

# Reduced Cold-induced Vasodilation at altitude: due to hypoxic or hypobaric circumstances?

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## INTRODUCTION

Cold exposure leads to a sympathetically mediated vasoconstrictor response that causes a virtual shutdown of peripheral blood flow. When the skin temperature ( $T_{sk}$ ) remains low for a period of 5-10 min the vasoconstriction may be interrupted by a phase of peripheral vasodilation that leads to an increase in local skin temperature (Lewis 1930, Grant and Bland 1931). It is thought that this Cold Induced Vasodilation (CIVD) response provides an important protective function to maintain tissue integrity and minimize the risk of cold injuries (e.g., Daanen and Van der Struijs 2005). However, upon exposure to prolonged cold and/or altitude exposure, where the risk of cold injury is highest, the CIVD reaction and magnitude is often reduced (Daanen et al., 1997; Daanen and Ducharme, 1999, Daanen and Van Ruiten, 2000; Felicijan et al., 2008; Mathew et al., 1977; Takeoka et al., 1993). However, despite the increased risk of cold injury at altitude surprisingly little research has been undertaken into the effect of altitude on the CIVD response. Daanen and Van Ruiten (2000) controlled for ambient temperature and still observed a decrease in the CIVD response at altitude compared to sea-level. These data provide evidence that hypobaric hypoxic circumstances may impair the CIVD response independently of thermal effects. The main physiological stressors of a hypobaric environment are: (1) a reduced partial pressure of oxygen, and subsequent tissue hypoxia and; (2) a dominant effect of negative pressure on the body (Conkin 2008). It has not been determined whether the reduced CIVD response at altitude is attributable to hypoxia alone or whether the lower atmospheric pressure contributes. Whilst hypoxia leads to vasodilation in the skin, skeletal muscle, cerebral and splanchnic regions of the body a vasoconstriction response usually occurs in the fingers and toes (Blauw et al 1995, Crawford et al 2009, Golja et al 2002). Consequently, the reduced CIVD at altitude may be attributable to hypoxia. No studies have assessed the affect of hypobaria *per se* on the CIVD response. Thus, the purpose of this study is to systematically evaluate the affect of hypoxia, hypobaria and their interaction on the CIVD response.

## METHODS

### *Subjects*

Nine healthy, well-trained male subjects participated in the experiment. Their physical characteristics were: (mean  $\pm$  SD) body mass  $77.8 \pm 6.7$  kg, stature  $185 \pm 0.1$  cm, age  $25.2 \pm 2.9$  yr,  $VO_{2max}$   $57.2 \pm 4.9$  ml $\cdot$ kg $\cdot$ min $^{-1}$ . The subjects signed an informed consent prior to the experiment. The experiment was approved by the independent Medical Ethical Commission of Tilburg University. The subjects did not perform strenuous exercise 24 hours prior to the experiment.

### *Experimental conditions*

Subjects undertook a familiarisation trial in a normobaric normoxic environment prior to the first experiment. At intervals, of at least 70hr, subjects visited the laboratory, at the same time of day, on four separate occasions and undertook a test to evaluate their CIVD response in each of the following four experimental conditions: normobaric normoxia (NN), normobaric hypoxia (NH), hypobaric (11000 ft) normoxia (HN) and hypobaric hypoxia (HH). Table 1 presents an overview of the experimental conditions.

**Table 1.** Experimental conditions

Condition	Abbreviation	Oxygen (%)	Simulated Altitude (m)
Normobaric normoxia	NN	21	0
Normobaric hypoxia	NH	14	0
Hypobaric normoxia	HN	21	3353
Hypobaric hypoxia	HH	14	3353

To avoid any order effects, subjects undertook each experimental trial in a balanced order. All experiments were done at room temperature (about 22°C).

### *Protocol*

During each trial subjects dressed in underwear, T-shirt, shorts, combat suit, socks and sport shoes and were seated on a comfortable chair. Each trial comprised a 20 min control period, where subjects became accustomed to the ambient temperature and pressure conditions, followed by a CIVD test. During the control period subjects inspired the specified mixed gases in the NH and HN trials and room air in the NN and HN trials.. Hereafter, the CIVD test was started. The CIVD test consisted of immersing the middle finger of the right hand in 5°C water for 30 minutes. During the CIVD test subjects wore a neoprene glove with the middle finger cut off at the base to ensure that only the middle finger was cooled. Previous experiments showed no significant differences between the fingers in CIVD response (Van der Struijs et al., 2008).

### *Conditions*

The hypobaric measurements were performed in a hypobaric chamber pressurized to a simulated altitude of 3353 m; all other measurements were performed in a climatic chamber at 22°C. In each condition subjects wore a facelet which was open in the NN and HH trials. During the NH trials the facelet was connected to a mixed gas and subjects breathed a hypoxic gas mixture containing 14% O<sub>2</sub> (PI, O<sub>2</sub> = 0.08 ATA). During the HN trial subjects breathed, via the facelet, a mixed gas containing 31.8% O<sub>2</sub>.

### Measurements

Finger skin temperature was determined using small thermistors (ITC limited, Tokyo, Japan) connected to a Mobi8 reading unit ([www.tmsi.com](http://www.tmsi.com), Oldenzaal, The Netherlands). The sensors were taped to the finger using water permeable tape. A rectal probe (YSI 701, Yellow Springs, USA) was inserted at least 12 cm beyond the sphincter prior to the test. Mean skin temperature was determined using i-buttons (Marken Lichtenbelt et al., 2006) on the shin, shoulder, left hand and neck according to ISO 9886. Finger skin temperature and rectal temperature was measured each second, skin temperatures were measured every 15 seconds. Systolic and diastolic blood pressure (Omron MX3) were measured throughout the experiment.

### Statistics

The effect of each condition was determined via a within subject repeated measures study. All statistical analysis was performed in Statistica (Statsoft, 2009). A two way (hypobaric/hypoxia) analysis of variance (ANOVA) was used to determine whether there were any significant, main or interactive, effect on skin temperatures, prior to and during the CIVD test. All results are presented as mean  $\pm$  standard deviation. Significance is accepted at  $P < 0.05$ .

### RESULTS

The mean finger  $T_{sk}$  was not different between conditions prior to the CIVD test. Mean values corresponded to (NN)  $31.6 \pm 0.5$ ; (NH)  $30.9 \pm 0.7$ ; (HN)  $28.4 \pm 1.6$ ; (HH)  $30.3 \pm 1.0$ . Data recorded during the CIVD test are presented in Table 2. During the CIVD test, neither the onset time, minimum or peak finger  $T_{sk}$  were affected by hypoxia or hypobaric. Mean finger temperature during 30 min immersion in cold water was not different between any condition. ANOVA showed a significant effect of hypoxic, but not hypobaric circumstances on the amplitude of the CIVD response. The amplitude was reduced with hypoxia by  $1^\circ\text{C}$ . Rectal temperature, mean skin temperature and blood pressure during the CIVD test did not differ between the conditions (Table 2).

**Table 2.** Temperature response and blood pressure during cold water immersion under different conditions

	Normobaric normoxia (NN)	Normobaric hypoxia (NH)	Hypobaric normoxia (HN)	Hypobaric hypoxia (HH)
CIVD onset (min)	$6.3 \pm 0.3$	$6.2 \pm 0.4$	$7.4 \pm 0.8$	$6.4 \pm 0.3$
Minimum $T_{fi}$ ( $^\circ\text{C}$ )	$7.9 \pm 0.2$	$8.1 \pm 0.6$	$7.3 \pm 0.5$	$7.9 \pm 0.5$
Peak $T_{fi}$ ( $^\circ\text{C}$ )	$16.6 \pm 1.2$	$15.4 \pm 1.2$	$15.5 \pm 0.9$	$15.4 \pm 0.7$
Amplitude $T_{fi}$ ( $^\circ\text{C}$ )*	$8.6 \pm 1.1$	$7.3 \pm 1.1$	$8.2 \pm 0.7$	$7.5 \pm 0.8$
Mean $T_{fi}$ ( $^\circ\text{C}$ )	$12.0 \pm 0.5$	$11.1 \pm 0.6$	$11.5 \pm 0.8$	$11.5 \pm 0.6$
Rectal ( $^\circ\text{C}$ )	$37.7 \pm 0.3$	$37.5 \pm 0.4$	$37.5 \pm 0.4$	$37.7 \pm 0.4$
Mean skin ( $^\circ\text{C}$ )	$33.5 \pm 0.7$	$33.8 \pm 0.6$	$33.4 \pm 0.8$	$33.8 \pm 0.6$
$P_{syst}$ (mm Hg)	$116 \pm 8$	$116 \pm 10$	$119 \pm 12$	$120 \pm 9$
$P_{diastol}$ (mm Hg)	$68 \pm 9$	$72 \pm 8$	$74 \pm 6$	$74 \pm 11$

Values are presented as mean  $\pm$  SD. Mean finger skin temperature during cold water immersion is determined from minute 5 to 30.  $T_{fi}$  = finger skin temperature;  $P_{syst}$  = systolic blood pressure;  $P_{diastol}$  = diastolic blood pressure; \* = significantly different between normoxia and hypoxia.

## CONCLUSIONS

The main finding of this study is that in hypoxic conditions the amplitude of the CIVD response is reduced. Hypobaric conditions *per se* do not have any effect on the CIVD response in healthy well trained subjects.

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