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Exposure to hypobaric hypoxia results in higher oxidative stress compared to normobaric hypoxia

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ABSTRACT

Sixteen healthy exercise trained participants underwent the following three, 10-h exposures in a randomized manner: (1) Hypobaric hypoxia (HH; 3450 m terrestrial altitude) (2) Normobaric hypoxia (NH; 3450 m simulated altitude) and (3) Normobaric normoxia (NN). Plasma oxidative stress (malondialdehyde, MDA; advanced oxidation protein products, AOPP) and antioxidant markers (superoxide dismutase, SOD; glutathione peroxidase, GPX; catalase; ferric reducing antioxidant power, FRAP) were measured before and after each exposure. MDA was significantly higher after HH compared to NN condition (+24%). SOD and GPX activities were increased (vs. before; +29% and +54%) while FRAP was decreased (vs. before; −34%) only after 10 h of HH. AOPP significantly increased after 10 h for NH (vs. before; +83%), and HH (vs. before; +99%) whereas it remained stable in NN.

These results provide evidence that prooxidant/antioxidant balance was impaired to a greater degree following acute exposure to terrestrial (HH) vs. simulated altitude (NH) and that the chamber confinement (NN) did likely not explain these differences.

1. Introduction

Exposure of humans to environmental hypoxia can be achieved either by reducing the ambient pressure (hypobaric hypoxia; HH) or by reducing the fraction of inspired oxygen (normobaric hypoxia; NH). It was long thought that the reduction of the partial pressure of inspired O_2 (P_iO_2) was the unique modulator of hypoxia-induced physiological responses. However, a growing body of evidence suggests that the difference in barometric pressure (BP) between HH and NH at the same P_iO_2 may induce different physiological responses regarding ventilation (Loeppky et al., 1997), nitric oxide (NO) metabolism (Hemmingsson and Linnarsson, 2009) and acute mountain sickness (Fulco et al., 2011). Although the underlying mechanisms of the differences between HH and NH are not yet fully understood, it was hypothesized that oxidative stress could be one of the key biological parameters involved in these processes (Millet et al., 2013). In this context, we recently reported higher select plasmatic oxidative stress markers during 24-h exposure to HH (3000 m natural altitude) compared to a simulated NH equivalent to 3000 m altitude in a hypoxic chamber (Faiss et al., 2013). It could, however, be argued that the observed oxidative stress in NH may, at least partially, result from the confinement in the chamber per se. Especially, since no control group that would be submitted to normobaric normoxia (NN) was employed. Accordingly, the aim of this study was to evaluate the effects of different modes of hypoxia (HH & NH) as well as the potential effects of confinement per se on prooxidant/antioxidant balance changes.

2. Methods

2.1. Participants

Sixteen healthy, trained male volunteered for this study (mean ± SD; age 34.7 ± 9.5 years, body weight 75.2 ± 7.2 kg, height 179.7 ± 5.7 cm, peak oxygen consumption (VO_{2max}) 60.2 ± 9.9 ml kg^{-1} min^{-1}). All participants gave written informed consent before participation. They were all non-smokers, and neither acclimatized nor recently exposed to altitude. The subjects were asked

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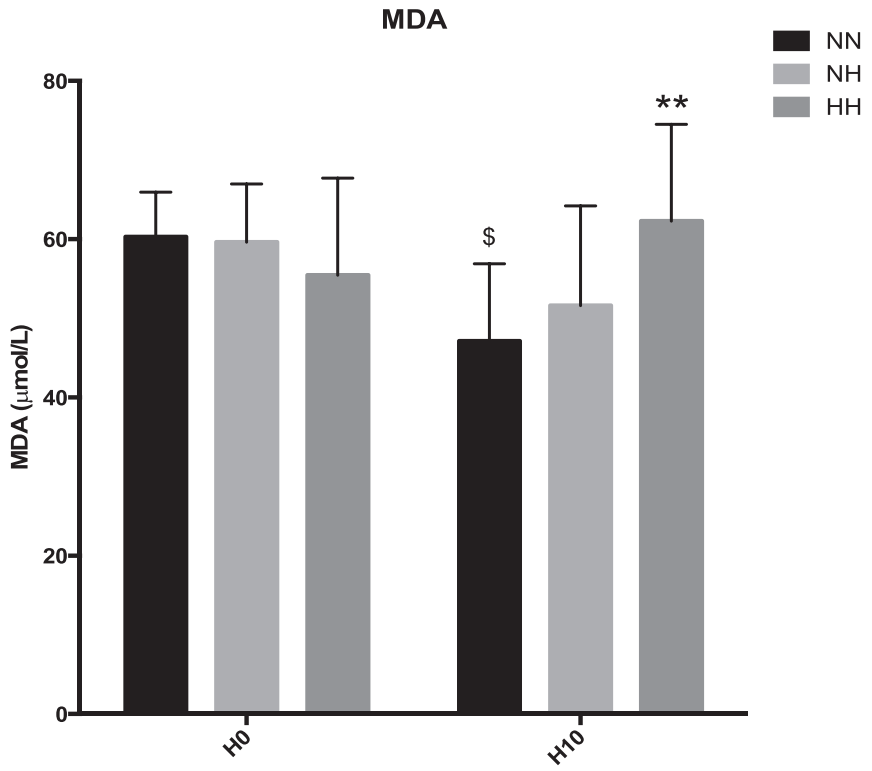

Fig. 1. Plasma concentration of malondialdehyde (MDA) before (H0) and after (H10) in hypobaric hypoxia (HH), normobaric hypoxia (NH) and normobaric normoxia (NN). Data are presented as means ± SD. $^{**}p < 0.01$ significant difference with corresponding NN; $^{\$}p < 0.05$ significant difference with corresponding H10.

Table 1
Environment conditions during the hypobaric hypoxia (HH), normobaric hypoxia (NH) and normobaric normoxia (NN) sessions.

	F_iO_2 (%)	BP (mm Hg)	P_iO_2 (mm Hg)	Temperature (°C)	Humidity (%)
HH (3450 m terrestrial altitude)	20.9	481.5 ± 4.7	90.9 ± 1.0	21.3 ± 0.6	42.8 ± 4.4
NH (3450 m simulated altitude)	13.6	715.8 ± 3.8	91.0 ± 0.6	22.7 ± 0.8	41.0 ± 4.8
NN (485 m terrestrial altitude)	20.9	718.1 ± 3.3	140.5 ± 0.6	23.0 ± 1.0	45.1 ± 8.3

Fraction of inspired oxygen: FiO_2; barometric pressure: BP; partial pressure of inspired oxygen; P_iO_2.

to maintain their usual training and physical activities during the whole experimental protocol to avoid fitness changes between sessions. The schedule and activities were exactly the same for all the conditions. The subjects completed the same diary, which was precisely controlled. The experimental protocol was conducted according to the Declaration of Helsinki and the study was approved by a local Medical Ethics Committee (Commission Cantonale Valaisanne d'Ethique Médicale, CCVEM; Agreement 051/09).

2.2. Experimental design

The experimental design consisted of three testing sessions preceded by a preliminary visit. Each testing session consisted of 10 h of exposure to the designated experimental condition (NN, NH, HH). During the preliminary visit, the participants were familiarized to the laboratory and perform baseline anthropometric and exercise testing. The following three exposure sessions were separated by at least 10 days and were performed in a randomized order. The HH session was performed at Altitude Research Station in Jungfraujoch (3450 m) while the NH and NN exposure sessions were performed in a hypoxic chamber (ATS Altitude, Sydney, Australia) at an altitude of 485 m (Sion, Switzerland) in a blinded manner. The hypoxic chamber is a well-ventilated room (2.4 m × 5.0 m × 2.5 m) with transparent glass panels (Faiss et al., 2013). The time spent in hypoxia was exactly the same for each session because of the very precise schedule. In addition, the progressive increase in altitude to access the Jungfraujoch by train during the HH sessions was simulated during the NH and NN sessions: For 45 min before entering the hypoxic chamber, the subjects breathed either room air (for NN) or hypoxic air (for NH) by using a mask and an Altitrainer.

Temperature inside the chamber was maintained at 22° in average maintained by an internal air conditioning system. The F_iO_2 within the chamber was controlled regularly with an electronic device (GOX 100 oximeter, Greisinger, Regenstauf, Germany). In order to blind participants to either the NH or NN exposure, the system was also running normoxic airflow into the chamber during the NN sessions.

During all sessions, peripheral blood oxygen saturation (SpO_2) was monitored continuously using a finger pulse oxymeter (WristOx2™, Model 3150, Nonin, Nonin Medical, Inc., Minnesota, USA).

The environmental conditions during the exposure sessions were the following are detailed in Table 1.

2.3. Plasma oxidative stress and antioxidants assays

A 5-mL blood sample was obtained at rest from the antecubital vein before (H0) and immediately after the 10 h exposure (H10). After centrifugation, 400 µL aliquots of plasma were frozen and stored at 80 °C until blinded analysis performed less than 6 months after the experiment in the same laboratory.