EXERCISE EFFICIENCY AND MITOCHONDRIAL COUPLING IN THE ELDERLY

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INTRODUCTION

Low locomotory efficiency has been found to have important impact on activities of daily living of the elderly. A difference of 30% in the energetic cost of walking has been found between young and elderly subjects and suggests that muscle energetic changes are a major contributor to age-related inefficiency of locomotion. A change in contractile efficiency is the conventional explanation for differences in exercise efficiency, but elderly muscle has a greater content of the more efficient type I fibers than younger muscle and therefore would be expected to become more efficient - not less. Thus a shift in muscle fiber type does not explain reduced exercise efficiency in elderly subjects.

A role of mitochondria in exercise efficiency comes from Whipp and Wasserman’s evaluation of the cascade of efficiencies that underlie exercise. Their analysis revealed that contractile (0.5) and mitochondrial (0.6) efficiencies contributed equally to cycling efficiency (so-called delta efficiency, 0.3) in human quadriceps (i.e., 0.3 = 0.5 x 0.6). The lower mitochondrial coupling efficiency evident in elderly muscle of humans and animals would therefore have the potential to reduce the power output per O2 in exercising elderly. Thus, the mitochondrial uncoupling found with age in humans is a likely contributor to the reduced exercise efficiency of elderly subjects.

To evaluate the contribution of contractile and mitochondrial coupling efficiency to exercise efficiency, we determined the underlying efficiencies in adult and elderly subjects. First, we determined exercise efficiency (i.e., delta efficiency) from oxygen uptake and power output measured on the cycle ergometer. Second, we used a simple method to estimate contractile efficiency of the quadriceps in vivo. Third, we determined mitochondrial coupling efficiency using a combination of in vivo and biopsy determinations.

Oxygen consumption on a cycle ergometer was evaluated in 9 adult (mean: 38.8 yrs) and 39 elderly subjects (mean: 68.8 yrs), revealing a decline in exercise efficiency (delta efficiency, εd) from 0.27±0.01 (mean+SEM) to 0.22±0.01 between age groups (Figure 1). Contractile-coupling efficiency (εC) determined from leg power output at VO2max and ATP generation determined from magnetic resonance spectroscopy yielded values in adults (0.50±0.05) and elderly (0.58±0.04) in agreement with independent measures. Mitochondrial coupling efficiency (εM) was determined from εd/εC to yield values reflective of well-coupled mitochondria (0.58±0.08) in adults, but indicative of significant uncoupling in the elderly (0.44±0.03). These εM values were confirmed in measurements from muscle biopsy material from these subjects (adult: 0.57±0.08; elderly: 0.41±0.03) consistent with uncoupling as the basis of the mitochondrial dysfunction in these elderly. Thus, reduced mitochondrial efficiency (εM) is a key part of the exercise inefficiency found in the elderly subjects and may be an important part of the loss of exercise performance with age. The new insight from this analysis is the role of mitochondrial efficiency in the decline in exercise efficiency in the elderly.

REVERSAL OF MITO DYSFUNCTION IMPROVES EXERCISE PERFORMANCE IN ELDERLY.

Recent studies suggest that mitochondrial uncoupling may improve with an endurance training program based on the increase in coupling reported
in isolated mitochondria in young subjects \(^{11}\). To evaluate the impact of exercise training, 39 male and female subjects (69.2 ± 0.6 yr) were divided into groups for a 6-month program of no training, endurance training (ET) or resistance training (RT). Only ET elevated the oxidative phosphorylation capacity in vivo (\(\text{ATP}_{\text{max}}\)). Improved mitochondrial function was evident from muscle biopsies based on the greater \(\text{ATP}_{\text{max}}\) per mitochondrial content (\(\text{ATP}_{\text{max}}/V_{\text{f}}\)). No change in muscle fiber type was found \(^{12}\). These results suggest that reduced mitochondrial functional capacity (low \(\text{ATP}_{\text{max}}/V_{\text{f}}\), consistent with uncoupling of ATP from \(O_{2}\) uptake) can be reversed.

Our second question was whether improved \(\text{ATP}_{\text{max}}/V_{\text{f}}\) elevated exercise efficiency and the coupling of power output of the legs, \(P_{\text{max}}\), to \(V_{\text{O}2\text{max}}\) to improve exercise performance. Again, ET alone significantly improved delta efficiency (\(\varepsilon_{\text{D}}\), \(\Delta^2\%\)) as well as \(P_{\text{max}}\) (17%) without a significant change in \(V_{\text{O}2\text{max}}\). This rise in \(P_{\text{max}}\) per \(V_{\text{O}2\text{max}}\) paralleled the greater mitochondrial coupling (\(\text{ATP}_{\text{max}}/V_{\text{f}}\)) in the vastus lateralis in these subjects with ET (Figure 2). This association suggests that improved coupling of leg power output per \(V_{\text{O}2}\) both during exercise (\(\varepsilon_{\text{D}}\)) and at the aerobic limit \(\Delta(P_{\text{max}}/V_{\text{O}2\text{max}})\) reflects an elevation in mitochondrial coupling, as evidenced by \(\Delta(\text{ATP}_{\text{max}}/V_{\text{f}})\) in the vastus lateralis. Thus, a substantial increase in exercise performance as measured by greater leg power output per \(V_{\text{O}2\text{max}}\) in the elderly resulted from improvements in mitochondrial coupling efficiency after ET. These results demonstrate that mitochondrial uncoupling plays an important role in the reduced exercise efficiency with age and that the reversal of this uncoupling with ET can raise exercise performance that was lost with age in these elderly subjects.

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Figure 2. Improved exercise (\(\Delta(P_{\text{max}}/V_{\text{O}2\text{max}})\)) and mitochondrial coupling (\(\Delta(\text{ATP}_{\text{max}}/V_{\text{f}})\)) in the ET group (Jubrias et al., 2001). *P<0.05.