Altered Ca^{2+}-handling in human skeletal muscle to alleviate Ca^{2+}-induced damage in the days associated with delayed onset muscle soreness

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High-force eccentric exercise results in sustained increases in the Ca^{2+} levels in the cytoplasm ($[Ca^{2+}]_{cyto}$), which potentially may cause damage to the muscle. The muscle has been observed to form vacuoles which remained in contact with the plasmalemma post-eccentric contraction, in mouse studies (Yeung *et al.*, 2002). The plasmalemma of skeletal muscle mostly consists of tubules that are invaginations of the outer membrane. This membrane network inside the fibres is commonly referred to as the tubular (t-) system. Three-dimensional reconstruction of the human muscle fibre t-system showed regular, transverse tubules and series of longitudinal tubules that often join transverse tubules across misregistered sarcomeres. Longitudinal tubules were prevalent at the periphery of the fibre. A heavy-load strength training bout caused the loss of the predominantly transverse organisation of the t-system and an increase in the propensity of the longitudinal tubules to form a series of large vacuoles across adjacent sarcomeres. Acute application of high $[Ca^{2+}]_{cyto}$ could also induce vacuolation. The transverse tubules and vacuoles displayed distinct Ca^{2+}-handling properties. Both components of the t-system could take up Ca^{2+} from the cytoplasm but only transverse tubules supported store-operated Ca^{2+} entry (SOCE) during Ca^{2+} release. The retention of significant volumes of Ca^{2+} within vacuoles during SOCE provides an effective buffer of $[Ca^{2+}]_{cyto}$ to reduce the total content of Ca^{2+} within the fibre. These results indicate that the human muscle t-system can alter its structure to change its Ca^{2+} handling properties. We propose this ability can reduce or limit resistance exercise-induced, Ca^{2+}-dependent damage to the fibre by the reduction of $[Ca^{2+}]_{cyto}$ to help maintain fibre viability during the period associated with delayed onset muscle soreness.

Yeung EW, Balnave CD, Ballard HJ, Bourreau J-P & Allen DG (2002). Development of T-tubular vacuoles in eccentrically damaged mouse muscle fibres. *J Physiol* **540**, 581-592.