maximal isometric contractions, there would need to be about 1 cm of internal shortening of the muscle. The stiffness of the tendons of the first dorsal interosseous has been estimated to be of the order of 100 N mm^{-1} (Cook, Santello & McDonagh, 1995). If the tendons of the adductor pollicis are similar there would be no more than about 1 mm internal shortening in response to the maximum tetanic forces. Observation of the hand as it was being stimulated revealed a certain amount of movement, generally extension of the wrist, but the insertion and attachment of the adductor pollicis did not obviously change their relative positions so it is difficult to see how there could have been more than, at most, 2–3 mm internal shortening of the muscle.

It would seem likely that the high energy cost and consequent rapid fatigue of the muscle undergoing intermittent brief isometric contractions may be due to a combination of two factors, a longer duration of muscle activation compared with the actual time of stimulation, and an increased energy cost as a result of work done during internal shortening. Neither by themselves seems sufficient but in combination they may account for the observed behaviour.

In summary, the present results demonstrate two points. The first is that the energy cost of a human muscle undergoing shortening contractions is approximately twice that of maintaining a steady isometric contraction. The second point is that if the contraction pattern consists of repeated brief isometric contractions the energy costs are very similar to those of a muscle shortening against an external load. There is no simple explanation of the last observation, but two possible contributory factors have been discussed.

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