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Sample Entropy Analysis of Heart Rate Variability during Rest and Exercise in Hypoxia

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Abstract

In this paper, the aim was to study Heart Rate Variability during rest and exercise in normobaric hypoxia environment using sample entropy. Sample entropy is a powerful way to analyze non-linear biological system, it's the first time to analysis hypoxia exercise HRV signal by sample entropy.12 healthy males took part in the experimentation, some of them were asked to stay in the hypoxia cabin for 150 min every day. It's divided into three 30 min rest periods and three 20 min exercise periods, the rest and exercise period was across. Subjects' heart rate and SaO_2 *data were collected. The sample entropy of rest period was compared with exercise period, there's statistical difference between them. Our results indicate that hypoxia exerts an influence on HRV, it also suggest that acute exposure to normobaric hypoxia induce increases in sympathetic vasomotor activity and cardiac sympathetic dominance result an increased heart rate.*

Keywords: *Hypoxia, Sample Entropy, Exercise, Heart Rate Variability (HRV)*

1. Introduction

With increased travel all over the world, high altitude sojourns are more and more common for different populations. The hypoxia physiology has become important in aviation and high altitude medicine [1]. For the body, the main problem of altitude exposure is less of oxygen, exposure to decreased partial pressures of O_2 induces hypoxemia in humans.

The neurological regulation of cardiovascular factors is systematically altered by hypoxemia. Using spectral analysis of oscillations in heart rate, such cardiovascular neuroregulation can be non-invasively analyzed [2]. Assessing heart rate variability (HRV) can measure autonomic nervous activity, the reliability of this method has already been examined in various studies, including large-scale ischemic heart disease studies [3].

Most biological signals are nonlinear and non-stationary time series, such as HRV. Nonlinear dynamic analysis is a useful approach to understanding biological system. Sample entropy is one way of nonlinear dynamic analysis, this method is not sensitive to missing points [4].

Exercise is another load which is known to deteriorate acute high altitude mountain sickness [5]. Petra Zupet studied the influence of hypobaric hypoxia on HRV during physical exercise to determine whether HRV changes due to the exercise induced heart rate (HR) increase or whether hypoxia itself exerts an influence [6]. Fumihiko analyzed the impact of acute hypoxia

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on heart rate and blood pressure variability in conscious dogs by frequency domain analysis [7].

Most of the researches about hypoxia are studied by time or frequency domain, as HRV is not stationary time series, in this paper, sample entropy is used to estimate the HRV in hypoxia. Through this method, more detail about the nonlinear specialty is looking forward to be observed.

2. Subjects and Method

2.1 Hypoxia cabin and subjects

In this research, hypoxia cabin was designed by control the flowing ratio of nitrogen and air. Different altitude from 0 to 8000 meters can be simulated in it. There's a power bicycle inside to perform the exercise.

Healthy males participated in the study, each subject gave his written informed consent prior to the commencement of the experimental procedures. None of the subjects had cardiovascular or pulmonary disease, and none took any drugs during this period. The subjects refrained from heavy exercise and from consuming caffeinated or alcohol beverages for at lease 24 hours before the test. All subjects lived at an altitude of about 80m, and none was acclimatized to high altitute before the experiment.

2.2 Experimental protocol

The experiment was given in a quiet, environmentally controlled laboratory. Every training lasted 150 minutes in a day. It's divided into six consecutive experimental periods, three rest period of 30 min for each and three exercise period of 20 min for each, the rest and exercise period was across, as was shown in Figure 1.The first three days belonged to an progress course, the other days belong to the maintain course. The subjects completed rest measurement with the upright sitting position in hypoxia cabin, they exercised with the bicycle.

All data were acquired using an analog-to-digital converter interfaced with a computer. Measured R-R intervals were determined from the electrocardiogram, there's a HR data of one experiment in Figure 2. HR variability data were sampled at 1000 Hz and stored for subsequent analysis. Arterial oxygen saturation SaO_2 was monitored using a portable monitor, the SaO_2 probe was set on the right index finger.

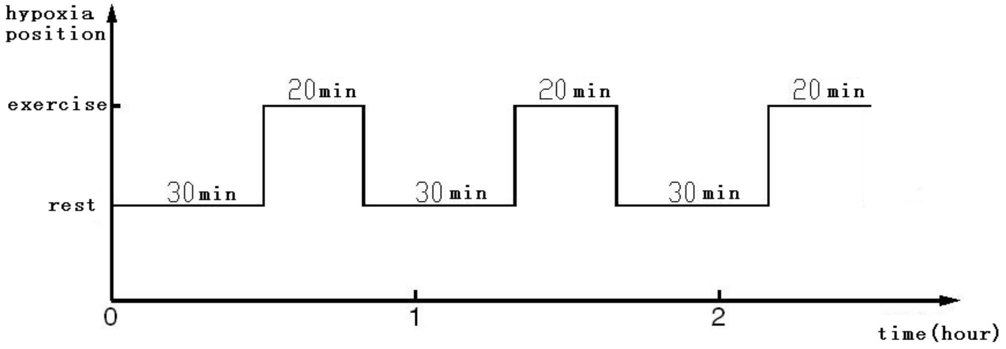


Figure 1. Schematic Diagram of Experiment Protocol

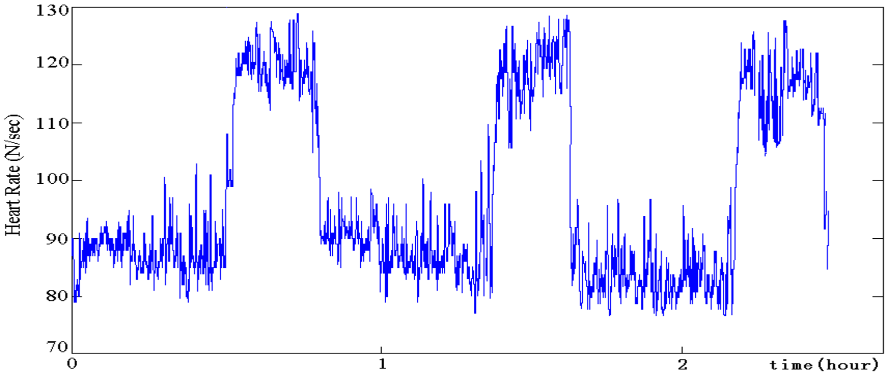


Figure 2. Heart Rate Data of an Experiment

2.3 Sample entropy

Sample entropy is a algorithm to measure the complexity of time sequence, which is developed by Richwman based on approximate entropy [8]. Sample entropy has two important properties. First, it is simpler than the approximate entropy algorithm, that is because of the largely independent on the record length and eliminate self-matches. Second, the meaning of sample entropy is the rate of generation of new information, which can be applied to the typically short and noisy time series of clinical data. This method was used to analysis the neonatal heart rate variability [4].

For a time series of N points, u(1),u(2),⋯u(N),sample entropy was proceed as follows[8]:

(1) forms the N-m+1 vectors Xm(i) for i=1~N-m+1, where Xm(i)= [u(i),u(i+1),⋯ u(i+m-1)] is the vector of m data points from u(i) to u(i+m-1).

(2) The distance between two such vectors is defined to be d[x(i),x(j)] =max[u(i+k)-u(j+k)], i, j=1~N-m+1,k=1~m-1. It is the maximum difference of their corresponding scalar components.

(3) Let Bi be the number of vectors Xm(j) within r of Xm(i) and let Ai be the number of vectors Xm+1(j) within r of Xm+1(j). Define the function

$$B_i^m(r)=\frac{B_i}{N-m}$$

In calculating $B_i^m(r)$, the vector Xm(i) is called the template, and an instance where a vector Xm(j) is within r of it is called a template match. $B_i^m(r)$ is the probability that any vector Xm(j) is within r of Xm(i).

(4) Calculate the average of the natural logarithms of the functions $B_i^m(r)$

$$B^m(r)=\frac{1}{N-m+1}\sum_{i=1}^{N-m+1}B_i^m(r)$$

(5) Let m change to m+1, repeat the above steps to calculate $B_i^{m+1}(r)$.

(6) Theoretically, the sample entropy of this series is

$$SampEn(m,r) = \lim_{N\to\infty}\left\{-\ln\left[\frac{B^{m+1}(r)}{B^{m}(r)}\right]\right\}$$

(7) When the length of this time series N is limited, the above formula can be estimated by

$$SampEn(m,r,N) = -\ln\left[\frac{B^{m+1}(r)}{B^{m}(r)}\right]$$

It is important to choose two parameters: r and m. For larger m, too much calculation are given, time will be long. In general, m is 1or 2. For smaller r values, one usually achieves poor conditional probability estimate, while for larger r values, too much detailed system information is lost. Pincus give a preliminary conclusion that to produce reasonable statistical validity, the range of r was from 0.1 to 0.2 SD of the u(i) [9]. In this research, r chooses 0.2 SD of u(i), m chooses 2.

2.4 Statistical analysis

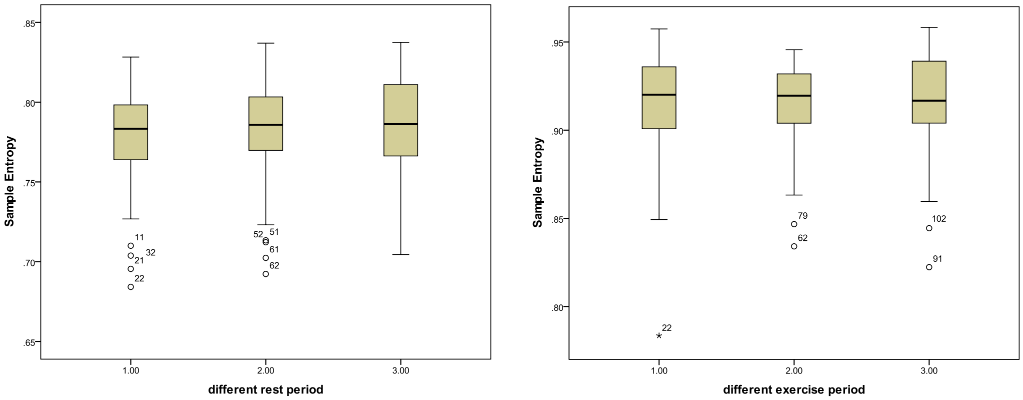
The middle 5 min heart rate signal of every period was chosen to insure the tranquilization. To every selected heart rate data, the sample entropy was computed as introduced before.

The SPSS software for Windows was used for calculations. Changes in Sample entropy associated with rest or exercise were estimated with Student t test. The results were denoted as an arithmetic mean and standard deviation. Differences below the confidence limit α =5% were considered statistically significant.

3. Result

3.1 Contrast of three different periods

The analysis to sample entropy of the three different rest periods in one experiment indicated there’s no statistical difference among them. The same result was received in the three different exercise periods too. The results were shown in Figure 3.

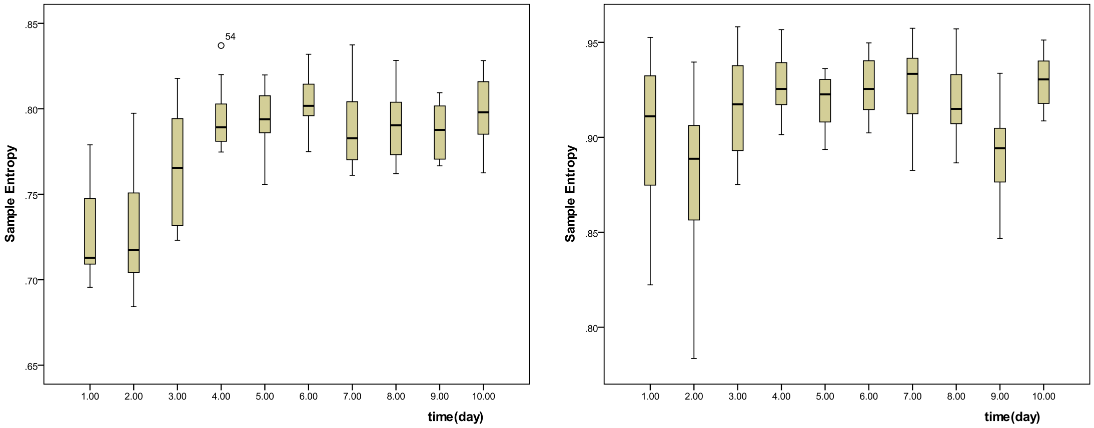


(a) (b)

Figure 3. Contrast of three different periods. (a). rest period, (b).exercise period

3.2 Contrast of 10 days difference

The difference of sample entropy was shown in Figure 4. In the first three days, sample entropy was increasing, the other days, actually it's after acclimation, although there was fluctuation, it arrived to a stability area ultimately.



(a). (b).

Figure 4. 10 days tendency of Sample Entropy (a). rest period, (b).exercise period

3.3 Contrast of rest and exercise period

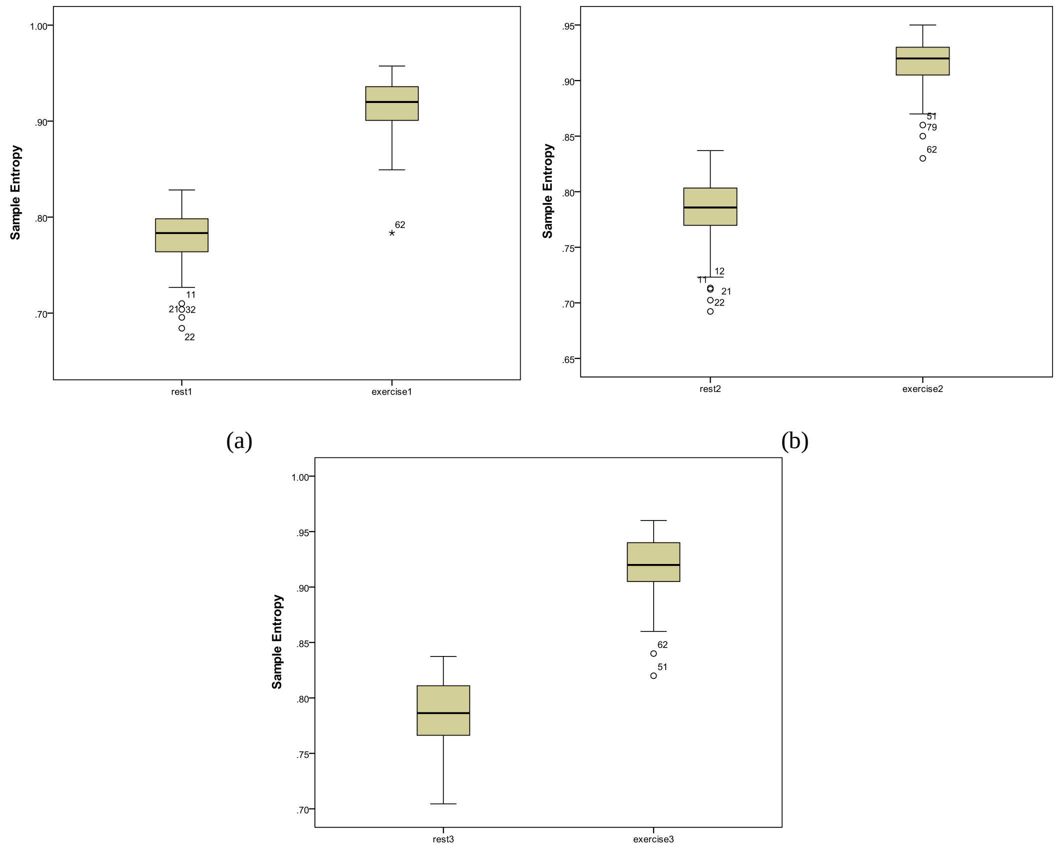
The stable days were chosen, sample entropy of the rest and exercise periods were compared, There was statistical difference between them, as was shown in Figure 5.

4. Discussion

HRV is one of the noninvasive and real-time evaluation parameter of autonomic nervous system. HRV is the beat to beat alteration of the R-R intervals in an electrocardiogram, and it's the consequence of heart rate modulation by both branches of the autonomic nervous system. HRV can be reduced in stressful situations, such as exposure to hypoxia, while the heart rate is increased at the same time [6]. It is a non-invasive indicator of cardiac activity, previous observations on HRV suggest increased sympathetic and decreased parasympathetic modulation in altitude [10].

According to some researchers, the reduction in the responsiveness of the autonomic nervous system can indicate an inability of the body to adapt to challenging conditions, such as exposure to hypobaric hypoxia [3]. While in another article, the low responsiveness of the autonomic nervous system at high altitudes was regarded as an advantage in the protection of the organs against an excessive and uninterrupted sympathetic stimulation during a long stay at high altitudes [6].

Most studies explored autonomic nervous activity by assessing HRV through time or frequency domain [11, 12]. Power of HRV was quantified by determining the areas of the spectrum in two component widths: LF and HF. High-frequency components are considered to be associated solely with cardiac parasympathetic activity, whereas the low-frequency components are associated with both parasympathetic and sympathetic activity. The LF/HF ratio is an index of cardiac sympathetic tone [11].



(a) (b)

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(c)

Figure 5. compare of three rest and exercise periods .(a)the first rest and exercise periods,(b)the second rest and exercise periods, (c)the third rest and exercise periods

The influence of hypoxia on heart rate variability has been studied under resting conditions with mixed results. Differences have been found in physiological responses to normobaric versus hypobaric hypoxia. Petra Zupet investigated the influence of hypoxia to pilot, his aim was to study the influence of hypobaric hypoxia on HRV during physical exercise to determine whether HRV changes due to the exercise-induced heart rate (HR) increase or whether hypoxia itself exerts an influence. His results indicated that hypobaric hypoxia itself exerts an influence on HRV at a moderate HR [6]. Jason studied the intermittent hypoxia and respiratory plasticity, to make sure the effect of intermittent hypoxia exposure to sleep apnea [13].

Buchheit observed the HRV responses to acute hypoxia at rest and during exercise to infer sympathovagal balance from it. He used a standardized hypoxic tolerance test, the exercise was moderate exercise. All absolute HRV indexes were strongly reduced during exercise with no further changes under additional stimulus of hypoxia. His research indicated a vagal control withdrawal under hypoxia at rest, HRV indexes can not adequately represent cardiac autonomic adaptation to acute hypoxia, due to the dominate effect of exercise [5]. But his research used the hypoxia veil, there were probably some differences between hypoxia veil and hypoxia chamber.

Camilo Povea took stock of the changes in HRV arosed by an intermittent exposure to hypoxia in 20 national elite athletes, evaluated the difference between two groups: LLTL(live low, train low) and LHTL(live high, train low). Acclimatization modified the correlation between the ventilatory response to hypoxia at rest. The increase in total power suggests that intermittent hypoxic increased the response of the autonomic nervous system mainly through increased sympathetic activity. Exposure to acute hypoxia during exercise resulted in a significant decrease in spectral components of HRV in comparison with exercise in normoxia [14].

Sample entropy is a nonlinear signal processing method, it’s easy to be computed. It’s used as a measurement of signal complexity here, to evaluate the dynamical system components of heart rate variability in simulated hypoxia. The nonlinear methods differ from the linear measures in that they do not attempt to assess the magnitude of HRV but instead describe the complexity or fractal dynamics of R-R intervals. Undoubtedly, nonlinear analysis methods may provide a different picture of HR behavior and more valuable information regarding cardiovascular regulation that is not obtainable with conventional linear methods. Among numerous nonlinear indexes, sample entropy are commonly used to uncover complexity in HR dynamics [15].

Frequency domain analysis of HRV dissects sympathetic and parasympathetic activity [6, 14], but it is very sensitive to data point missing [16, 17]. Loss of data point is irrelevant to the calculation of Sample Entropy, the research of [18] shown that Sample Entropy little affected by loss of more than one-third of the data. The finding is consistent with other results presented here that Sample Entropy of HR records reports on spikes as well as regularity. It is surprising, since loss of small amounts of data significantly impaired the detection of regularity in truly deterministic data. But missing data is the practical limit that everyone might encounter, so not sensitive to missing points is a good character to Sample entropy analysis of HRV.

Cardiovascular autonomic nerve modulation and balance will be changed by acute exposure to normobaric hypoxia. Increased sympathetic vasomotor activity will be induced by hypoxia, and an increased heart rate will appear by sympathetic dominance on the cardiac autonomic nerve activity. These modulations were displayed through the change of sample entropy. When first go to intermittent hypoxia, the balance of cardiovascular autonomic nervures system was broken, that was incorporated by the increasing of sample entropy at the first days. Then, after progress course, new balance was rebuilt again, acclimation changed the vitality of sympathetic nerve and parasympathetic nerve, so the sample entropy only changed in a small area finally.

Exercise was another important influence factor to cardiovascular autonomic nerve system. During exercise periods, the Sample Entropy was strongly higher than the rest periods. The analogous results can be found from [14], which says exercise during hypoxia causes an important supplementary desaturation in comparison to rest in hypoxia and an additional decrease in HRV in comparison to exercise in normoxia. Exercise in hypoxia also causes an additional increase in the sympathoadrenergic response in comparison to the same effort in normoxia.

5. Conclusion

In this research, changes of heart rate variability induced by exposure to intermittent hypoxia during exercise and rest were estimated in healthy males. Sample entropy was used to analysis heart rate signal, the outcomes of this research illuminated that hypoxia per se affects the functioning of the autonomic nervous system under the simulated hypoxia conditions, especially with the collaborate of exercise. Further studies are needed to substantiate the results, especially to different intermittent altitude and more subjects. Sample entropy and other nonlinear methods could be useful tools to study hypoxia acclimation.

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