Does antioxidant supplementation reduce skeletal muscle mitochondrial biogenesis?

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Mitochondria are the primary controllers of cellular metabolism and the mitochondrial content within the cell is a balance between mitochondrial biogenesis (synthesis) and its degradation *via* mitophagy (Yan *et al.*, 2012). Endurance exercise potently stimulates increases in skeletal muscle mitochondrial content and the increased mitochondrial biogenesis following endurance training is largely attributed to the cumulative effects of each acute bout of exercise (Perry *et al.*, 2010).

Reactive oxygen species (ROS) are produced during skeletal muscle contraction (Bailey *et al.*, 2007) and have a regulatory role in the adaptations of skeletal muscle to endurance training such as increased mitochondrial biogenesis and improved antioxidant defences (Silveira *et al.*, 2006; Irrcher *et al.*, 2009). However, there is controversy in the literature regarding whether or not oral antioxidant supplementation can prevent the adaptive response of skeletal muscle to endurance training by attenuating ROS (Gomez-Cabrera *et al.*, 2008; Ristow *et al.*, 2009; Yfanti *et al.*, 2010; Holloszy *et al.*, 2012; Paulsen *et al.*, 2014). Research on the impact of antioxidants on exercise-induced mitochondrial biogenesis have used vitamins C and E (alone or in combination), coenzyme Q10, N-acetylcysteine, resveratrol, β-carotene and α-lipoic acid in rats and humans (Mankowski *et al.*, 2015). However the findings are mixed and depend on the species, the type of antioxidant and the dosage used.

Vitamins C and E are the most prevalent supplements, with approximately 20% of the population reported to use vitamin C and/or E (Rock *et al.*, 2004). A recent study by Paulsen *et al.* reported that some favourable cellular responses to endurance training are blunted by daily supplementation with combined 1g vitamin C and 260IU vitamin E (Paulsen *et al.*, 2014). Whether this extends to commonly used markers of mitochondrial content, such as citrate synthase activity and also to antioxidant enzyme activity has been unclear. Therefore, we conducted a double-blinded, placebo-controlled randomized control trial in eleven healthy young males. Vitamin C (2×500mg/day) and E (400IU/day) supplementation did not attenuate skeletal muscle oxidative stress or the increase in gene expression of mitochondrial biogenesis markers following acute exercise in healthy young males (Wadley *et al.* unpublished observations). However, vitamin C and E supplementation did attenuate some of the cellular adaptations in skeletal muscle following four weeks of endurance training, such as the increased protein abundance of mitochondrial transcription factor A and enzymatic activity of superoxide dismutase ($P<0.05$, Wadley *et al.* unpublished observations). Nevertheless, most of the skeletal muscle adaptations related to oxidative capacity such as citrate synthase activity and the whole-body adaptations to endurance training such as maximal oxygen uptake were not hampered by vitamin C and E supplementation (Wadley *et al.* unpublished observations). In summary, evidence from our own group and others (Paulsen *et al.*, 2014) supports the hypothesis that 1 g/day vitamin C and >260IU/day vitamin E can hamper some of the cellular processes involved in increased mitochondrial biogenesis and antioxidant defences following endurance training in human skeletal muscle. However, there is no compelling evidence that these antioxidants impair skeletal muscle mitochondrial content or endurance performance in humans.

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