ATP requirements of mammalian skeletal muscle Na^+/K^+-ATPase

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Repeated vigorous action-potential (AP) stimulation can reduce K^+ and Na^+ gradients, leading to long-lasting depolarization of the membrane and reduced muscle excitability. The Na^+/K^+-ATPase requires sufficient ATP to maintain these gradients. This study compared the effectiveness of 'local' ATP (produced glycolytically in the triad junction) *versus* 'global' (cytoplasmic) ATP at meeting the Na^+/K^+-ATPase's energy requirements. Long-Evans hooded rats were killed by an overdose of halothane and single EDL fibres were mechanically skinned and electrically stimulated (75 V cm^{-1}, 1 ms pulse) in potassium HDTA solution to produce twitch or tetanic force responses under various conditions (e.g. 66 or 126 mM K^+ with 10 or 40 mM phosphocreatine (CP), with/without 1 or 5 mM phosphoenol pyruvate (PEP), creatine phosphokinase (CK) or pyruvate kinase (PK)). The repriming period for action potential generation, an indicator of membrane potential, was determined by applying paired pulses at varying intervals. Twitch and tetanic peak force were reduced to 70% and 60% respectively at 66 mM K^+ (compared to 126 mM K^+) and this was significantly ameliorated by 5 mM PEP/PK. The repriming period in 126 mM K^+ was 4.1±0.1 ms (n=31) and 7.3±0.3 ms (n=19) in 66 mM K^+. Addition of 5 mM PEP/PK to the 66 mM K^+ solution reduced the repriming period to 5.8±0.2 ms (n=11). When 5 mM PEP was added to the 66 mM K^+ solution without exogenous PK, repriming was still increased (8.8±0.2 ms and 6.7±0.3 ms without/with PEP, n=3). In summary, Na^+/K^+-ATPases function better when ATP is produced glycolytically in the triad junction instead of by CP/CK. Furthermore, after skinning, some PK remains bound within the fibre and this is sufficient to produce ATP near the Na^+/K^+-ATPases.