Comparison of Baroreflex Sensitivity Gain during Mild Lower Body Negative Pressure in Presence and Absence of Long Duration Bed Rest

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Abstract

Lower body negative pressure (LBNP) and head down bed rest (HDBR) are protocols used to simulate hypovolemia and cardiovascular deconditioning, causing an alteration of autonomic control of circulation. The objective of this study was to investigate the combined effects of LBNP and bed rest on cardiac baroreflex sensitivity (BRS). RR and systolic blood pressure (SBP) recordings from seven volunteers were analyzed during a mild LBNP protocol consisting of three different levels of LBNP (-10 mmHg, -20 mmHg, -30 mmHg) before (pre-HDBR) and on day 50 of a HDBR study. Spectra of RR and SBP were computed and BRS was assessed in the low frequency (LF) and high frequency (HF) bands through a bivariate model that takes into account the causal relationships between heart rate (HR) and arterial blood pressure. HR significantly increased from BL in HDBR for LBNP≤-20 mmHg. BRS gain decreased significantly in the LF band with increasing levels of LBNP in both conditions. BRS gain was significantly lower on day 50 of HDBR with respect to pre-HDBR at -20 mmHg. These data suggest that BRS in the LF range is reduced in bed rest, and these changes may be due primarily to a reduction in plasma volume associated with bed rest, which impact the physiological responses of autonomic control of circulation.

1. Introduction

Lower body negative pressure (LBNP) and head down bed rest (HDBR) are protocols used to simulate hypovolemia and cardiovascular deconditioning, causing an alteration of autonomic control of circulation.

Low levels of LBNP have been considered to selectively unload cardiopulmonary baroreceptors [1,2], resulting in reflex peripheral vasoconstriction without changes in heart rate (HR) and unchanged mean arterial pressure (MAP), this has been supposed not to involve arterial baroreceptors. However, there is evidence about the engagement of arterial baroreflex during mild LBNP procedure as well. For instance, Taylor et al. [3] demonstrated a decrease in systolic ascending aortic area, which is a measure of aortic baroreceptor input, during low levels of LBNP despite the maintenance of arterial blood pressure (ABP), whereas Fu et al. [4] showed a transient reduction in systolic blood pressure (SBP) and diastolic blood pressure (DBP) which were restored presumably through the arterial baroreflex feedback mechanism, after about 15 heartbeats during mild LBNP.

On the other hand, high levels of LBNP have been associated with unloading of arterial and cardiopulmonary baroreceptors [5].

Regarding baroreflex sensitivity (BRS) during mild LBNP, there are controversial results some authors have reported an enhancement or increase in arterial baroreflex [6] while others have reported no change [7], whereas Barbieri et al [8] reported a decrease in baroreflex gain at -30 mmHg of LBNP in both feedback and feedforward pathways.

In addition, exposure to bed rest has been characterized by a deconditioning of autonomic nervous system and a reduction in BRS has been reported after HDBR [9].

The goal of this paper is to assess the combined effects of LBNP and bed rest on cardiac baroreflex sensitivity (BRS) and to contribute in elucidating the controversial results about these maneuvers.

2. Method

2.1. Experimental protocol

A subset of data from Women's International Space

Simulation for Exploration (WISE-2005) study was analyzed. More details of protocol description are reported in [10]. The selected subset of data consisted of seven healthy women (age 33 ± 1yr, height 165 ± 4cm, weight 59 ± 3kg). All procedures were approved by Ethics Committee from University of Waterloo, Canada, and the French Committee for Health, in agreement with the Helsinki convention, and informed written consent was obtained from all participants.

Subjects were placed in a custom-made LBNP chamber and sealed at the iliac crest with a neoprene "skirt". The subjects were monitored by an ECG (Colin, St. Antonio, TX, USA), a respiration belt (PowerLab), a finger blood pressure cuff (Finometer, FMS, Amsterdam, The Netherlands) and by a catheter inserted in the right antecubital vein for the acquisition of central venous pressure (CVP). All these signals were collected at 1000 Hz on a PowerLab Data Acquisition System running Chart software (PowerLab, Sydney, Australia).

Incremental levels of lower body pressure (0, -10, -20, -30 mmHg) were progressively applied to subjects, at least 2 min per level, and with transition time between each level <5 s. The experiment was completed once before entry into bed rest and then repeated again on day 50 of 6° HDBR.

2.2. Signal preprocessing and spectral analysis

RR series were extracted from ECG waveforms by identification of QRS complexes and of R peaks. Beat-by-beat series of SBP, DBP, MAP, and pulse pressure (PP), computed as the difference between SBP of the current cardiac cycle and DBP of the previous cycle, were extracted. Beat-by-beat series of CVP were obtained as the mean value of continuously recorded CVP over each cardiac cycle, i.e., between two consecutive R peaks. The signals were pre-processed with an adaptive filter in order to remove artifacts or ectopic beats. Stationary segments of two minutes were selected for each LBNP phase. Beat-by-beat series were detrended, divided by mean value and resampled in the time domain at 1 Hz in order to perform spectral analysis. Power spectral density was computed via autoregressive (AR) estimation and powers in low frequency (LF) band ($0.04 < f < 0.15$ Hz) and high frequency (HF) band ($0.15 < f < 0.4$ Hz), were calculated. The values of total power (TP) were computed as well. The AR model order range was between 8 and 12, and the optimal model order was chosen according to the Akaike Criterion.

2.3. Baroreflex sensitivity gain

BRS gain was assessed by means of a bivariate model considering the causal relationship from SBP to RR, i.e. the feedback mechanism, and RR to SBP, i.e. the feedforward mechanism. An autoregressive bivariate model of order comprised between 8 and 12 was computed as follows:

$$Y[n] = \sum_{k=1}^{p} A[k]Y[n-k] + W[n], \quad (1)$$

where

$$\mathbf{A}[k] = \begin{bmatrix} a_{11}[k] & a_{12}[k] \\ a_{21}[k] & a_{22}[k] \end{bmatrix}, \mathbf{Y}[n] = \begin{bmatrix} RR[n] \\ SBP[n] \end{bmatrix},$$

$$\mathbf{W}[n] = \begin{bmatrix} W_{RR}[n] \\ W_{SBP}[n] \end{bmatrix} \quad (2)$$

The gains are computed as follows:

$$G_{SBP \to RR}(f) = \frac{A_{12}(f)}{1 - A_{11}(f)} \quad (3)$$

$$G_{RR \to SBP}(f) = \frac{A_{21}(f)}{1 - A_{22}(f)} \quad (4)$$

where,

$$A_{ij}(f) = \sum_{k=1}^{p} a_{ij}[k] e^{-j2\pi fk} \quad (5)$$

The relationship SBP→RR represents the cardiac baroreflex, i.e. the actual feedback mechanism, whereas the relationship RR→SBP represents the direct influence of RR interval on SBP, which is mediated by a perturbation mechanism based on the Starling law (a longer RR induces an increased left ventricular end-diastolic volume and, in turn, a larger stroke volume) and diastolic runoff (a longer RR induces a larger decay of diastolic pressure and, thus a smaller SBP, keeping constant the other variables like stroke volume) [11].

A two-way repeated-measures ANOVA test was performed, with LBNP epochs being the repeated factor and pre-HDBR and HDBR conditions the second factor. One-way repeated-measures ANOVA was applied to the indices obtained both in pre-HDBR and HDBR. Post hoc comparisons were performed by Fisher's least significant difference test to verify significant differences between a specific level of LBNP and baseline (BL). Paired two-sample Student's t-test was used to compare pre-HDBR and HDBR for each LBNP epoch (e.g., BL pre-HDBR vs. BL HDBR). Statistical significance was considered for two tailed p-values<0.05.

3. Results

HR significantly increased during HDBR from BL to -20 mmHg and -30 mmHg of LBNP, while SBP decrease from BL to -30 mmHg LBNP in pre-HDBR. CVP significantly decreased from BL, progressively with increasing intensities of LBNP, before and during HDBR. HR was significantly lower in each of the four experimental epochs in pre-HDBR with respect to

HDBR. These results are shown in Table 1.

Total RR power tended to decrease at the onset of LBNP in pre-HDBR and to increase again for larger levels of LBNP. A significant increase in LF% of RR was found on day 50 of HDBR at -30mmHg with respect to BL, possibly as a reflection of the reduced variability of HR and respiration, which can also reduce the power of RR in the respiratory band. A significant increase in total power of SBP was reported at -10 mmHg with respect to BL in pre-HDBR, while this was not the case in HDBR. Total power of SBP at BL and at -20mmHg was significantly smaller before bed rest than during HDBR. A significant higher value of SBP LF% at -20 mmHg on day 50 HDBR with respect to pre-HDBR condition was found. LF power of SBP showed a significant smaller value in pre-HDBR in comparison with HDBR, in BL and during LBNP (Table 2).

Table 1. Time domain indices before (PRE) and during bed rest (HDBR), in each of the four experimental epochs of the continuous LBNP maneuver

	BL	**-10**	**-20**	**-30**
HR, bpm [a,b]				
PRE‡	64± 6.8[#]	62± 6.2[#]	65±4.7[#]	70± 3.2[#]
HDBR‡	71± 4.7	75± 6.9	81±8.4[§]	89±11.1[§]
SBP, mmHg [a]				
PRE‡	127± 7.2	124± 7.7	119±8.0	117± 7.9[§]
HDBR‡	118±13.2	117±11.1	114±9.6	110±12.4
DBP, mmHg				
PRE‡	74±6.7	72± 6.1	71±5.4	71± 5.3
HDBR	74±8.9	73± 8.6	74±7.9	73± 9.6
MAP, mmHg				
PRE‡	94± 6.3	91± 6.0	88±5.5	88± 5.0
HDBR‡	91±10.0	90± 9.0	89±8.1	87±10.0
CVP, mmHg [a,b]				
PRE‡	7.3± 0.9	4.8± 0.9[§]	3.3±1.5[§]	2.2± 2.6[§]
HDBR‡	6.7± 1.3	5.5± 1.5	5.1±1.4[§]	4.4± 1.3[§]

Values are expressed as mean ± SD. [a]Two-way ANOVA row factor (effect of bed rest), p-value < 0.05. [b]Two-way ANOVA column factor (effect of LBNP), p-value <0.05. ‡One-way ANOVA, p-value<0.05. [§]significant post-hoc comparison between each LBNP level and BL (in PRE and HDBR condition). [#]Paired t-test between the same LBNP phase (PRE vs HDBR) p-value < 0.05.

BRS gain (SBP→RR) estimated in the LF band decreased with increasing levels of LBNP, in pre-HDBR a significant decrease was found at -30mmHg, while on day 50 of HDBR significant lower values were found at -20mmHg and -30mmHg in comparison with baseline. Furthermore, at -20mmHg BRS gain resulted significantly lower on day 50 of HDBR with respect to pre-HDBR condition (Figure 1). During HDBR in the HF band, a significant reduction of the BRS gain ($G_{SBP \rightarrow RR}$) was observed at the three different levels of LBNP (Figure 1). Regarding the feedforward pathway, no changes were reported.

Table 2. Main frequency domain indices of hemodynamic variability before (PRE) and during bed rest (HDBR) in each epoch of LBNP

	BL	**-10**	**-20**	**-30**
LF RR, 10^{-3} [a]				
PRE	86± 43.4	81±81.2	79± 44.8	82± 56.3[#]
HDBR	184±148	89±66.5	139± 70	315± 289
LF SBP, 10^{-3} [a]				
PRE	26± 15.9[#]	34±19.4[#]	28± 18.7[#]	35± 19.3[#]
HDBR	131± 71.9	91±58.3	131± 84.7	243± 195
LF % RR [a,c]				
PRE	73±10.1	74± 8.9	74±10.1	65±11.1[#]
HDBR	77± 9.8	77±11.2	84± 6.9	88± 6.1[§]
LF % SBP [a]				
PRE	72±12.4	68± 8.4	71±10.7[#]	74±15.3
HDBR	74±14.7	79±16.4	87± 6.8	83±18.4
TOTAL POWER RR, 10^{-3} [a]				
PRE	197±126	138±134	152± 87	213± 156
HDBR	319±207	157±120	217± 120	442± 383
TOTAL POWER SBP, 10^{-3} [a]				
PRE	51± 23.9[#]	109± 87[§]	58± 33[#]	71± 39
HDBR	398±282	204±187	206± 106	437± 392

Values are expressed as means ± SD. [a] Two-way ANOVA row factor (effect of bed rest), p-value <0.05. [b]Two-way ANOVA column factor (effect of LBNP), p-value < 0.05. [c] Two-way ANOVA interaction, p-value < 0.05. ‡One-way ANOVA, p-value < 0.05.[§]Significant post hoc comparison between each LBNP level and BL. [#]Paired t-test between the same LBNP phase, PRE vs HDBR p-value < 0.05

4. Discussion and conclusion

The goal of this paper was to assess the effects of LBNP and HDBR on cardiac BRS through a bivariate model that considers the casual effects between HR and SBP. BRS has been explored during LBNP or during HDBR in other works, but separately. To our knowledge, only the work of Hughson et al. [12] performed a similar analysis, but the estimation of BRS was obtained by means of the sequence method, which is a technique unable to separate the SBP and RR oscillations from different origin from baroreflex mediated ones.

The changes in CVP, which are related to central volume variations, resulted as was expected with

significant reductions during incremental LBNP levels; however, no significant differences were found between pre-HDBR and day 50 of HDBR. HR was significantly increased at -20 mmHg and -30 mmHg in HDBR condition which could suggest that arterial baroreflex is active at these LBNP levels.

BRS gain decreased during high LBNP levels in pre and HDBR conditions in LF band, whereas for HF band significant decreases were found at the three different LBNP intensities only in HDBR. These data suggest that BRS is reduced in bed rest, and these changes may be due primarily to a reduction in plasma volume associated with bed rest, which impacts the physiological responses of autonomic control of circulation.

Our findings, i.e. the decrease of BRS gain during HDBR and during LBNP is consistent with other works [12,13]. In this work the feedforward mechanism was also evaluated as well, but no changes were reported in this pathway. This result may be expected, as the mechanical coupling between HR (thus cardiac output) and ABP should not be altered by bed rest, while the main changes are known to affect neural regulation of cardiovascular function.

Further works are necessary in order to assess the interaction of cardiac baroreflex and cardiopulmonary baroreflex during these maneuvers as both baroreflexes play an important role.

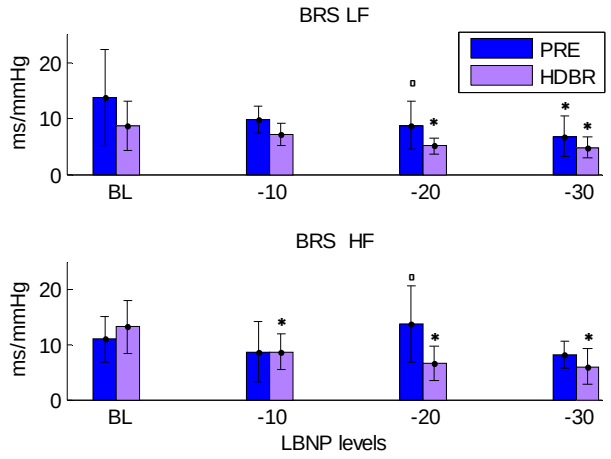

Figure 1. Bivariate model gain values estimated in LF and HF bands in each LBNP epoch before and after bed rest. The symbol * marks the significant post hoc comparison between each LBNP level and BL (p-value <0.05). ° marks the significant differences between the same LBNP phases, PRE vs HDBR (p-value < 0.05).

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