Time Course of Change in the Level of Autonomic Nervous Activity during the Exposure to High Altitude Environment

Yuji Takemura, Hisashi Hirose
and Shigeru Sugano

Department of Animal Environmental Physiology, Faculty of Agriculture, The University of Tokyo, Bunkyo-ku, Tokyo 113

(Received November 11, 1985)

Abstract An attempt was made to elucidate how the autonomic nervous activity of animals alters with the progress of exposure to a high altitude environment. Six out of 30 male Wistar rats were examined at 5 weeks old. The others were exposed to a hypobaric-hypoxic condition equivalent to 2,500 m in altitude (barometric pressure 561 mmHg, partial pressure of oxygen 117 mmHg; exposed group, n=12) or to a normobaric-normoxic condition equivalent to the sea level (barometric pressure 760 mmHg, partial pressure of oxygen 159 mmHg; control group, n=12) in a control chamber, and 6 animals of each group were examined after the 3- and the 6-week-exposure, respectively. Heart rates of animals after the 4 kinds of treatments were examined under a normobaric-normoxic condition: 1) heart rate after sympathetic blockade (HRsx) by propranolol (4 mg/kg, i. p.); 2) heart rate after parasympathetic blockade (HRpx) by atropine (2 mg/kg, i. p.); 3) heart rate after sympathetic and parasympathetic blockade (HRspx) by propranolol and atropine (4 and 2 mg/kg, respectively, i. p.); 4) heart rate after control treatment (HRsp) by saline (1 ml/kg, i. p.). The HRspx of the exposed group was lower than that of the control group after the 3-week-exposure. The level of HRsp was higher than that of HRspx in both the control and the exposed group, and the difference between HRsp and HRspx became larger in the exposed group than in the control group during the first 3 weeks of exposure but contrarily smaller during the latter 3 weeks. The difference between HRpx and HRspx became larger during the first 3 weeks but contrarily smaller during the latter 3 weeks. The difference between HRsx and HRspx became smaller during the first 3 weeks but contrarily larger during the latter 3 weeks. It was suggested from the results obtained that at the early stage of exposure to high altitude, the balance of the autonomic nervous activity shifted to the direction that the sympathetic nervous activity became preponderant, but thereafter, contrarily to the direction that the parasympathetic nervous activity became preponderant.


Key words: high altitude, autonomic activity, autonomic blockade, heart rate, rat.

In our previous reports1,2,3), we suggested that the autonomic nervous function of animals was influenced by a high altitude environment, that is, the activity of the autonomic nervous system was altered with the progress of exposure to high altitude. In recent years, the examination of the effect of autonomic nervous blockade on heart rate has been attempted to estimate the autonomic nervous function4,5). In this study,
therefore, we observed the heart rates after the sympathetic and/or parasympathetic nervous blockades in the rats chronically exposed to simulated high altitude and tried to elucidate how the autonomic nervous activity of animals alters with the progress of exposure to high altitude.

**Materials and Methods**

Thirty male Wistar rats were raised for one week preliminarily from 4 to 5 weeks old in a control chamber (Shimadzu, SCA 102 Z)* under a normobaric-normoxic condition (barometric pressure 760 mmHg, partial pressure of oxygen 159 mmHg, simulated sea level), and then divided into the following 5 groups (6 animals in each group): C₀, non-exposed and examined at 5 weeks old; T₃, T₆, exposed to a hypobaric-hypoxic condition (barometric pressure 561 mmHg, partial pressure of oxygen 117 mmHg, simulated high altitude equivalent to 2,500 m above the sea level) and examined after the 3- and the 6-week-exposure (8 and 11 weeks old), respectively; C₃, C₆, control groups for T₃ and T₆, respectively, raised under the normobaric-normoxic condition. In both simulative conditions, ambient temperature, relative humidity and CO₂ concentration were continuously maintained at 25°C, 60% and 500-1,500 ppm, respectively, and light control (12 L: 12 D in 100 lux) was also performed. The exposed groups were returned to the normobaric-normoxic condition every 2 days for about 1.5 hours to be managed with the control groups. The animals were raised in solid bottom plastic cages (3 animals in each cage). They were fed commercial pellet (CLEA Japan Inc., CE-2) and watered ad libitum.

All examinations were carried out in the laboratory room, the temperature of which was controlled at 25°C, under a normobaric-normoxic condition out of the chamber. The heart rates after the 4 kinds of treatments (abbreviated as follows) were examined on the animals under an unanesthetized condition: 1) heart rate after sympathetic nervous blockade (HRsx) by the intraperitoneal administration of dl-propranolol (SIGMA Chemical Co., 4 mg/kg); 2) heart rate after parasympathetic nervous blockade (HRpx) by the intraperitoneal administration of atropine sulfate (Tokyokaseikogyo Co., 2 mg/kg); 3) heart rate after sympathetic and parasympathetic nervous blockade (HRspx) by the intraperitoneal administration of the combined doses of propranolol and atropine (4 and 2 mg/kg, respectively); 4) heart rate after control treatment (HRsp) by the intraperitoneal administration of saline (1 ml/kg). The doses of the blocking agents were determined according to our preliminary examinations and referring to other investigators’ reports in rats. The drugs used in 1), 2) and 3) were dissolved in distilled water and the administration volume was arranged at 1 ml per 1 kg of body weight. For each animal, one of those examinations was made per day at a fixed time. All the examinations were completed in both the control and the exposed group within the same successive 4 days. The order of the treatments was randomized to eliminate the influence of the habituation of the animal to the examination.

---

*: installed in the Center of Environment Regulation System for Biology, Faculty of Agriculture, The University of Tokyo.
After each treatment, the animal was confined in a Bollman's cage and needle electrodes were attached subcutaneously. Electrocardiogram in II limb lead was recorded with a biophysiograph (San-ei, 180 system) every 5 minutes during the 40 minutes after the onset of the treatment. Heart rate (beats/min) was determined as the multiple of 10 by the count of the heart beats in the 6 seconds of electrocardiographic recording.

**Results**

Heart rate changes during the 40 minutes after the sympathetic and/or parasympathetic nervous blockades are shown in Fig. 1. The change in HRspx was very smaller than those in HRsx, HRpx and HRsp. The heart rate after the sympathetic and parasympathetic nervous blockade is the heart rate due to the automatism of the heart and often called as intrinsic heart rate. In this report, therefore, intrinsic heart rate (IHR) is used instead of HRspx, hereafter. On the other hand, the heart rate of animals in normal condition is under the regulations of both the sympathetic and the parasympathetic nervous system, therefore, normal heart rate (NHR) is used instead of HRsp, hereafter.

Fig. 2 presents the changes in NHR and IHR during the 6 weeks exposure to simulated high altitude. After the 3-week-exposure, the IHR of the exposed group was significantly lower than that of the control group, however, no significant dif-

![Fig. 1](image-url)
High Altitude Environment and Autonomic Activity

Fig. 2. Changes in normal heart rate and intrinsic heart rate during the 6 weeks exposure to simulated high altitude. Each plot represents a mean±or−S.D. of 6 animals. The average heart rate during the 40 minutes observation was used as the representative value for each animal. *: significant difference between C₃ and T₃ by t-test (p<0.05).

Fig. 3. Changes in ΔHRₜ, ΔHRₛ and ΔHRₚ during the 6 weeks exposure to simulated high altitude. ΔHRₜ = HRₜ − IHR. ΔHRₛ = NHR − IHR. ΔHRₚ = HRₚ − IHR. Each plot represents a mean of 6 animals. The average heart rate change from IHR during the 40 minutes observation was used as the representative value for each animal. C₃T₃ = C₅T₅

- C₇C₇. C₆T₆ − T₃T₄ − C₇C₇. C₅C₅/T₃T₃.

Difference was observed in NHR between the two groups. After the 6-week-exposure, no differences were observed between the control and the exposed group in both NHR and IHR.

Differences between HRₜ and IHR, NHR and IHR, HRₛ and IHR were calculated and abbreviated as follows; ΔHRₜ: HRₜ − IHR. ΔHRₛ: NHR − IHR. ΔHRₚ: HRₛ − IHR. Changes in ΔHRₜ, ΔHRₛ and ΔHRₚ during the 6 weeks exposure to simulated high altitude are indicated in Fig. 3. By comparing the changing process in each parameter between the control and the exposed group, it was revealed that all the values of these parameters in the exposed group shifted to the plus direction during the first 3 weeks of exposure, but contrarily to the minus direction during the latter 3 weeks.

Discussion

ΔHRₜ and ΔHRₚ are considered to be the heart rate change from the IHR produced by the positive chronotropic action of the sympathetic nervous system and that produced by the negative chronotropic action of the parasympathetic nervous system, respectively, so that they are regarded respectively as the parameter indicating the
level of the sympathetic nervous activity (SNA) and that indicating the level of the parasympathetic nervous activity (PNA). On the other hand, $\Delta HR_{sp}$ is regarded as the parameter indicating the balance of the autonomic nervous activity, because it is considered to be the heart rate change due to the chronotropic actions of both the sympathetic and the parasympathetic nervous system. In this simulative study, all the values of these parameters were shifted by the exposure to the plus direction during the first 3 weeks but contrarily to the minus direction during the latter 3 weeks (Fig. 3). It is suggested from the results that at the early stage of exposure to high altitude, the balance of the autonomic nervous activity shifts to the direction that the SNA becomes preponderant owing to the facilitation in the SNA and the depression in the PNA, but thereafter, contrarily to the opposite direction that the PNA becomes preponderant owing to the depression in the SNA and the facilitation in the PNA. The changing process of the autonomic nervous activity obtained in the present study was in agreement with those obtained in our previous studies: We indicated in our study on the cattle raised at high altitude based on the somato-autonomic reactions that the SNA was facilitated by a high altitude environment especially at the early stage of residence at high altitude\(^2\); Moreover, we presumed in our simulative study on rats based on the cardiovascular responses to sympathomimetic and parasympathomimetic drugs that the SNA was facilitated but the PNA was depressed at the early stage of exposure to high altitude and both the SNA and the PNA were reciprocally altered with the progress of exposure\(^3\). It was confirmed by the present study that the balance of the autonomic nervous activity was altered with the progress of exposure to high altitude.

The exposed group showed a significantly lower IHR than the control group after the 3-week-exposure, but no difference was observed after the 6-week-exposure between the two groups. It is considered from the result that the cardiac function itself free from the regulation of the autonomic nervous system is also influenced by a high altitude environment. We reported previously in our study on rats carried out under the same experimental conditions with the present study\(^6\) that the relative weight of the right ventricular free wall to that of the left ventricular free wall plus the ventricular septum was greater in the exposed group than in the control group, but this tendency was more clearly observed after the 3-week-exposure than after the 6-week-exposure. These results suggest that the heart of animals is greatly influenced by a high altitude environment especially at the early stage of exposure to high altitude.

From the results obtained in this study, it was considered that in the adaptation to a high altitude environment, animals achieved the new stable conditions at high altitude after the process of the dynamical changes in the physiological functions not only of the regulation side but also of the effector one.

Acknowledgments

We are much grateful to Prof. Dr. Hiroshi SAWAZAKI, Faculty of Agriculture, The
High Altitude Environment and Autonomic Activity

University of Tokyo, for his helpful advice for this study.

References


高地環境暴露に伴う自律神経活動レベルの推移

竹村勇司・広瀬 昌・菅野 茂
東京大学農学部，東京都文京区 113

著者らは，先に，自律神経作動薬投与に対する心血管系反応に基づいて高気圧環境下での自律神経系の活動性に変
化の生じることを示唆したが，本研究では，自律神経系
の活動性と暴露期間との関係を明らかにするためにコン
トロールチェンバーを用いて実験を行なった。

Wistar 系雄ラット 30 匹を用い，6 匹を 5 週齢で試験
した後，12 匹を暴露群として標高 2,500 m 相当の低圧低
酸素分圧条件（気圧 561 mm Hg，酸素分圧 117 mm Hg）
下で，同数を対照群として海面相当の常圧常酸素分圧条
件（気圧 760 mm Hg，酸素分圧 159 mm Hg）下で飼育し，
両群とも 3 および 6 週間飼育した後に，各 6 匹ずつを試
験に供した。試験は常圧常酸素分圧条件下で行ない，動作
物に以下の 4 種類の処置を施した時心拍数を調べた。
1) 交感神経遮断（propranolol 4 mg/kg，i. p.）時心拍数
（HRsx）。2) 副交感神経遮断（atropine 2 mg/kg，i. p.）
時心拍数（HRax）。3) 両神経遮断（propranolol 4 mg お
および atropine 2 mg/kg，i. p.）時心拍数（HRspx）。4) 対照処置（saline 1 ml/kg，i. p.）時心拍数（HRsp）。

暴露群の HRspx は，対照群と比べ 3 週暴露後に低い
値を示した。両群とも HRsp のレベルは HRspx よりも
高く，その差は暴露の前半で暴露群が対照群と比べ大き
くなり，後半では逆に小さくなった。HRsx と HRspx と
の差は，暴露の前半で大きく，後半では逆に小さくなる。

以上の成績から，高地環境暴露の初期には，交感神経
活動レベルの上昇と副交感神経活動レベルの減少が生じ
るが，その後は，逆に交感神経活動レベルの減少と副交
感神経活動レベルの上昇が生じ，両神経の活性性のパラ
ンスは，暴露の時間経過に伴い変化することが示唆され
た。

日畜会報，57 (7): 608-613，1986