Acute incubation with creatine protects against muscle fatigue in an isolated skeletal muscle preparation

S.I. Head, B. Greenaway, School of Medical Sciences, Unsw, Sydney, NSW, Australia

Fatigue can be defined as the inability of a muscle to maintain maximal force production as a result of repeated activity. It is the graded failure of calcium release from the sarcoplasmic reticulum (SR) during fatigue that is primarily responsible for the decline in maximal force. This failure of calcium release from the SR is thought to be due to the increased P_i in the myoplasm entering the SR and precipitating free calcium. In the present study we used an isolated fast twitch muscle preparation (edl) from the mouse to examine the effect of incubating with creatine on the rate and extent of the force loss during muscle fatigue. In addition, we used an isolated fast twitch single fibre preparation (fdb) loaded with the calcium sensitive dye Fura-2 to measure the effect of incubating with creatine on intracellular calcium concentration during fatigue. In each case the muscle or isolated fibre was used as its own control (pre- and post- incubation). All animals were killed with Halothane prior to removing tissue. We demonstrated that creatine incubation significantly increased the amount of force produced during fatigue, as a result of increasing the amount of calcium released from the SR and improved the resistance of the muscle to fatigue. Creatine incubation also decreased the slowing of relaxation of the twitch which occurs in fatigue and increased the time to peak of the twitch. *(Creatine, control respectively: 12.0± 0.8 Ncm^{-1}, 6.1± 0.9 Ncm^{-1}; 0.56 ±.064 Ca^{2+} ratio, 0.39 ±.042 Ca^{2+} ratio; the time taken for the maximal force to drop to 50% improved by 21.7% in creatine; 18N/ms±3.1, 8N/ms±1.1; 25N/ms±2.9, 16N/ms±1.9.)* Creatine via the reaction ADP+PCATP+Cr may improve calcium handling by maintaining high levels of ATP at the SR calcium pump and the contractile proteins and by preventing a local rise in ADP at these sites. Importantly the increased creatine phosphorylation reaction will lower levels of P_i thus reducing the calcium failure due to the ppt of insoluble calcium phosphate in the SR.