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ORGINAL RESEARCH

Alterations in autonomic nervous control of heart rate among tourists at 2700 and 3700 m above sea level

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Objectives.—Many travelers who are not specially trained for activities at high altitude are at risk of physical problems, including cardiovascular disorders, when exposed to high-altitude environments. In the present study, we investigated how actual acute exposure to altitudes of 2700 and 3700 m affected the autonomic nervous control of heart rate in untrained office workers.

Methods.—Physiological parameters (heart rate, respiratory rate, arterial blood oxygen saturation, and end-expiratory carbon dioxide tension) were measured at sea level, 2700 m, and 3700 m. The power of heart rate variability was quantified by determining the areas of the spectrum in 2 component widths: low frequency (LF; 0.04–0.15 Hz) and high frequency (HF; 0.15–0.5 Hz). The ratio of LF power to HF power (LF:HF), which is considered to be an index of cardiac sympathetic tone, was also assessed.

Results.—Both HF and LF heart rate variability decreased according to the elevation of altitude. High- and low-frequency powers at 3700 m were significantly lower than those at sea level ($P < .01$ for HF, $P < .05$ for LF). The LF:HF ratio at 2700 m was not significantly different from that at sea level. However, it was significantly increased at 3700 m ($P < .01$).

Conclusions.—At 2700 and 3700 m, the activity of the autonomic nervous system measured by heart rate variability was decreased in untrained office workers. The sympathetic nervous system was dominant to the parasympathetic at 3700 m. These alterations in the autonomic nervous system might play some role in physical fitness at high altitudes.

Key words: heart rate variability, highland trekking, spectrum analysis

Introduction

Because of advances in transport technology, a large number of travelers are able to visit a moderate altitude of approximately 3000 m above sea level without any difficulty. This traveling population may include older people and people with medical problems. Although previous reports demonstrated that acclimatization to a high altitude requires a relatively long exposure time,[1] most travelers do not have enough time to adapt to the environment, where the oxygen tension is lower than that of sea level. Accordingly, many travelers who are not specially trained for activities at high altitudes are at risk for physical problems, including high-altitude disorders.[2] In a previous study, we demonstrated that the rate pressure product (heart rate multiplied by mean blood pressure, an indicator of oxygen demand of the heart) increased at a moderate altitude and more than doubled after exercise at 3700 m.[3] Electrocardiographic abnormalities were also observed in some cases. The results suggested that the oxygenation status of the heart might be at risk in many travelers and workers at an altitude of approximately 3000 m.

Recent technological advances in physiological monitoring have made it possible to evaluate the activities of autonomic nervous systems noninvasively and in a real-time manner.[4] Heart rate variability, which is the beat-to-beat alteration of the R-R intervals in an electrocardiogram, is commonly used to monitor autonomic nervous system activities.[5] In this method, the time se-

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ries of R-R interval data is analyzed by the fast Fourier transformation method for spectral analysis[5] or by a combination of the maximum-entropy method for spectral analysis and the nonlinear least squares method for fitting analysis, as described previously.[6,7] Power of heart rate variability was quantified by determining the areas of the spectrum in 2 component widths: low frequency (LF; 0.04–0.15 Hz) and high frequency (HF; 0.15–0.4 Hz). High-frequency components are considered to be associated solely with cardiac parasympathetic activity, whereas the LF components are associated with both parasympathetic and sympathetic activity.[8] The ratio of LF power to HF power (LF:HF) is an index of cardiac sympathetic tone.

The reliability of this method has already been examined in various studies, including large-scale studies regarding ischemic heart disease.[9] A recent multicenter study trial, named ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction), revealed that the measurement of heart rate variability is useful in assessing the activity of the autonomic nervous system and in predicting the risk of life-threatening arrhythmias in ischemic heart disease patients.[10] Rovere et al[10] described that the depressed autonomic nervous system responsiveness has significant prognostic value for cardiac mortality after myocardial infarction. Several other studies demonstrated positive correlation between the heart rate variability change and cardiac mortality.[11,12] Therefore, it is possible that such estimation of the autonomic nervous system activity is helpful for understanding the risk of circulatory disorders among travelers at a moderate or high altitude.

Until now, however, a limited number of studies have investigated the alteration of autonomic nervous system activity at high altitudes by heart rate variability measurement. Hughson et al[13] demonstrated changes in heart rate variability in subjects exposed to an altitude higher than 4000 m for more than 10 days. Farinelli et al[14] and Perini et al[15] independently reported changes in autonomic regulation of heart rate among trekkers exposed to 5050 m for almost a month. However, these studies were conducted for the purpose of studying the physiological changes during gradual high altitude acclimatization, therefore it is impossible to apply these conclusions to untrained trekkers who are exposed acutely to high altitudes. More recently, Yamamoto et al[16] described the effects of acute exposure to simulated altitude on heart rate variability by using a hypobaric chamber. In the present study, to assess the alteration in autonomic nervous control of the heart during high-altitude traveling, we investigated how actual acute exposure to altitudes of 2700 and 3700 m affect the heart rate variability of untrained office workers with no habitual physical exercise regimen.

Subjects and methods

The approval of the local human ethics committee and the informed consent of the experimental subjects were obtained prior to this study. The total number of subjects in the study was 36, and the subjects were divided into 3 groups. Each of the 3 groups consisted of completely different subjects. All of the subjects were office workers with no habitual physical exercise regimen, and none of the subjects had been exposed to an altitude above 2000 m within a year prior to the study. None of the subjects had medical complications, such as cardiovascular and pulmonary diseases, and none smoked. Physiological parameters were measured at sea level, 2700 m, and 3700 m. The barometric pressures at these altitudes were 760, 540, and 480 mm Hg, respectively. In the experiments at 2700 m and 3700 m, subjects reached 1500 m and 2500 m by car, respectively, and ascended another 1200 m on foot, trekking for 4 hours without any weight load. In both cases, total duration times required for the ascent from sea level to 2700 m or 3700 m were approximately 6 hours. All of the experiments were performed in wind-sealed constructions, and the temperature was maintained at 18° Celsius. After arrival at a new altitude, the subjects were permitted 2 hours of resting time prior to experimental measurements.

Electrocardiograms were recorded with standard limb lead II (MWM01; GMS Inc, Tokyo, Japan) and were analyzed by the MemCalc system (MemCalc, TARAWA/WIN; GMC) on an on-line computer (FMV-MC30; Fujitsu Inc, Tokyo, Japan). In the program, the time series of R-R interval data was analyzed by the maximum-entropy method with high resolution as described previously.[17] Power of heart rate variability was quantified by determining the areas of the spectrum in 2 component widths: LF (0.04–0.15 Hz) and HF (0.15–0.5 Hz).[18] The ratio of LF power to HF power (LF:HF) was also assessed. Arterial blood oxygen saturation (Spo_2), end-expiratory carbon dioxide tension ($Etco_2$), and respiratory rate were monitored using a handheld intensive care monitor (NPB-75; Nellcor Puritan Bennett Inc, Pleasanton, CA). An Spo_2 probe was set on the right index finger, and airway gas was sampled through a dual-inlet nostril cannula. During the measurement, subjects were resting quietly in supine, and were shielded against auditory and visual stimulation. Subjects were advised to breath regularly without intermittent deep breaths. Data were collected after the stable electrocardiographic baseline was recorded for 10 minutes.

All data except demographics are expressed as mean

Data recorded at sea level, 2700 m, and 3700 m*

	Altitude		
	0 m	*2700 m*	*3700 m*
Age (y)	31 ± 5	35 ± 5	34 ± 14
No. of men/No. of women	7/5	7/5	7/5
Heart rate (beats/min)	70 ± 10	78 ± 9	89 ± 10†
Respiration rate (breaths/min)	11 ± 1	12 ± 1‡	14 ± 2‡
Spo_2 (%)	98 ± 1	94 ± 2	81 ± 6§
$Etco_2$ (mm Hg)	35 ± 2	34 ± 3	31 ± 2‖

*Values are reported as mean ± SD. Spo_2 indicates arterial blood saturation; $Etco_2$, end-expiratory carbon dioxide tension.

†Significant change compared with the value at 0 m ($P < .01$) and 2700 m ($P < .05$).

‡Significant change compared with the value at 0 m ($P < .01$).

§Significant change compared with the value at 0 m and 2700 m ($P < .01$).

‖Significant change compared with the value at 0 m ($P < .05$).

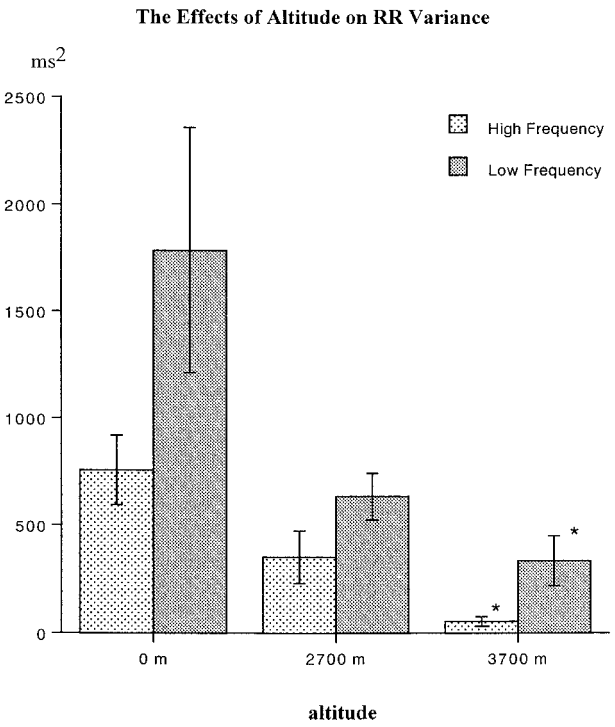

Figure 1. The effects of altitude on R-R variance. Both high- and low-frequency heart rate variability decreased according to the elevation of altitude. High- and low-frequency powers at 3700 m were significantly lower than those at sea level (asterisk indicates $P < .01$ for high frequency, $P < .05$ for low frequency).

± SEM. Statistical comparisons of mean values were assessed using analysis of variance with a Scheffe modification.

Results

No significant difference was found between groups for age and gender distribution (Table). No subject had symptoms of high-altitude sickness at the time of measurement. Two subjects at 3700 m complained of slight headaches immediately after arrival at the altitude, but the symptoms dissipated within 30 minutes without medical therapy.

Heart rates increased according to the altitude. At 3700 m above sea level, the value was significantly higher than that at sea level ($P < .01$) and 2700 m ($P < .05$). Respiratory rate was also slightly increased at 2700 m and 3700 m compared to the value at sea level ($P < .01$). Both Spo_2 and $Etco_2$ decreased at 3700 m compared to the values at sea level ($P < .01$ for Spo_2 and $P < .05$ for $Etco_2$) (Table).

None of the subjects showed signs of electrocardiographic abnormalities, such as premature ventricular beats or ST-T segment change, even at high altitudes. Both HF and LF heart rate variability decreased at 2700 and 3700 m. High- and low-frequency powers at 3700 m were significantly lower than those at sea level (Figure 1; $P < .01$ for HF, $P < .05$ for LF). The LF:HF ratio at 2700 m was not significantly different from that at sea level. However, it acutely increased according to the elevation from 2700 to 3700 m (Figure 2; $P < .01$).

Discussion

Acute exposure to high altitude induces abrupt physiological change in the untrained human. In this study, we observed alterations in heart rates, respiratory rates, Spo_2, and $Etco_2$. These alterations are consistent with the results of previous studies.[1,2] The results of this study demonstrated that heart rate variability, an indicator of the activity of the autonomic nervous system, was also altered by exposure to altitudes of 2700 and 3700 m above sea level.

Few reports describing alterations in activity of the autonomic nervous system measured by heart rate variability have been published to date. Hughson et al[13] studied the effect of long-term exposure to an altitude above 4000 m and the role of the β-adrenergic system in high-altitude acclimatization. They observed increased sympathetic nervous system and decreased parasympathetic nervous system activities in the early phase of acclimatization. Farinelli et al[14] and Perini et al[15] in-

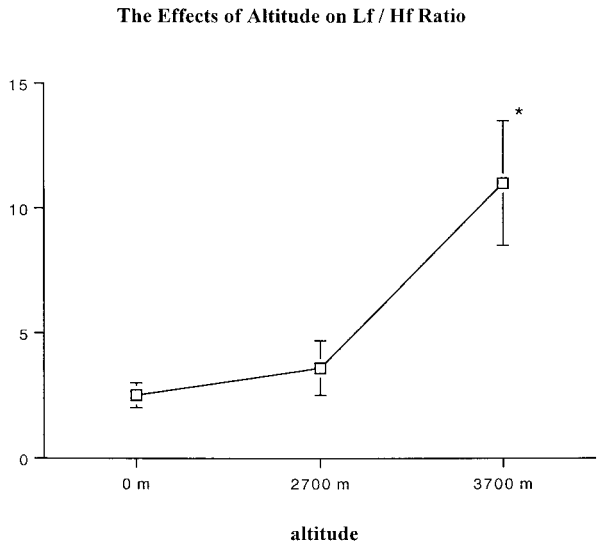

Figure 2. The effects of altitude on low-frequency (LF)-high-frequency (HF) ratio. The LF:HF ratio at 2700 m was not significantly different from that at sea level, but was acutely increased according to the elevation from 2700 m to 3700 m (asterisk indicates $P < .01$).

dependently reported alterations in heart rate variability during a long-term sojourn above 5000 m. Both of these studies demonstrated that the sympathetic system is dominant compared to the parasympathetic at a high altitude. Recently, Yamamoto et al[16] reported that exercise in a hypobaric chamber comparable to the altitude of 3500 m provoked an increase in the sympathetic nervous system indicator and a decrease in the parasympathetic nervous system indicator. Since these studies were conducted under completely different circumstances, it is impractical to compare the results of these studies directly. However, overall trends of these results indicate that the sympathetic nervous system is dominant compared to the parasympathetic system at high altitude. The drastic increase in the LF:HF ratio observed in our study is also consistent with this finding.

Hyperactivity of the sympathetic nervous system and down-regulation of the β-adrenergic receptor system has already been established as a phenomenon observed during high-altitude acclimatization.[2] This alteration is considered to be beneficial in protecting organs, including the heart, from long-term sympathetic stimulation at high altitude. Several previous studies, conducted before the development of heart rate variability analysis, demonstrated the phenomenon with various sophisticated approaches.[19–21] Maher et al[19] measured the concentration of plasma catecholamines and β-adrenergic responsiveness of the heart in dogs. Voelkel et al[20] and Light et al[21] independently reported down-regulation of the cardiac β-adrenergic receptors in rats and guinea pigs. Recent studies with heart rate variability measurement further support the previous findings by the novel noninvasive machinery. This noninvasive and convenient measurement might facilitate study of the autonomic nervous system at high altitude.

The effect of acute exposure to higher altitudes on heart rate variability has been assessed previously only by Yamamoto et al.[16] In their experiments using a hypobaric chamber, the effect of higher altitudes was observed only after an exercise load. The resting values of heart rate variability were not influenced by the simulated altitude exposure. The results of our study were not consistent with those of Yamamoto et al. However, the differences in these results may be explained by the significant differences in the ages of subjects and the altitude-exposure protocol. In the present study, to simulate the situation of office workers participating in a trek, we adopted the actual exposure to altitudes after 4 hours of trekking. Although the data in this study were obtained after a resting period of 2 hours, the physical workload during the ascent and the psychological effects of the actual stay at high altitude must have some significant effects on the physiological parameters at high altitudes. In a previous study, we found that exercise at altitudes around 3000 m induced a drastic decrease in Spo_2 and cerebral regional oxygen saturation measured by a near-infrared spectrophotometer.[22] Although we did not measure the effect of workload in the present study, it is highly possible that additional physical exertion provokes further alteration in the autonomic nervous system activity as measured by heart rate variability.

In the present study, both HF and LF powers were decreased at 3700 m above sea level. Changes in respiratory mode have been reported to influence heart rate variability, especially high-frequency components.[23,24] However, considering that the changes in respiratory rate in this study were minor, and the subjects in this study were breathing regularly without deep breaths, the effects of respiration on the heart rate variability would be minimal.

A reduction in heart rate variability has been noted after both major surgery[25] and myocardial infarction.[9] Some researchers have proposed that a decrease in heart rate variability indicates a reduction in the autonomic nervous system responsiveness and an inability to adapt the body to challenging conditions.[9,11,12] In contrast, previous studies implied that the low responsiveness of the autonomic nervous system at a high altitude could be advantageous in protecting organs from excessive and continuous sympathetic stimulation during a long-term stay at high altitude.[20] Since the number of subjects in this study was limited, it is impossible to relate the re-

duction in heart rate variability observed in this study and the risks of high-altitude trekking of untrained office workers. A larger scale study is needed to clarify the mechanism of alterations in the autonomic nervous system. The alterations found immediately after a high-altitude exposure and those noted during a long-term stay at high altitude may be different and may be derived from different mechanisms. A thorough understanding of the alterations in the autonomic nervous system at high altitudes could prove helpful in determining a safe strategy for high-altitude traveling.

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