A single bout of high intensity interval training reduces the autophagosome content in type I and type II muscle fibres

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Autophagy is a dynamic intracellular recycling process which can dismantle old or damaged organelles and provide substrate for protein synthesis and energy metabolism. Autophagy is activated during periods of energetic imbalance and the activation of autophagy in skeletal muscle following exercise has been linked to endurance training adaptations (Lira *et al.*, 2013) and related improvements in glucose homeostasis (He *et al.*, 2012). The aim of this study was to investigate the fibre type specific autophagy response to an acute bout of moderate intensity continuous (MICT) and high intensity interval training (HIT) in human skeletal muscle.

Eight recreationally active individuals (aged 25±6 years, BMI 24.8±1.0 $kg.min^{-2}$, VO_{2max} 48.4±4.0 $ml.min^{-1}.kg^{-1}$) completed two exercise bouts on a cycle ergometer following an overnight fast. The trial order was randomised and separated by ≥7 days. HIT sessions involved 5 x 4 min bouts performed at 75% peak power output whereas MICT was performed at 50% of peak power output, and matched to the HIT session for total work. Muscle biopsies were collected prior to exercise, immediately post-exercise and 3 h post-exercise. Single muscle fibres were isolated and muscle fibre type was assessed using immunoblotting. Single muscle fibres of the same fibre type were pooled before analysis of the autophagy marker LC3-I/II. The content and localisation of LC3-I/II was further investigated in membrane, cytosolic and myofibrillar enriched fractions. Additional autophagy markers (GABARAP and p62) and upstream signalling pathways were analysed by immunoblotting in whole muscle.

LC3-II abundance, which is indicative of autophagosome content, tended to be higher in type I muscle fibres in the basal state (P=0.09). There was no significant change in LC3-II abundance in response to MICT immediately or 3 hours post-exercise. In contrast, there was a reduction in LC3-II abundance in type I (P=0.06) and type II muscle fibres (P=0.02) immediately post-HIT which returned to baseline values at 3 hours post-exercise. There were no changes in LC3-I content and no significant differences in GABARAP or p62 abundance following either exercise mode ($P > 0.05$). Approximately 80% of the total LC3-I pool was in the cytosolic fraction whereas LC3-II was found exclusively in the membrane-enriched fraction.

These results demonstrate that acute exercise can modulate skeletal muscle autophagy in an intensity dependent manner. The enhanced autophagosome clearance may contribute to the superior adaptations of skeletal muscle previously observed with HIT. Furthermore, this study shows that the lipidation of LC3 determines its localisation to the membrane fraction, indicative of its presence on the autophagosomal membrane.

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Lira VA, Okutsu M, Zhang M, Greene NP, Laker RC, Breen DS, Hoehn KL, Yan Z. (2013) Autophagy is required for exercise training-induced skeletal muscle adaptation and improvement of physical performance. *FASEB J* **27**:4184-4193.