Effects of Normobaric and Hypobaric Hypoxia on Mitochondrial Related Gene Expression

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ABSTRACT

Environmental stimuli such as temperature and hypoxia can influence cellular signaling in the skeletal muscle. Previously we have reported no changes in gene expression related to mitochondrial development with acute exposure to normobaric hypoxia. However, exposure to hypobaric hypoxia may elicit different physiological responses. **Purpose:** To determine the response of skeletal muscle mitochondrial related gene expression after 4 h of exposure to normobaric normoxia (NN), normobaric hypoxia (NH), and hypobaric hypoxia (HH) after exercise. **Methods:** Recreationally trained participants (8 male, 7 female) each completed three trials of 1-h cycling at 70% of W_{max}. Following exercise, participants sat in an environmentally controlled chamber for a 4-h recovery period in NN (975 m), NH (4,420 m), or HH (4,420 m) environmental conditions. Muscle biopsies were taken from the *vastus lateralis* pre-exercise and after a 4-h environmental exposure period. Samples were analyzed using qRT-PCR to assess gene expression related to mitochondrial development. **Results:** There were no differences in mRNA between trials or times in PGC-1α ($p = 0.804$), GABPA ($p = 0.650$), ERRα ($p = 0.956$), or NRF1 (0.563). TFAM mRNA increased in NH from pre-exercise to post-exercise ($p = 0.036$) and NH was higher compared to NN ($p = 0.011$) and but not HH ($p = 0.053$). **Conclusion:** These data indicate that gene expression related to mitochondrial development is only marginally affected (TFAM) by the type of hypoxic environment after a 4-h treatment despite differences in arterial oxygen saturation.

INTRODUCTION

- Normobaric and hypobaric hypoxia and are both used in laboratory settings with the assumption that both have similar physiological effects.
- Hypoxic conditions are known to cause decreased muscle mass and decreased mitochondrial function.
- It is not known if mitochondrial gene expression of the skeletal muscle is altered between different modes of hypoxia.
- The purpose of this study was to determine if recovery in normobaric hypoxia and hypobaric hypoxia alter gene expression associated with mitochondrial biogenesis compared to that of normobaric normoxia.

METHODS

- Fifteen recreationally trained participants (8 male, 7 female) each completed three experimental trials in a randomized, counterbalanced order.
- Subjects cycled for 1 h on an electronically braked cycle ergometer (Velotron, Racermate Inc., Seattle, WA) at approximately 70% of work rate associated with VO_{2peak} followed by 4 h of supine recovery.
- The recovery took place in either an altitu de tube to simulate hypobaric hypoxia (HH, 4,420 m; Engineering Innovations, LLC, Littleton, CO), an environmental chamber to simulate normobaric hypoxia (NH, 4,420 m; Tescor, Warminister, PA), or in ambient conditions for normobaric normoxia (NN, 975 m).
- A pulse oximeter (Nonin, Plymouth, MN) was used to assess blood oxygen saturation (SaO_2) during the trial.
- Muscle biopsies were taken from the *vastus lateralis* pre-exercise and 4 h post-exercise.
- Gene expression analysis was performed with qRT-PCR.

RESULTS

Table 1. SaO_2 (%) during each hour of recovery in NN, NH, and HH

Hour	1	2	3	4
NN	96.4 ± 0.3	96.3 ± 0.4	96.5 ± 0.3	96.1 ± 0.4
NH	79.8 ± 1.3*	77.3 ± 1.2*	79.9 ± 1.0*	79.8 ± 1.2*
HH	75.6 ± 1.5*†	77.1 ± 1.5*	77.1 ± 1.1*†	76.2 ± 1.0*†

Data are mean ± SE. * $p < 0.05$ from NN. † $p < 0.05$ from NH.

RESULTS

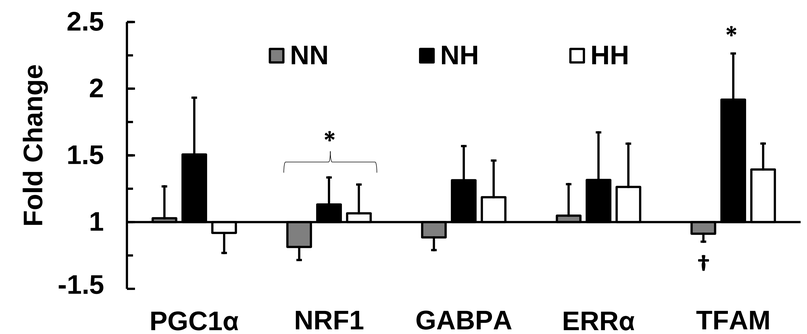

Figure 1. Gene expression after 4 h recovery. $p < 0.05$ from pre-exercise. † $p < 0.05$ from other trials. PGC-1α, Peroxisome proliferator-activated receptor gamma coactivator 1 alpha; GABPA, GA-binding protein alpha chain; ERRα, Estrogen related receptor alpha; TFAM, Mitochondrial transcription factor A. Data are mean ± SE.

Table 2. Participant descriptive data

Age (y)	Height (cm)	Weight (kg)	Body Fat (%)	VO_2 peak ($L \cdot min^{-1}$)	Power at VO_{2peak} (W)
24 ± 4	178 ± 12	72.5 ± 13.8	14.5 ± 6.8	3.60 ± 0.83	274 ± 72

Data are mean ± SE.

CONCLUSIONS

- Despite differences in SaO_2 during the 4 h recovery period, only TFAM mRNA was increased in hypoxia.
- PGC-1α, GABPA, ERRα, and TFAM mRNA were not affected by exercise or hypoxia. NRF1 mRNA increased from pre-exercise.
- Further work is needed to determine the impact of long term hypoxia exposure on transcriptional responses related to mitochondrial biogenesis.
- Funded by Department of Defense United States Army Medical Research and Materiel Command.