Skeletal muscle energy metabolism and fatigue during intense contraction in man

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The rate of skeletal muscle anaerobic ATP resynthesis is rapid when compared with aerobic resynthesis, however a high rate of anaerobic resynthesis can only be maintained for short periods of time. Table 1 shows the rates of ATP resynthesis from phosphocreatine (PCr) and glycolysis during 30s of near maximal isometric contraction in man. After only 1.3s of contraction the rate of PCr utilisation begins to decline, while the corresponding rate from glycolysis does not peak until after 3s of contraction This suggests that the rapid initial utilisation of PCr may buffer the momentary lag in energy provision from glycolysis. There is also a progressive decline in ATP provision from both substrates after their initial peaks e.g. the rates of ATP provision from PCr and glycolysis during the final 10s of contraction amount to 2 and 40%, respectively of their respective peak rates of production. Similar findings, involving isokinetic and dynamic exercise, have been reported by other research groups (Boobis et al. 1982, Jones et al. 1985). Interestingly, in all of these studies, in conjunction with the decline in anaerobic ATP production was a decline in force production and power output. It is tempting to postulate therefore, that the development of fatigue was attributable to the decline in ATP provision. Alternatively however, the decline in energy provision may simply be a function of a decline in the rate of ATP utilisation which will accompany any decline in force production.

Table 1. Rates of anaerobic ATP resynthesis from phosphocreatine (PCr) degradation and glycolysis during intense contraction in man. Values were calculated from muscle metabolite changes measured in muscle biopsy samples obtained during intense intermittent electrically evoked (50Hz) isometric contraction (Hultman and Sjöholm 1983, Hultman et al. 1990).

	ATP production (mmol/kg dm/s) from:	
Duration (s)	PCr	glycolysis
0-1.3	9.0	2.0
0-2.6	7.5	4.3
0-5	5.3	4.4
0-10	4.2	4.5
10-20	2.2	4.5
20-30	0.2	2.1

The values shown in table 1 were calculated from the metabolite changes measured in muscle biopsy samples obtained from the quadriceps femoris muscle of normal healthy volunteers. However, it is known that human skeletal muscle is composed of at least two functionally and metabolically different fibre types. Type I fibres have been shown to have a high aerobic capacity, to be slow contracting with a low power output and to be fatigue resistant. Conversely, type II fibres have a high anaerobic capacity, are fast contracting with a high peak power output and fatigue rapidly (for comprehensive review see Green 1986). Evidence from

animal studies performed on muscles composed of predominantly type I or type II fibres (Barany 1967, Hintz et al. 1982) and from one study performed using bundles of similar human muscle fibre types (Faulkner et al. 1986), suggest that the rapid marked rise and subsequent decline in maximal power output observed during intense muscle contraction in man may be closely related to activation and rapid fatigue of type II fibres during contraction.

Recently we have attempted to relate the decline in whole muscle force production during intense contraction in man to the metabolic changes occurring in individual muscle fibre types (Greenhaff et al. 1991, Hultman et al. 1991, Söderlund et al. 1992). These studies have involved individual muscle fibre fragments being dissected from biopsy samples and, after fibre type characterisation, being used to determine single fibre ATP, PCr and glycogen concentrations. The latter study involved muscle biopsy samples being obtained from the quadriceps muscle group before and after 10 and 20s of intense isometric contraction, induced by intermittent percutaneous electrical stimulation (50Hz; 1.6s stimulation, 1.6s rest). During the initial 10s of stimulation, the rates of PCr utilisation in type I and II fibres were 3.3 and 5.3 mmol/kg dm/s, respectively. During the subsequent 10s of stimulation, the rate of PCr utilisation in type I fibres remained fairly constant, declining by ~15%. However, the corresponding rate in type II fibres declined by ~60% and, at the end of the stimulation period, the PCr store of this fibre type was close to zero.

The rate of glycogen utilisation over the 20s stimulation period in type II fibres (6.3 mmol/kg dm/s) was rapid when compared to the negligible rate observed in type I fibres (0.6 mmol/kg dm/s), and was in excess of both the measured and calculated maximal rates of glycogen utilisation determined for mixed fibred muscle. Unfortunately, the rate of single fibre glycogen utilisation was not determined for the initial 10s of contraction, therefore it is not possible to determine whether the decline in glycogenolysis observed in mixed fibred muscle (Table 1) occurred solely in type II fibres. However, in an experiment where electrical stimulation was maintained for 30s (Greenhaff et al. 1991), the rate of glycogenolysis in type II fibres was 3.5 mmol/kg dm/s over the stimulation period, and the corresponding rate in type I fibres was 0.2 mmol/kg dm/s. It is plausible to suggest therefore that the observed decline in glycogen utilisation in mixed fibred muscle during intense electrical stimulation is probably restricted to type II fibres. The relatively low rate of ATP utilisation by type I fibres, together with their high capacity to resynthesise ATP aerobically, may explain the observed low rate of glycogen utilisation by these fibres during intense intermittent contraction. It is possible that the intermittent nature of the contraction (1.6s stimulation, 1.6s rest) may be important in dictating the oxygen availability to this fibre type.

In parallel with the decline in whole muscle force production during intense isometric contraction is a marked decline in the rates of PCr and glycogen utilisation in type II fibres. In the case of type I fibres, the corresponding rates of utilisation remain relatively unchanged. Evidence suggests that after ~20s of intense contraction the PCr store of type II fibres will be almost totally depleted and the rate of glycogen utilisation will be close to maximal or even on the decline in this fibre type. At this point, no alternative mechanisms will be available for type II fibres to maintain the required ATP resynthesis rate and compensate for the depleted PCr stores and declining, or soon to be declining, rate of glycogen utilisation. In short therefore, the declining rate of ATP resynthesis will be insufficient to maintain force production and fatigue will occur.

References

Barany M (1967). ATPase activity of myosin correlated with speed of muscle shortening. *Journal of General Physiology* **50** (suppl 2), 197-218.

Boobis LH, C Williams & SA Wooton (1982). Human muscle metabolism during brief maximal exercise in man. *Journal of Physiology (London)* **338**, 21-22P.

Faulkner JA, Claflin DR & McCully KK (1986). Power output of fast and slow fibres from human skeletal muscles. In: *Human Muscle Power*. Eds, Jones NL, McCartney N & McComas AJ, Human Kinetics Publ., Champaign, IL. pp81-89.

Green HJ (1986). Muscle power: Fibre type recruitment, metabolism and fatigue. In: *Human Muscle Power*. Eds, Jones NL, McCartney N & McComas AJ, Human Kinetics Publ., Champaign, IL. pp65-80.

Greenhaff PL, Ren J-M, Söderlund K & Hultman E (1991). Energy metabolism in single muscle fibres during contraction witout and with epinephrine infusion. *American Journal of Physiology* **260**, E713-E718.

Hintz CS, Chi MM-Y, Fell RD, Ivy JL, Kaiser KK, Lowry CV & Lowry OH (1982). Metabolite changes in individual rat muscle fibres during stimulation. *American Journal of Physiology* **242**, C218-C228.

Hultman E & Sjöholm H (1983). Substrate availability. In: *Biochemistry of Exercise, International Series on Sport Sciences*. Eds, Knuttgen HG, Vogel JA, & J Poortmans, **13**, Human Kinetics Publ., Champaign, IL. pp 63-75.

Hultman E, Bergstrom M, Spreit LL & Söderlund K (1990). Energy metabolism and fatigue. In: *Biochemistry of Exercise, International Series on Sport Sciences*. Eds, Taylor AW, Gollnick PD, Green HJ, Ianuzzo CD, Noble EG, Metivier G, & Sutton J, **21**, Human Kinetics Publ., Champaign, IL. pp 73-92.

Hultman E, Greenhaff PL, Ren J-M & Söderlund K (1991). Energy metabolism and fatigue during intense muscle contraction. *Biochemical Society Transactions* **19**, 347-353.

Jones NL, McCartney N, Graham T, Spriet LL, Kowalchuk JM, Haigenhauser GJF & Sutton JR (1985). Muscle performance and metabolism in maximal isokinetic cycling at slow and fast speeds. *Journal of Applied Physiology* **59**, 132-136.

Söderlund K, Greenhaff PL & Hultman E (1992). Energy metabolism in type I and type II human muscle fibres during short term electrical stimulation at different frequencies. *Acta Physiologica Scandinavica* **144**, 15-22.