Original Article

Effect of hypoxia on modulation of pressor responses to isometric handgrip with low atmospheric pressure

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ABSTRACT

Heart Rate (HR) and Blood Presure (BP) responses during sustained isometric contractions (at 30% MVC) were measured in Normoxic Normobaria (NN) and after 30 min of exposure to Hypoxic Hypobaria (HH - air at 15,000' simulated altitude) and Non-Hypoxic Hypobaria (NH -60-70% of oxygen at 15,000 ft) in healthy, male, human volunteers. Heart Rate Variability (HRV) indices were derived from ECG recordings of 2 min duration in resting sitting and during second to fourth min of handgrip in all the three conditions. Results were analyzed using ANOVA with Greenhouse Geisser correction. Individual comparisons were made using Least Significance Difference (LSD) test. HR, DBP and PP exhibited a significant main effect of both atmospheric pressure (p=3.27E-04 for HR; p=0.031 for DBP and p=0.060 for PP) and isometric contraction (p=1.19E-07 for HR; p=2.61E-10 for DBP and p=0.020 for PP). The attenuation in blood pressure was comparable in both hypoxic and non-hypoxic hypobaria. Changes in HR were opposite in HH and NH with a significant increase in the former and decrease in the latter. Arterial saturation was significantly less in hypoxic hypobaria compared to either normoxic normobaria (p= 0.00E+00) or non-hypoxic hypobaria (p=1.48E-18). Amongst the HRV indices, only high frequency (HF, 0.15-0.50 Hz) power showed a significant main effect of handgrip (p=0.008) with a decrease during contraction. In view of a comparable attenuation of pressor responses to handgrip in hypoxic and non-hypoxic hypobaria, the effect was attributed to low atmospheric pressure rather than alveolar oxygen tension. The effect was uniformly present on BP in resting sitting and during handgrip as apparent from an insignificant interaction effects. Comparable decrease in HF power in HRV in all the three conditions was corroboratory to it. It could be concluded that low atmospheric pressure attenuates blood pressure and the effect is not mediated through hypoxia.

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Key words: Hypoxia, Non-hypoxic hypobaria, Heart Rate Variability, Handgrip Test.

Introduction

Earlier studies [1,2] have demonstrated a significant attenuation of pressor responses to isometric muscle contraction (in the form of handgrip) during exposure of human volunteers to non-hypoxic hypobaria (breathing ~60-70% oxygen-air mixture while decompressed to 429 mm Hg, equivalent to 15,000 ft). Fitting the effect into physiological model, proposed by Burton [3] for predicting group tolerance to positive acceleration, authors conceived it to be relevant in operational terms as it could reduce the efficacy of Anti-G Straining Maneuver (AGSM) by ~50 mm Hg.

However, the mechanisms involved in attenuating pressor responses to isometric contraction during exposure to non-hypoxic hypobaria are poorly understood. The attenuation could not be ascribed to mild hyperoxia (rather than strict normoxia) or variation in ambient temperature in these experiments. Merely by exclusion, and not with any direct evidence, the effect was attributed to changes in baroreceptor loading [4] consequent upon a change in atmospheric pressure. Such a loading should also result into deceleration of heart rate and vasodilatation. The latter is actually seen

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during acute hypoxic exposure [5]. However, it is attributed to a '*functional sympatholysis*' which is traditionally conjectured to be mediated through the effect of local metabolites [6]. In view of the above, to further probe into the mechanisms involved, the present study examined if the above attenuation is modulated with/without hypoxia in a comparable hypobaric environment.

Material and Methods

Subjects & Protocol

18 healthy male volunteers, in the age of 20-40 years served as subjects. Female subjects and individuals with middle ear disease, Eustachian tube dysfunction, upper respiratory tract infection, allergic rhinitis and those on any medication(s) were excluded from the study. A written consent was obtained after the experimental protocol was explained. Ability to ventilate middle ears was ensured through the examination of the mobility of tympanic membranes with the Valsalva manoeuvre on ground and a standard 'ear clearance' run in the Decompression Chamber.

Experimentation was conducted between 1400h-2000h in a post absorptive state in an altitude chamber installed in the Department of High Altitude Physiology and Hyperbaric Medicine at Institute of Aerospace Medicine (IAM), Bangalore situated at an elevation of approximately 963 meters (3,159 ft) from the mean sea level. Subjects were asked not to consume alcoholic beverages the previous night and avoid tea, coffee and smoking from 1000h in the morning on the day of experimentation.

For experimentation in normoxic normobaria i.e. while breathing air at ground level (3,159 ft AMSL; 0.92 ATA), doors of the chamber were closed and measurements taken after about 15 min in order to maintain the thermal ambience comparable with that during hypobaric evaluations at '*high altitude*'. Experimentation in normoxic normobaria was followed by that in hypoxic or non-hypoxic hypobaria. One of these experiments was done on the same day and the other was accomplished on a separate occasion. Minimum separation between the two hypobaric experiments was two days.

For hypobaric conditions, the subject was decompressed to 15,000 ft in the altitude chamber with an '*ascent*' rate of 3000 ft/min. After completion of the test procedure, the subject was '*brought down*' to ground level at the rate of 3000 ft/min. For evaluation in hypoxic hypobaria, the subjects breathed chamber air and for evaluation in non-hypoxic hypobaria they were made to breathe air oxygen mixture using an oxygen mask (ABEU MK II) and regulator (MK-17E) assembly.

To prevent any 'carry over' effects, the sequence of evaluation was counterbalanced as :-

Group A (n=6)	Normoxic normobaria, hypoxic hypobaria, non-hypoxic hypobaria
Group B (n=6)	Hypoxic hypobaria, Non-hypoxic hypobaria, Normoxic normobaria
Group C (n=6)	Non-hypoxic hypobaria, normoxic normobaria, hypoxic hypobaria

In each of the above conditions, handgrip test was performed as described below.

A continuous recording of electrocardiogram (in Standard Lead-II configuration) was made for 2 min in resting sitting before the grip and for the same duration from second to fourth minute of the grip. It was accomplished for the analysis of heart rate variability (HRV).

Handgrip Test

Subject was given instruction for the proper use of dynamometer and not to hold breath during the procedure. Maximal voluntary contraction (MVC) was evaluated in the dominant hand for a few seconds. The best of the 3 readings was taken as MVC. Thereafter, subjects maintained a hand grip at 30% of their MVC for 4 min. Heart rate (HR) and blood pressure (BP) were recorded, on non exercising arm, at the end (last 30s) of first, second to fourth minutes during the contraction (i.e. before the release of handgrip) and sixth min (i.e. during recovery after release of the grip). Measurements of BP were made using a standard sphygmomanometer.

Analysis of Heart Rate Variability

Sequence of beat to beat R-R intervals was manually examined and edited for artifacts or ectopics following which this discrete event series (DES) was transformed into an evenly sampled time signal at 4 samples/sec by linear interpolation using Matlab® (Version 6.5.0.180913a Release 13) software. This transformation into a real time signal allowed the power spectra of R-R interval to be represented as a function of true frequency in units of cycles per second (Hz) as opposed to cycles per beat. Subsequent to removal of mean from the series, estimates of HRV were made using Matlab® through parametric (maximum entropy method) technique. Parameters of autoregressive model were calculated with 'AR' command using 'forward-backward' approach. Model order was determined by minimizing Akanke information criterion. 'PMEM' command was employed to calculate power spectrum estimates via Maximum Entropy Method. It permitted a frequency resolution of 0.002 Hz

Power in spectra was integrated as follows:-

Low Frequency (LF) - 0.040 - 0.150 Hz.

High Frequency (HF) - 0.150 - 0.500 Hz

To account for the variation in the R-R interval during experimentation, power was normalized to square of mean R-R interval as suggested by Taha et al [7]. Thereafter, for appropriate scaling, the normalized values were multiplied by 10^6.

Statistical Analysis

The data were, first, examined for normality using Shapiro Wilk's 'W' statistic. Logarithmic transformation was done for HRV indices, since they were found to deviate significantly from normality. One way, repeated measures analysis of variance (ANOVA) was used for determination of statistical significance of HRV indices. For heart rate and blood pressure values during handgrip test in normobaria, hypoxic hypobaria and non-hypoxic hypobaria, a two way, repeated measures ANOVA with Greenhouse-Geisser correction was employed. The two factors were- experimental conditions (with three levels viz, normobaria, hypoxic hypobaria and non-hypoxic hypobaria) and isometric muscle contraction (with five levels viz. resting sitting, first, second to fourth minute during handgrip and recovery in 6^{th} min). Greenhouse-Geisser correction was employed due to significant departures from the assumption of sphericity. Level of significance was set at $p<0.05$.

It is pertinent to note that Blood pressure could not be recorded during handgrip for one subject during non-hypoxic hypobaria and for two subjects during hypoxic hypobaria due to chamber noise/ movement. Therefore, number of subjects was effectively reduced to 15 in case of BP data.

Table 1: HR and BP responses to isometric handgrip during Normoxic Normobaria (NN), Non-Hypoxic Hypobaria (NH) and Hypoxic Hypobaria (HH)

		Resting Sitting	During Handgrip			Recovery 6 min
			1 min	2 min	4 min	
HR (bpm)	NN	82 ± 10	85 ± 10	87 ± 11	86 ± 10	84 ± 11
	NH	78 ± 8	80 ± 11	83 ± 10	84 ± 9	79 ± 10
	HH	88 ± 13	91 ± 13	90 ± 14	93 ± 13	90 ± 13
SBP (mm Hg)	NN	123 ± 14	128 ± 13	132 ± 14	134 ± 13	123 ± 12
	NH	121 ± 10	128 ± 11	127 ± 12	133 ± 11	122 ± 10
	HH	123 ± 14	126 ± 16	126 ± 15	133 ± 17	120 ± 15
DBP (mm Hg)	NN	83 ± 12	91 ± 12	93 ± 16	94 ± 15	84 ± 14
	NH	76 ± 9	83 ± 11	82 ± 11	86 ± 12	78 ± 9
	HH	78 ± 14	82 ± 15	83 ± 17	86 ± 16	79 ± 17
PP (mm Hg)	NN	39 ± 11	37 ± 10	39 ± 9	40 ± 11	39 ± 9
	NH	45 ± 8	45 ± 9	44 ± 10	48 ± 10	43 ± 8
	HH	45 ± 6	44 ± 10	43 ± 9	47 ± 11	41 ± 8
MAP (mm Hg)	NN	94 ± 13	101 ± 12	104 ± 16	105 ± 14	95 ± 14
	NH	89 ± 10	96 ± 11	95 ± 11	100 ± 13	91 ± 9
	HH	91 ± 13	94 ± 15	96 ± 15	100 ± 15	93 ± 15

Results of statistical analysis

	Pressure condition	Handgrip	Pressure condition xHandgrip
HR	F=10.26; p=3.27E-04	F=12.44; p=1.19E-07	F=0.97; p= 0.465
SBP	F=0.43; p=0.652	F=45.86; p=1.52E-12	F=1.25; p= 0.272
DBP	F=3.92; p=0.031	F=26.720; p=2.61E-10	F=1.371; p= 0.217
PP	F=3.12; p=0.060	F=3.63; p=0.020	F=0.612; p=0.766
MAP	F=1.71; p=0.201	F=31.12; p=1.51E-10	F=1.334; p= 0.235

Individual comparisons for pressure effects (using LSD test)

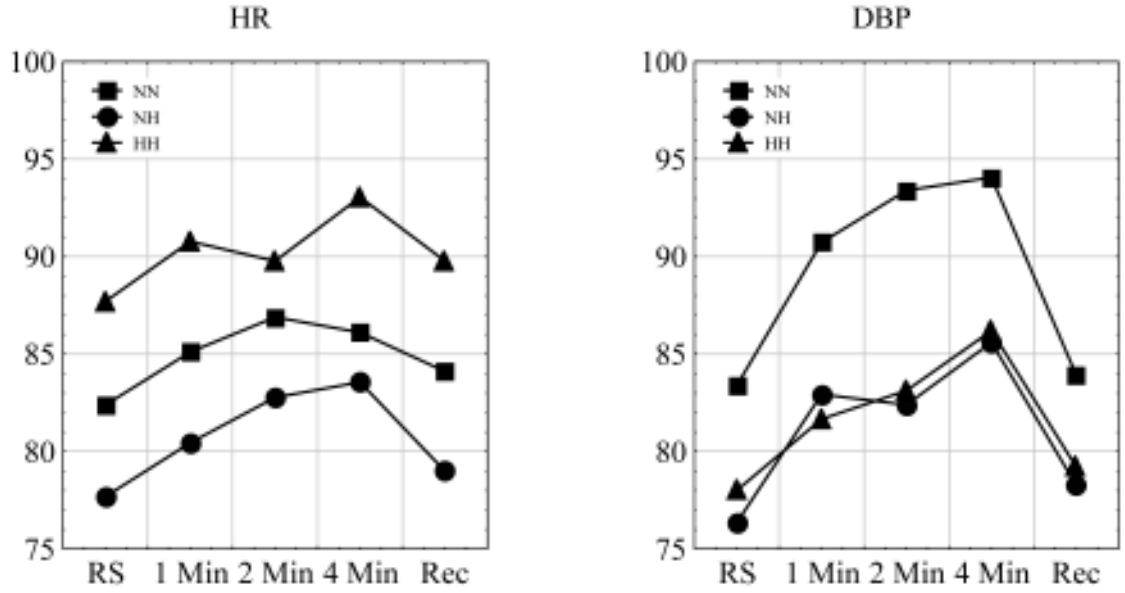
	NN vs NH	NN vs HH	NH vs HH
HR	p = 0.053	p = 0.017	p = 7.14E-05
DBP	p = 0.018	p = 0.027	p = 0.868
PP	p = 0.027	p = 0.063	p = 0.689

Degrees of freedom have been adjusted accordingly. Analysis of HRV was performed in 10 subjects only.

Results

HR and BP responses to isometric handgrip (HGT) during Normoxic Normobaria (NN), Hypoxic Hypobaria (HH) and Non-hypoxic Hypobaria (NH) are given in Table 1 and Figure1. There was a significant main effect of both atmospheric pressure (F=10.26; p=3.27E-04) and isometric contraction (F=12.44; p=1.19E-07) on heart rate (HR). There was no significant interaction between the effects of handgrip and

Figure 1: HR and DBP responses to isometric handgrip during Normoxic Normobaria (NN), Non-Hypoxic Hypobaria (NH) and Hypoxic Hypobaria (HH)



Note - On the 'x' axis, 1 min, 2 min & 4 min represent values during handgrip, RS and Rec are values during resting sitting (before grip) and recovery at 6th min. On the 'y' axis, values are expressed in bpm/mm Hg for HR/DBP.

hypobaria on HR (F=0.97; p=0.465). Similarly, DBP and PP showed a significant main effect of isometric contraction (F=26.720; p=2.61E-10 for DBP, and F=3.63; p=0.020 for PP) and atmospheric pressure (F=3.92, p=0.031 for DBP and F=3.12; p=0.060 for PP). Again, no significant interaction effect was discernible (F=1.371; p=0.217 for DBP and F=0.612; p=0.766 for PP) between the two. On the other hand, SBP exhibited only a significant main effect of isometric contraction (F=45.86; p=1.52E-12). Effect of hypobaria and that of interaction were insignificant (F=0.43; p=0.652 for hypobaria and F=1.25; p= 0.272 for interaction).

All the three experimental conditions had comparable thermal ambience (F=0.028, p=0.972 for Tdb; F=5.49E-29, p=1.000 for Twb and F=0.001, p=0.99 for Oxford Index). Table-2 refers for details. Table 2 also presents arterial saturation in the three experimental conditions. Saturation exhibited significant effect of experimental conditions (F=23119.1; p= 0.00E+00) with a significant reduction (p=0.00E+00) during exposure to hypoxic hypobaria and significant increase (p=1.48E-18) during exposure to non-hypoxic-hypobaria.

Absolute values of total power and that in the HF band showed significant main effect of hand grip (F=12.048; p=0.007 for total power and F=18.368; p=0.002 for HF power). The effect persisted even after normalization of the power to R-R^2 (F=4.982; p=0.053 for total power and F=11.628; p=0.008 for HF power), Table-3 refers for details. Grand average of HRV power spectra (across subjects) during three experimental conditions are shown in Figure1.

Discussion

Overall pattern of cardiovascular responses during handgrip and their modulation in non-hypoxic and hypoxic hypobaria

There was a significant main effect of

Table 2: Arterial saturation and ambient temperature during experimentation in Normoxic Normobaria (NN), Non-Hypoxic Hypobaria (NH) and Hypoxic Hypobaria (HH)

	NN	NH	HH	Statistical Comparison
SaO_2 (%)	97.1±0.2	98.1±0.2	86.0±0.2	F=23119.1; p= 0.00E+00 Individual comparisons – NN vs NH; p= 1.48E-18 NH vs HH; p= 0.00E+00 NN vs HH; p= 0.00E+00
T_{db} (°C)	30±1	30±2	30±2	F=0.03; p= 0.972
T_{wb} (°C)	25±1	25±1	25±1	F= 5.49E-29; p= 1.000
Oxford Index (°C)	26.0±1.3	26.0±1.3	25.9±1.3	F=0.001; p= 0.99

isometric muscle contraction (handgrip) on all the cardiovascular variables examined (Table 1 refers for details). Main effect of pressure condition was significant on HR (F=10.26, p=3.27E-04), DBP (F=3.92, p=0.031) and marginal on PP (F=3.12, p=0.060 for PP). Notably, no significant interaction effect (pressure condition x handgrip) was observed for any of the cardiovascular variables. A significant interaction effect implies that the difference among levels of one factor (handgrip) is not constant at all levels of the second factor (pressure condition). Therefore, a significant effect of pressure condition in the absence of a significant interaction, observed in the present study, suggests that, even though, the two pressure conditions had a significant effect on these variables, both during resting sitting and during isometric muscle contraction (handgrip), the overall pattern of responsiveness was not significantly modulated. In other words, relative changes in these cardiovascular variables during handgrip were comparable in the three experimental conditions (viz. normoxic normobaria, non-hypoxic hypobaria and hypoxic hypobaria) despite a significant shift in the absolute values. The effect (absence of an interaction effect) is at variance with the observation made earlier in the studies by Tripathi et al [1] and Prasanth [2]. It could be due to use of a standard (mercury) sphygmomanometer in the present study. Earlier studies used a non invasive blood pressure monitor (Agilant M3046 A) which was more sensitive, especially in the noisy hypobaric conditions. Since the pattern of changes in HR and BP were different in the different experimental conditions, these are discussed separately in the succeeding paragraphs.

Changes in Heart Rate

Changes in HR were qualitatively different in hypoxic hpobaria from those in non-hypoxic hypobaria. HR increased in hypoxic hypobaric (p=0.017) and decreased in non-hypoxic hypobaria. However, the decrease in non-hypoxic hypobaria was just short of significance (p=0.053). Such an increase in HR during hypoxia is shown to be due to sympathetic activation directly via stimulation of peripheral chemoreceptors and vagal withdrawal indirectly via increases in ventilation, for a review, refer to Wolfel & Levine [6]. The extent of change in heart rate (~7%) is also comparable to what is reported after an acute exposure to 15,000 ft altitude [8].

During exposure to non-hypoxic hypobaria, the HR tended to be lower. It was because the subjects were maintained in mild hyperoxia, rather than strict normoxia. Such an effect of hyperoxia on HR is also well established [9]. An objective evidence of the maintenance of subjects in mild hyperoxia (rather than strict normoxia) during exposure to non-

hypoxic hypobaria and hypoxia during exposure to hypoxic hypobaria was available from SaO_2 which was significantly higher (p=1.484E-18) in non-hypoxic hypobaria (98.1±0.2%) and significantly lower (p=0.00E+00) in hypoxic hypobaric (86±0%) compared to that in normobaria (97.1±0.2%).

Changes in Blood Pressure

Unlike HR, BP exhibited changes which were qualitatively and quantitatively similar in non-hypoxic and hypoxic hypobaria. As stated above, DBP and PP exhibited significant main effect of pressure condition. SBP was largely unaffected with hypobaria (F=0.43, p=0.652) and changes in MAP could not attain statistical significance (F=1.71, p=0.201). It is to be appreciated that, while examining pressor responses to isometric muscle contraction (handgrip), it is the DBP which merits greatest importance.

A significant reduction in DBP during hypoxic hypobaria could be conceived, at the first instance, to be a result of '*functional sympatholysis*' which offsets the effects of sympathetic activation. Nonetheless, a comparable (p=0.868) reduction of DBP was noted also in non-hypoxic hypobaria. In view of the above, it will be un-parsimonious to conceive that the effect was secondary to hypoxia. Low atmospheric pressure, the stressor which is common to both the conditions, seems to be more probable candidate. Such an effect is consistently demonstrable in previous studies [1,2]. Mediation of vasodilatation through accumulation of local metabolites (the proposed mechanism underlying '*functional sympatholysis*') seems to be less probable a mechanism also from the observations that high energy phosphates, measured in skeletal muscle of humans, show no significant decrement in hypoxia at rest or even after exhaustive exercise. Green et al [10] investigated adaptations in skeletal muscle in response to progressive hypobaria in eight male subjects over 40 days of progressive decompression to the stimulated altitude of the summit of Mount Everest. Samples of the vastus lateralis muscle extracted before decompression (SL-1), at 380 and 282 Torr and on return to sea level (SL-2) indicated that maximal activities of enzymes representative of the citric acid cycle, beta-oxidation, glycogenolysis, glycolysis, glucose phosphorylation, and high-energy phosphate transfer were unchanged (p>0.05) at 380 and 282 Torr compared with initial SL-1 values.

Thermal ambience in the three experimental conditions

It is noteworthy that, in their study by Tripathi et al [1], there was a mild, yet statistically significant, increase in the ambient temperature during exposure to non-hypoxic hypobaria compared to normoxic normobaria (Tdb and Twb in the chamber varied between 27-30°C and 22-26°C in normobaria and 28-30°C and 22-27°C in hypobaria, respectively). Even though such a mild increase in temperature could not have affected the blood pressure during exposure to hypobaria, it was a desirable control. The present study maintained the thermal ambience (F=0.028, p=0.972 for Tdb; F=5.49E-29, p=1.000 for Twb and F=0.001, p=0.99 for Oxford Index; Table 2 refers for details) in all the experimental conditions and qualifies to be an ideal one from an academic point of view.

Changes in Spectral Indices of HRV

Absolute value of total power and that in the HF band showed significant main effect of hand grip (F=12.048; p=0.007 for total power and F=18.368; p=0.002 for HF power). The effect persisted even after normalization of the power to mean R-R^2 (F=4.982; p=0.053 for total power and F=11.628; p=0.008 for HF power). These observations are appreciable as a significant

Table 3: Heart Rate Variability (HRV) spectral indices during Normoxic Normobaria (NN), Non-Hypoxic Hypobaria (NH) and Hypoxic Hypobaria (HH) : Resting sitting and average values during HGT

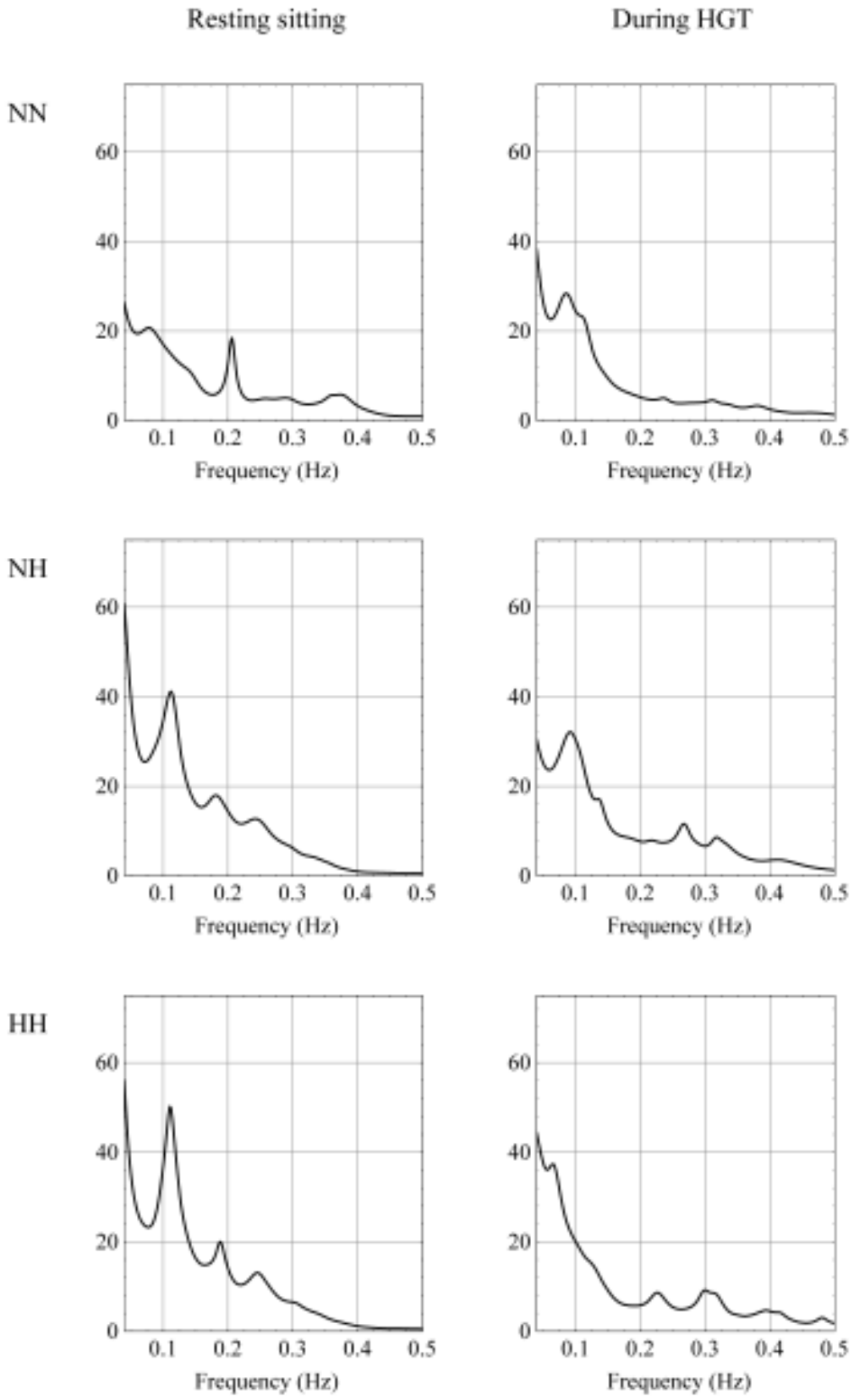
	NN		NH		HH	
	Resting Sitting	HGT	Resting Sitting	HGT	Resting Sitting	HGT
TP (0.04-0.50 Hz) Absolute values in ms^2	2.970±0.132	2.963±0.267	3.189±0.288	3.071±0.214	3.184±0.301	2.832±0.241
LF Power (0.04-0.15 Hz) Absolute values in ms^2	2.712±0.087	2.767±0.268	2.941±0.330	2.834±0.140	2.952±0.318	2.6702 ±0.232
HF Power (0.15-0.50 Hz) Absolute values in ms^2	2.578±0.263	2.509±0.286	2.806±0.262	2.636±0.371	2.792±0.286	2.307±0.291
TP (0.04-0.50 Hz) Values normalised to R-R^2	3.198±0.129	3.219±0.257	2.940±0.111	3.024±0.255	2.806±0.259	2.766±0.280
LF Power (0.04-0.15 Hz) Values normalised to R-R^2	3.367±0.334	3.310±0.213	3.119±0.374	3.073±0.131	2.984±0.307	2.875±0.371
HF Power (0.15-0.50 Hz) Values normalised to R-R^2	3.352±0.353	3.072±0.261	3.120±0.370	2.911±0.253	2.960±0.336	2.548±0.306

Results of statistical analysis of data presented in Table-4

	Pressure condition	Handgrip	Pressure condition x Handgrip
TP (0.04-0.50 Hz) Absolute values in ms^2	F = 3.290; p = 0.061	F = 12.048; p = **0.007**	F = 3.576; p = **0.049**
LF Power (0.04-0.15Hz) Absolute values in ms^2	F = 2.510; p = 0.109	F = 3.915; p = 0.079	F = 3.393; p = 0.056
HF Power (0.15-0.50Hz) Absolute values in ms^2	F = 3.452; p = 0.054	F = 18.368; p = **0.002**	F = 3.973; p = **0.037**
TP (0.04-0.50 Hz) Values normalised to R-R^2	F = 2.346; p = 0.124	F = 4.982; p = **0.053**	F = 2.435; p = 0.116
LF Power (0.04-0.15Hz) Values normalised to R-R^2	F = 1.541; p = 0.241	F = 0.941; p = 0.357	F = 2.151; p = 0.145
HF Power (0.15-0.50Hz) Values normalised to R-R^2	F = 2.770; p = 0.089	F = 11.628; p = **0.008**	F = 3.049; p = 0.072

reduction in the vagal modulations in heart rate control during handgrip. No significant effect of either pressure condition or handgrip was observed on LF power. Table 3 refers for these details. The latter observation, even though seem to be intriguing at the firs instance, is supported from recent reports which have shown that LF may be a poor marker of sympathetic activity [11,12]. A few studies are worth discussion and are presented here. After selective sinoatrial parasympathectomy, Randall et al [13] observed that low-frequency power in dogs was a reflection of multiple components. The authors synthesised that the total low-frequency power was composed of 50% parasympathetic activity, 25% sympathetic activity, and 25% other 'yet to be identified' factors. Grasso et al [14] performed autoregressive transfer function analysis of RR interval, and systolic & diastolic arterial pressure in a group of 10 healthy human subjects during supine rest and while standing, both before and after â1-selective blockade (with atenolol). Beta-blockade failed to induce systematic changes on the power of the LF peak of R-R, in any condition. The coherence between R-R and systolic

Figure 2: Grand average of HRV power spectra (across subjects) during Normoxic Normobaria (NN), Non-Hypoxic Hypobaria (NH) and Hypoxic Hypobaria (HH)



arterial pressure in the same region remained high and a constantly negative phase (approximately 50-60 degrees, corresponding to a delay of 1-2 heart beats of RR on SAP) was always seen. Beta-blockade decreased the power of the LF peak of systolic arterial pressure, increased the transfer function gain between systolic arterial pressure and R-R at LF, and the HF power of R-R. Authors concluded that LF oscillations of R-R were not directly generated by the sympathetic drive to the heart but reflect mainly the parasympathetic activity. The observations of the present study further indicate inadequacy of HRV spectral indices as markers of autonomic activity (at least in hypobaric conditions). This inference derives enough support from literature and is believed to be due to above effects and additional confounding effects of ventilatory volume, respiratory rate, cardiac volume & mechanical function, arterial stiffness, arterial baroreflex function and responsiveness of sinus node, for a review, refer to Wolfel & Levine [6].

Present study further endorses the attenuating effect of low atmospheric pressure on the efficacy of AGSM. Even though the experiment design of the present study does not permit a direct visualization of the mechanisms involved in vasodilatation induced by hypobaria (measurements of muscle sympathetic nerve activity, forearm blood flow or autonomic blockade were not possible due to non availability of these facilities), it is clear, from the observations that hypobaria exerts an effect on peripheral vasculature and the effect remains unvarying whether the subjects are maintained in hypoxia or non-hypoxia. This is the singular strength of this study. It also provides a valuable insight into the mechanism(s) involved in vasodilatation after acute induction to high altitudes.

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