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Whole-body and muscle responses to aerobic exercise training and withdrawal in ageing and COPD

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Muscle mitochondrial function is not impaired in age or COPD. Whole-body and mitochondrial exercise training adaptations are robust in young, evident in older and deficient in COPD. COPD adaptation may require high-intensity exercise training programmes. https://bit.ly/3oe0k0S

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Abstract

Background Chronic obstructive pulmonary disease (COPD) patients exhibit lower peak oxygen uptake (V'_{O_2peak}), altered muscle metabolism and impaired exercise tolerance compared with age-matched controls. Whether these traits reflect muscle-level deconditioning (impacted by ventilatory constraints) and/or dysfunction in mitochondrial ATP production capacity is debated. By studying aerobic exercise training (AET) at a matched relative intensity and subsequent exercise withdrawal period we aimed to elucidate the whole-body and muscle mitochondrial responsiveness of healthy young (HY), healthy older (HO) and COPD volunteers to whole-body exercise.

Methods HY (n=10), HO (n=10) and COPD (n=20) volunteers were studied before and after 8 weeks of AET (65% V'_{O_2peak}) and after 4 weeks of exercise withdrawal. V'_{O_2peak}, muscle maximal mitochondrial ATP production rate (MAPR), mitochondrial content, mitochondrial DNA (mtDNA) copy number and abundance of 59 targeted fuel metabolism mRNAs were determined at all time-points.

Results Muscle MAPR (normalised for mitochondrial content) was not different for any substrate combination in HO, HY and COPD at baseline, but mtDNA copy number relative to a nuclear-encoded housekeeping gene (mean±SD) was greater in HY (804±67) than in HO (631±69; p=0.041). AET increased V'_{O_2peak} in HO (17%; p=0.002) and HY (21%; p<0.001), but not COPD (p=0.603). Muscle MAPR for palmitate increased with training in HO (57%; p=0.041) and HY (56%; p=0.003), and decreased with exercise withdrawal in HO (−45%; p=0.036) and HY (−30%; p=0.016), but was unchanged in COPD (p=0.594). mtDNA copy number increased with AET in HY (66%; p=0.001), but not HO (p=0.081) or COPD (p=0.132). The observed changes in muscle mRNA abundance were similar in all groups after AET and exercise withdrawal.

Conclusions Intrinsic mitochondrial function was not impaired by ageing or COPD in the untrained state. Whole-body and muscle mitochondrial responses to AET were robust in HY, evident in HO, but deficient in COPD. All groups showed robust muscle mRNA responses. Higher relative exercise intensities during whole-body training may be needed to maximise whole-body and muscle mitochondrial adaptation in COPD.