Inorganic phosphate reduces sarcoplasmic reticulum Ca^{2+} release in the presence and absence of cytoplasmic creatine phosphate in mammalian skeletal muscle

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Previous experiments[1,2] have shown that inorganic phosphate (P<sub>i) enters the sarcoplasmic reticulum (SR) of skeletal muscle and precipitates with Ca^{2+} to reduce the free [Ca^{2+}] available for release. This may underlie the reduction in Ca^{2+} release seen in the late stages of fatigue. These previous experiments were conducted in the absence of creatine phosphate (CP) to mimic fatigued muscle. However, a recent study has suggested that in the absence of CP, P<sub>i stimulates the reversal of the SR Ca^{2+}-ATPase which reduces the SR Ca^{2+} content independent of the formation of Ca^{2+}-P<sub>i precipitates[3]. Therefore, we sought to determine if under our conditions cytoplasmic CP alters the effect of P<sub>i on Ca^{2+} release observed previously[1,2].

Male Hooded Wistar rats were rapidly killed with CO_2 in accordance with the University of Adelaide's Animal Ethics guidelines. Mechanically skinned fibres were used here as previously described[1,2]. Skinned fibres were immersed in cytoplasmic-like solutions (K-HDTA)[1,2]; in some the [Pi] and [CP] were varied appropriately. Full SR Ca^{2+} release was elicited by using a K-HDTA solution containing 30 mM caffeine and low free [Mg^{2+}] (0.05 mM). The initial endogenous SR Ca^{2+} content was first determined and then fibres were Ca^{2+} loaded to the same level before exposure to P<sub>i solutions with or without CP (30s).

Ca^{2+} release from skinned fast-twitch fibres was equally reduced following a brief exposure to 50 mM Pi (30s) in the presence or absence of 10 mM CP. The absence of any difference in the effects of P<sub>i on Ca^{2+} release confirm our previous conclusions[1,2] that P<sub>i enters the SR where it precipitates with Ca^{2+} thereby reducing the amount of Ca^{2+} available for release.

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(2) Duke, A.M. & Steele, D.S. (2001). Journal of Physiology. 531.3, pp729-742.
(3) Fryer, M. W., et. al. (1995). Journal of Physiology. 482, pp123-140.