The effects of normobaric hypoxia on mitochondrial function in humans

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Introduction In response to stays at high altitude, contrasting mitochondrial changes have been reported. Mountaineers participating in extreme-altitude expeditions have an ~25% decrease in mitochondrial volume (Hoppeler *et al.*, 1990). In contrast, when the hypoxic exposure is limited to lower altitudes, there is no significant change in Citrate Synthase (CS) activity (Green *et al.*, 2000). However, it is difficult to know whether these contradictory findings can be attributed to different levels of hypoxia *per se*, and/or the accompanying changes in physical activity and nutrition. The purpose of this study was to investigate the effects of 15 days of normobaric hypoxia on mitochondrial content and function in humans when both physical activity and nutrition are tightly controlled.

Methods Eight untrained men lived in an altitude laboratory (3200 m), 24 h/day, for 15 consecutive days. Muscle biopsies were taken from the *vastus lateralis* muscle before and immediately following the stay. Mitochondrial respiration was determined on permeabilized muscle fibres. Both daily physical activity and caloric intake were monitored before entering the altitude laboratory, and were subsequently maintained at these levels for the duration of the stay. Gene and protein expression level, and CS activity was analyzed using biopsied muscle sample.

Results For most participants, 15 days of exposure to moderate hypoxia did not alter markers of mitochondrial volume (*i.e.* CS activity) or function (*i.e.* mitochondrial respiration), or genes and proteins associated with mitochondrial biogenesis. However, we report for the first time that some individuals had an increase in mitochondrial respiration, and these same individuals had a concomitant increase in both PGC-1α and p53 protein content.

Discussion The unchanged mitochondrial respiration, CS activity and mitochondrial respiratory complexes protein level could be due to the level of hypoxic stimulus and the length of exposure. Consistent with previous research (Levitt *et al.*, 2012), we observed considerable individual variation for changes in protein content following exposure to hypoxia. Our result suggested that the individual response to moderate hypoxia is characterized by a coordinated increase in mitochondrial respiration and protein content of both PGC-1α and p53.

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