Elevated $O_2^{\bullet -}$ production at 37°C reduces membrane excitability in isolated rat skeletal muscle

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When isolated mammalian skeletal muscle is exposed to 37°C, performance rapidly and irreversibly declines. Also, extracellularly measured superoxide ($O_2^{\bullet -}$) is markedly greater at 37°C than at 23°C. This can reduce muscle performance at temperatures above 40°C, by reducing contractile apparatus function. We investigate which excitation-contraction coupling steps contribute to the decline in performance at 37°C. Rats were killed by cervical dislocation or by halothane overdose. Single mechanically-skinned fibres were prepared from EDL muscles kept in Krebs-Ringer Solution (KRS) at 22°C or 37°C (30min). Skinned fibres were then activated at 22°C in solutions of different pCa. The resting membrane potential (RMP) and intracellular action potential (AP) were measured at 22°C in single fibres before and after 40min incubation in KRS at 22°C or 37°C. Results show that exposure to 37°C (30min) caused no significant effect on either the maximum Ca^{2+}-activated specific force or on the Ca^{2+}-sensitivity of the contractile apparatus. However, the RMP became depolarized (~10mV) and the AP amplitude was reduced by ~35mV following 37°C treatment (40min). Additionally, the depolarisation and repolarisation rate was significantly slower compared to control fibres (22°C). Tempol (1mM) largely ameliorated the effects of 37°C on the RMP, AP amplitude and maximum rate of repolarisation. In summary, the increased rate of $O_2^{\bullet -}$ production at 37°C significantly reduces membrane excitability, explaining to a large extent the concomitant reduction in tetanic force observed in the isolated rat EDL muscle under the same conditions.