



#### **A single session of high intensity interval exercise in hypoxia modulates changes in mitochondrial biogenesis related gene and protein in human skeletal muscle**

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Both high intensity interval exercise (HIIE) and hypoxia have been known as powerful inducers of mitochondrial biogenesis. But limited literature explored whether HIIE and hypoxia have synergistic effects on markers of mitochondrial biogenesis when combined. Methods: A total of ten healthy males (aged 18-37) completed three randomise HIIE sessions, two (one matched for absolute intensity, NA; and one matched for relative intensity, NR) in normoxia (Fraction of oxygen,  $FiO_2 = 0.21$ ) and one in hypoxia (HY,  $FiO_2 = 0.14$ , corresponding to a simulated altitude of ~3200m) condition. Skeletal muscle samples were collected before, immediately post, 3 hours and 24 hours post exercise.

Results: According to our previous study (Li, J., et al. (2020).), we hypothesis PGC-1 $\alpha$ , HIF-1 $\alpha$  and VEGF will be the main genes modulated by HIIE in hypoxia. The mitochondrial biogenesis genes PGC-1 $\alpha$ , and the isoforms PGC-1 $\alpha$ 1 and PGC-1 $\alpha$ 4 all have significant increase at 3h post HIIE in HY and NR ( $P < 0.01$  for all), but not in NA. However, the relative expression under HY and NR did not show any difference. The hypoxia sensitive genes HIF-1 $\alpha$  and VEGF at 3h post both increased in HY and NR in comparison to baseline, but not NA. Furthermore, HIF-1 $\alpha$  stayed in high level at 24h post HIIE in HY ( $P < 0.05$  for all), and the fold changes of HIF-1 $\alpha$  mRNA 24 post HIIE in HY is significantly higher than in NR ( $P = 0.02$ ). VEGF mRNA level in NR is significantly higher than in NA ( $P = 0.03$ ). PGC-1  $\alpha$  protein showed increase immediately post HIIE when compared with baseline in NR ( $P = 0.008$ ). And all other timepoints did not show any significant difference. No differences of fold changes were observed between three conditions in any timepoints. HIF-1 $\alpha$  and VEGF did not show differences at any timepoints in all conditions.

Conclusion: A single session of HIIE combined with hypoxia was sufficient to enhance the gene expression of markers of mitochondrial biogenesis and PGC-1 $\alpha$  protein. However, HIIE in hypoxia (HY) does not show synergistic effects on mitochondrial biogenesis more than NR. We believe that HIIE matched for absolute and relative intensity in normoxia (NR) led to distinct adaptations on mitochondrial biogenesis in human skeletal muscle.