Time to fatigue is increased in mouse muscle at 37°C; the role of iron and ROS

T.F. Reardon and D.G. Allen, Bosch Institute, School of Medical Sciences, University of Sydney, NSW 2006, Australia.

Studies exploring the rate of fatigue in isolated muscle at 37°C have produced mixed results. In the present study muscle fibre bundles from the mouse foot were used to study the effect of temperature on the rate of muscle fatigue. Provided iron was excluded from the solutions, time to fatigue at 37°C was increased compared to 22°C (125 ± 8 % of 22°C fatigue time, n = 7). In contrast, when iron was present (~1 μM), fatigue was accelerated (68 ± 10 %, n = 6). Iron can increase reactive oxygen species (ROS), which are believed to accelerate fatigue. The addition of 25-100 μM H_2O_2 at 22°C reduced time to fatigue to 80-20% of the control respectively (n = 15). Iron was added to cultured primary skeletal muscle cells to determine if iron could increase ROS production. Neither iron entry nor ROS production were detected in non-contracting muscle cells ($n \geq 6$). The addition of 8-hydroxyquinoline, which facilitates iron entry, to iron-ascorbic acid solutions caused a rapid rise in intracellular iron and ROS ($n \geq 9$). Our results indicate that time to fatigue *in-vitro* is increased at 37°C relative to 22°C, but the addition of ROS can accelerate fatigue. An increase in muscle iron can accelerate ROS production, which may be important during or following exercise and in haemochromatosis, disuse atrophy and sarcopenia.