AltitudeOmics: Effect of Exercise on Baroreflex Sensitivity at Sea Level and Altitude

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Abstract

Various studies have been performed to analyze and asses the baroreflex sensitivity (BRS) in different settings. Our study aims at analyzing the BRS at rest and during different exercise stages and altitudes. Twenty-one young, healthy subjects underwent experimental trials near sea level, and two times at high altitude. BRS was calculated using the sequence method (spontaneous trends of three or more inter-beat interval and systolic blood pressure) in order to analyze the baroreflex response at rest and during incremental exercise. Results show that BRS exponentially decreases during exercise at all altitudes. Moreover, BRS decays much faster with acute hypoxia (ALT1), indicating that the baroreceptors respond with a quick loss of sensitivity when exercising. After 16 days at high altitude (ALT16), BRS at rest resets to smaller values but the evolution of BRS during exercise has the same behavior as at SL, indicating BRS acclimation to altitude.

1. Introduction

Baroreflex sensitivity (BRS) is one of the two main markers (with heart rate variability, HRV) of the autonomic nervous system control on the cardiovascular function. BRS is a vital mechanism which has been shown to provide valuable information in cardiovascular diseases such as congestive heart failure and coronary artery disease [1] [2]. It depends on physiological and non-physiological factors such as age, gender [3] [4] [5] and physical exercise [1], but the effects of environmental hypoxia remain to be assessed [6].

Humans have a remarkable capacity to adapt to very high altitude (~5,000m), where ambient oxygen pressure is about half of the sea level value. Two of the main characteristics which accompany a healthy cardiovascular adaptation are an improvement in arterial oxygen content (CaO_2) and an improvement in exercise performance. However, the baroreflex is an essential homeostatic mechanism, which has rarely been studied during acclimation at very high altitude in humans and even more rarely during hypoxic exercise. Yet the baroreflex is primordial as it provides a rapid negative feedback loop that allows the maintenance of blood pressure at near constant level, compatible with adequate blood supply to any organ in the body. The aim of this study was to assess baroreflex sensitivity (BRS) in humans exercising at high altitude, when oxygen transport and exercise performance are severely challenged.

2. Methods

2.1. Ethical approval

This study was conducted as part of the AltitudeOmics project. Institutional ethics approval was obtained from the Universities of Colorado and Oregon and the U.S. Department of Defense Human Research Protection Office. This study follows the Declaration of Helsinki. All participants were first informed of the procedures of this study, and then gave written informed consent prior to participation.

2.2. Study design

Young, healthy sea level (SL) residents were recruited from the greater Eugene, Oregon, area (elevation 128 m) and screened to exclude anyone who was born or had lived at altitudes >1,500 m for more than 1 year or had traveled to altitudes >1,000 m in the past 3 months. SL measurements were performed in Eugene. Approximately 4 weeks following SL measurements, subjects were flown

to La Paz, Bolivia. They breathed supplemental oxygen during the drive to the Chacaltatya research station at 5,260 m. Acute responses to high altitude were assessed between 2 to 4 h after arrival and cessation of supplemental oxygen (ALT1). Subjects then acclimatized at 5,260 m over the next 15 days. On the 16th day (ALT16), measurements were repeated at 5,260.

This report focuses on novel data and novel analysis regarding BRS during incremental exercise, evaluated at fixed absolute workrates, as described further. The entire experimental protocol of the AltitudeOmics project is available in details elsewhere [7]. We have carefully avoided replication of data among reports, except where common variables were necessary to describe the physiological phenomena studied in the present work [e.g., heart rate (HR)].

2.3. Subjects

We studied 21 subjects (twelve men and nine women) at SL, ALT1 and ALT16, aged 21 ± 1 years old, height 175.8 ± 7.9 cm, weight 69.7 ± 9.0 kg, BMI 22.4 ± 1.8 kg/m^2, maximal wattage at SL 263 ± 58 W.

2.4. Measurements

All subjects were familiarized with study procedures at least 48 h prior to SL data recording. Subjects followed standardized exercise and dietary regimens for 24 h before each measurement period. At SL, ALT1 and ALT16, a 22-gauge catheter was inserted into a radial artery at least 1 h before instrumentation. Arterial blood pressure (ABP) was monitored via a fluid-filled pressure transducer (Deltran II; Utah Medical Products, Midvale, UT) attached to the radial artery catheter.

Continuous analog data for ABP were recorded at 200 Hz (PowerLab 16/30; ADInstruments) and directly stored on a dedicated computer for offline analysis.

2.5. Protocol

After the subjects were instrumented, they underwent a 3 min resting period, seated on an electrically-braked cycle ergometer (Velotron Elite, Racermate, Seattle, WA, USA). Immediately after the resting period, subject started pedaling at a self-chosen frequency. The subjects had to keep pedaling frequency constant throughout the 3-min stages at 70, 100, 130 and 160 W.

2.6. Methods

Extraction on Heartbeats. Heartbeats were extracted directly from the ABP recordings. Initially, systolic blood pressure peaks (SBP) were extracted from the ABP waveform with heartbeats representing the time of their occurrence. However, low sampling rates (< 250 Hz) may produce jitter in the estimation of peaks [8] [9]. For instance, at 200 Hz the highest time resolution is within a confidence interval of five ms. In order to refine the location of heartbeats and the SBP values, a second order polynomial was interpolated for each extracted peak using four neighbor samples from the ABP waveform (two immediately before and two immediately after). Heartbeats were selected as the location of the maximum of the interpolated polynomial. Furthermore, SBP values were updated as the maximum in their corresponding polynomial. Finally, the inter-beat intervals (IBI) were created as the interval between successive peaks.

Measuring Baroreflex Sensitivity. For this study, BRS was calculated using the sequence method [10]. This index works based on the identification of at least three consecutive beats in which strict increase (decrease) in SBP are followed by strict increase (decrease) in the IBI. Fixed minimal changes thresholds were considered for BP and IBI to validate a sequence. More specifically, a minimum change of 1 mmHg between two consecutive SBP values and five ms for IBI interval were considered as smallest increase (decrease) sequence. Furthermore, correlation coefficient between changes in SBP and IBI to validate a sequence was 0.85. Finally, a minimum number of five sequences was set to validate a BRS estimate.
For each SBP-IBI trend, the slope of the regression line between changes in SBP and IBI was calculated, and BRS was obtained as the average of all slopes.

3. Results

3.1. Cardiovascular data

Table 1- Cardiovascular data.

Parameter/Stage	SL	ALT1	ALT16
HR (bpm)			
Rest	77±17	90±15	97±16
70W	108±18	135±13	123±21
100W	125±21	149±14	138±19
130W	140±21	162±12	149±15
160W	155±20	167±9	157±15
Ex Int (% of max)			
70W	29±7	45±12	44±13
100W	41±10	64±17	62±18
130W	53±13	77±15	74±15
160W	66±16	95±19	91±19

HR: heart rate in beats per minute (bpm), Ex Int: Exercise Intensity in percentage (%) with respect to maximum exercise intensity in each altitude (Mean ± SD).

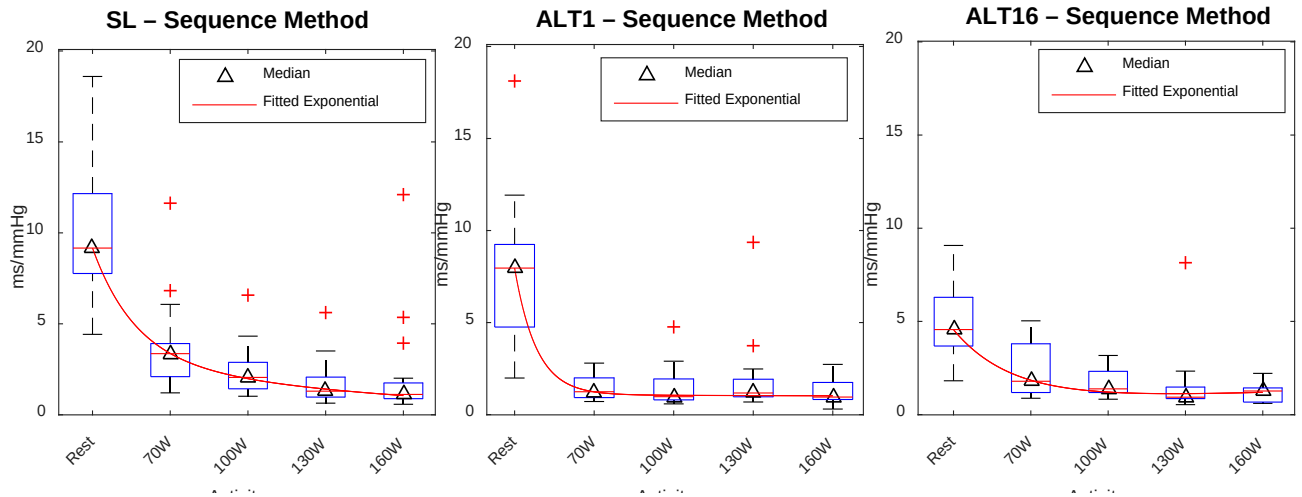

Figure 1- Box plot of the calculated BRS during exercise at each altitude.

3.2. Baroreflex sensitivity data

Baroreflex sensitivity was measured for the twenty-one subjects at SL, ALT1, and ALT16, separately for each exercise stage, including the resting period. Detailed BRS measurements are reported in Table 2.

Table 2- Baroreflex Sensitivity Data.

Parameter /Stage	SL (mean±std)	ALT1 (mean±std)	ALT16 (mean±std)
BRS (ms/mmHg)			
Rest	10.57±5.34	7.73±4.24	4.98±1.98
70W	3.64±2.35	1.48±0.70	2.37±1.37
100W	2.39±1.34	1.55±1.27	1.70±0.71
130W	1.69±1.11	2.08±2.45	1.64±2.01
160W	2.01±2.64	1.26±0.77	1.19±0.54

As reported in Table 2, BRS decreases as exercise starts and intensity incrementally increases. For better comparison of BRS behavior during exercise at SL, ALT1 and ALT16, an exponential fitting was performed on the calculated rest-exercise BRS, as illustrated by Fig. 1. Main decay constants of -1.8, -3.6 and -1.3 were obtained respectively for SL, ALT1 and ALT16.

4. Discussion

There are various methods to calculate the BRS. Apart from the sequence method, spectral methods, which are based on the square root of the ratio between IBI and SBP spectral components (in low- or high-frequency), with a minimum coherence, have been introduced [11]. Another method to measure the BRS is the transfer function method. This method calculates BRS by averaging the transfer function value between SBP and IBI in the frequency range of [0.07-0.14] Hz [12]. In this paper, the sequence method was used as the BRS is calculated based on standardized computations which removes inter-subject and intra-subject measurement variability [13]. It is noteworthy that the same BRS behavior was obtained when the sensitivity was calculated using spectral and transfer function methods.

In ALT1, the behavior of the BRS from rest to incremental exercise (up to 160 W) is strongly modified as indicated by the decrease in time decay from -1.8 to -3.6. This suggests either a partial failure of the BRS to respond acutely to very high altitude or that the baroreceptors respond with a quick loss of sensitivity when blood gases and blood pH regulation are severely challenged. Although the efficiency of a quick loss in BRS remains to be demonstrated, it may prevent blood flow (and thus oxygen delivery) to drop while CaO_2 is decreased. In ALT16, time decay goes back to SL values indicating that BRS behavior from rest to 160W partially recovers toward a normal shape, yet the starting point at rest (see Fig. 1) of the BRS is lower than in SL and ALT1. As the acclimation process normalizes CaO_2 and tolerates lower arterial CO_2 pressures, the BRS seems to reset to lower values but recovers normal behavior with regards to the transition from rest to incremental exercise.

5. Conclusion

This work studied the effect of exercise and acclimation to altitude on baroreflex sensitivity. BRS was calculated using the sequence method. Regardless of the altitude, the BRS exponentially decreased during exercise. In case of acute exposure to altitude, the BRS drops much faster compared to SL. Once subjects get acclimated, the BRS behaves comparably to SL, although starting from a lower level (approx. half of SL at rest) which suggests a resetting of the BRS to lower values.

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