Prognozing of the Resistance to Hypoxia in Military Pilots by Cardiovascular and Respiratory Parameters

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SUMMARY

The effect of hypoxic hypoxia on the autonomic cardiovascular response pattern and the prognosis of resistance to hypoxia were determined after exposure to hypoxic hypoxia in barochamber at simulated altitude 5000 m in 21 military pilots. Cardiovascular: heart rate variability (HRV) measures, heart rate, systolic and diastolic blood pressure, and respiratory parameters: arterial oxygen saturation were examined in pre-hypoxic and post-hypoxic exposure. Although mean values of cardiovascular and respiratory parameters corresponded to referents, hypoxia caused significant effect on HRV measures, diastolic blood pressure, and arterial oxygen saturation. Military pilots were tolerant to hypoxia and did not reveal symptoms of cardiovascular collapse. Hypoxic exposure induced integrated reflex response revealed by significant dependences of the arterial oxygen saturation on spectral power of the R-R intervals in the Respiratory Sinus Arrhythmia band (vagally mediated), and of the diastolic blood pressure on spectral power of the R-R intervals in the Traube - Hering - Mayer band (sympathetically and parasympathetically mediated). In post-hypoxic exposure we observed a pattern of increased both sympathetic and parasympathetic activities with prevailing relative dominance of the vagal cardiac activity over sympathetic one on the control of heart rate variations revealed by significant increase of the mean value of R-R intervals. Prognostic significance for determining of resistance to hypoxia possessed spectral power of the R-R intervals in the Temperature band (sympathetically mediated), and the level of physical training assessed by HRV index - PS. Post-hypoxic sympathetic activity evaluated by P_T could be predicted by pre-hypoxic level of the percent arterial oxygen saturation and diastolic BP; predictor of the post-hypoxic level of the physical training was pre-hypoxic level of P_T and systolic BP.

INTRODUCTION

Physiological stress of the high altitude flight has been the subject of intensive human factors research in aviation medicine. The high altitude exposure characterizes with different from pilot's habitual environment physical and physiological features. During military operations while flying or during physiological training these specific features can lead to hypoxia or risk from Decompression Illness, Mountain Sickness, Pulmonary Barotrauma and Cerebral Arterial Gas Embolism.

Tolerance to hypoxic hypoxia is used to control the physiological training of military pilots and to define their flight performance. During high altitude exposure physiological adjustments that improve pilot's hypoxic tolerance can be evaluated, and alternatively the early symptoms of hypoxic intolerance, resp. pilots predisposed to Barotrauma or Decompression Illness can be detected.

Hypoxic hypoxia is caused by the reduced oxygen partial pressure in inspired air. Exposure to hypoxic hypoxia induces a process of immediate physiologic responses to maintain an adequate tissues oxygen supply: respiratory, cardiovascular, cerebrovascular and visual responses (1; 13; 39; 41; 56; 66). Regardless of permanent studies the response pattern of the autonomic cardiovascular control to hypoxic hypoxia, and its dependence on the arterial oxygen saturation, heart rate, and systolic and diastolic blood pressure for prognozing of the pilot's resistance to hypoxia is not fully determined.

EFFECT OF HYPOXIA ON AUTONOMIC CARDIOVASCULAR CONTROL ASSESSED BY HEART RATE VARIABILITY

Changes in the oxygen partial pressure in the arterial blood perfusing the brain and the peripheral chemoreceptors affect the heart through autonomic nervous control. These indirect effects of hypoxia are dominant and determine response of cardiovascular parameters. Results of available studies will be reported below. Noninvasive mode to study the autonomic cardiovascular control: sympathetic and parasympathetic activity is to analyze components of Heart Rate Variability (HRV): Temperature component of heart rate fluctuations in the frequency band 0.01 - 0.05 Hz, mediated by sympathetic activity (2; 32); Traube-Hering-Mayer (T-H-M) wave component of heart rate fluctuations in the frequency band 0.06 - 0.14 Hz, mediated by sympathetic and parasympathetic activity (2; 42; 50), and Respiratory Sinus Arrhythmia (RSA) component of heart rate fluctuations in the frequency band 0.15 - 0.50 Hz, mediated by parasympathetic activity (2; 31; 50).

Acute hypoxia modulates the sympathetic and parasympathetic cardiac activity (24; 56; 57; 74; 78) but the pattern of changes in both autonomic activities under altitude-induced exposure at rest is not fully defined. To our knowledge there are a few studies of the effect of altitude hypoxia on autonomic cardiovascular control in healthy subjects. Prevailing part of the studies of the effect of hypoxia on autonomic cardiac activity in healthy subjects revealed increase of the sympathetic stimulation accompanied with parasympathetic withdrawal or no effect of hypoxia on

autonomic cardiac control whereas in animal studies co-activation of the activities of both autonomic branches is observed.

Comparing the effect of an exposure to hypoxia at 5050 m on HRV components, with their sea level values by postural manipulations demonstrated high values of the sympathetically/parasympathetically mediated T-H-M-/RSA spectral ratio which could be attributed to a shift of the sympathovagal interaction at rest towards sympathetic dominance (48). 24 h effect of the hypoxic hypoxia in barochamber at the simulated altitude of 4500 m decreased the spectral power in the RSA band and reduced the values of the time-domain HRV measures: standard deviation of the R-R intervals, percentage of differences between successive R-R intervals larger than 50 msec and mean R-R intervals compared with normobaric conditions (78). Reduction of the HRV, assessed by interpolated R-R intervals using cubic splines was attributed to hypoxia caused by the impact of breathing gas mixtures with less than 99.5 % oxygen content during rapid decompression in hypobaric chamber from simulated altitude of 6096 to 15239 m (9).

Contrary to these results other studies revealed that the chemoreceptors modulation caused by hypobaric hypoxia in barochamber did not affect significantly spectral powers in the HRV components, the spectral power in the RSA-band/total spectral power ratio (considered the spectral marker of the parasympathetic activity), the spectral powers in the frequency bands 0.00-0.15 Hz/RSA-band ratio (considered the spectral marker of the sympathetic activity), and heart rate at rest whereas during exercise hypoxia the induced responses were modified: decrease of the spectral power in the RSA-band/total spectral power ratio and increase of the spectral power in the frequency band 0.00-0.15 Hz/RSA-band ratio and heart rate (75). Similar results examining Gamma scaling properties of long-term HRV revealed preserved intrinsic dynamic property of heart function as a result of exposure to hypoxia at 5050 m (43).

In animal studies activation of the chemoreflex in response to decreased oxygen partial pressure under hypoxia caused activation of both sympathetic and parasympathetic cardiac activity (27; 28). Stimulation of the chemoreceptors elicited a simultaneous increase in vagal and sympathetic activity to the heart but activity of which autonomic branch dominated was not determined; the suggestion was vagal origin of activity as cardiac responses were little affected by beta-adrenoreceptor blockade (14; 39). The influence of the respiratory activity upon the magnitude of the excitatory sympathetic reflex was less than upon the cardiovagal chemoreceptor reflex (14).

The effect of an acclimatization process was associated with physiological responses of different character: immediate and long-term adjustments to altitude that improve human's tolerance to altitude hypoxia (41) . Studying of the autonomic cardiovascular responses to acclimatization with pharmaceuticals in different altitude phases revealed immediate compensatory responses: increasing of the spectral powers of the cardiointervals (R-R intervals) in the temperature and the T-H-M band, and decreasing of/in: the spectral power of R-R intervals in the RSA band, the total spectral power, the mean value of the R-R intervals and their standard deviation indicating sympathetic stimulation together with parasympathetic withdrawal whereas long-term adaptations characterized with opposite changes in the HRV components indicating reduction of the adrenergic activity and increased parasympathetic activity (56). Similar results were reported on exposure to acute hypobaric hypoxia at 6000 m (24). Reduced cardiac sensitivity to adrenergic stimulation investigated by postural manipulations was observed under chronic hypoxia (one month stay at 5050 m): evidence for decreased vagal tone was declining of the spectral power of the R-R intervals in the RSA component with little or no change in sympathetic activity examined by the spectral power of the R-R intervals in the T-H-M component (40). Adaptive response to high altitude hypoxia characterized with preserved or enhanced vagal tone evidenced by higher value of the spectral power in the RSA component and lower value of the T-H-M-/RSA-band ratio in high-altitude residents at 4800 m compared to acclimatized low-landers (44; 47).

EFFECT OF HYPOXIA ON SYMPATHETIC AND PARASYMPATHETIC CONTROL ASSESSED BY CARDIOVASCULAR AND RESPIRATORY PARAMETERS

Related to specific changes in autonomic cardiovascular control examined by HRV are adjustments in the cardiovascular and respiratory parameters as their response activation was caused also by stimulation of the chemoreceptors. Chemoreceptors activation induces changes in the autonomic function. Reduction in arterial oxygen partial pressure (PaO2) in the arterial blood stimulates the peripheral chemoreceptors in the carotid and aortic bodies. The resultant increase in the frequency of impulses in the afferent nerve fibres from the chemoreceptors stimulates the vasoconstrictor regions. Parallelly with chemoreflex activation, changes in the PaO2 modulate ventilation, heart rate, arterial pressure, vascular resistance, cardiac output and myocardial contractility via autonomic function.

Resting tachycardiac response to acute hypoxia in healthy subjects was discussed as due to increased activity in the medullary sympathetic centers occuring after stimulation of the peripheral chemoreceptors (5; 22; 24; 64; 67; 71) and/or parasympathetic withdrawal (24; 34). The underlying sympathetic stimulation, inducing cardiac acceleration, increased with acute exposure to hypoxia (15; 40; 53; 60) followed by progressive blunting of the sympathetic response with prolonged hypoxic exposure (57; 58). These alterations affected heart rate: heart rate was maximal after a few days at altitude and then decreased due to declining of the cardiac response to adrenergic activation (56) but did not always return to its basal normoxic value (25; 33; 72). Hypoxic tachycardiac response was not found to be a result from impaired baroreceptor reflex cardiac function (14). Hypoxia did not affect the baroreceptors when the arterial blood pressure did not alter (14; 39). Contrary to sympathetic, parasympathetic heart rate response to acute hypoxia continued

to be controversial, some studies revealed vagal withdrawal (24; 34), other - vagal dominance (21; 23). In animals heart rate response to hypoxia was bradycardiac (30; 35; 39; 45; 61; 65).

Differential response of heart rate was observed at exercise in hypoxic conditions. Exercise at altitude was a predisposing factor for Decompression Sickness (DCS) (36; 49; 54; 62) due to probability of gas emboli formation related to work load levels. Prior exercise at anaerobic threshold was found to have protective: increased blood flow to muscles and tissues facilitated gas elimination, and adverse effects: increased microbubbles formation in critical tissues influencing the incidence of DCS (10; 37). Medical issues associated with the effect of low barometric pressure on pilots (hypoxia and symptoms of Decompression Sickness), and technical aspects of oxygen system, and cabin pressurization inducing oxygen pressure disturbances were discussed extensively (3; 6; 7; 46; 59; 66; 68; 69; 70). During exercise heart rate was increased in hypoxia for low and moderate workloads, and was decreased for near maximal and maximal workloads (16; 55; 73). Alterations in cardiovascular parameters: heart rate and mean blood pressure were apparent only after exercise load occured at approximately 3000 m (63). Short-term exposure to hypoxia in hypobaric chamber at 4000 to 5000 m induced acclimatization to altitude and improved aerobic endurance affecting mainly the adaptive respiratory and circulatory responses (8; 77).

Peripheral chemoreceptors are related to the respiratory control causing increased depth of breathing, increased respiratory rate and pronounced hyperventilation when arterial oxygen saturation (SaO_2) decreased to 93 % at an altitude of 2400 m (66). Arterial oxygen saturation depends on the oxygen partial pressure of the arterial blood (PaO2). SaO_2 was a reliable parameter for studying of the effect of hypoxia and for the acute hypoxic tolerance (76). Declining of SaO_2 to 87 % indicated a status when hypoxic symptoms were obvious; further declining to 65 % was considered as critical for aircrews (66). Under hypoxia oxyhemoglobin dissociation curve was shifted slight to the right that decreased the oxygen affinity of hemoglobin and facilitated the release of available oxygen to the tissues.

In aircrews, reflex cardiovascular response to hypoxia induced increase of heart rate and moderate increase of systolic blood pressure (BP) (66). In military pilots under hypoxic esposure at 5000 m could be observed except tachycardia, moderate increase of systolic BP with 3-18 mm Hg, and decrease or increase of diastolic BP with no more than 10 mm Hg; however in most of the cases hypoxia caused no effect on systolic and diastolic BP (13). Breathing hypoxic mixtures revealed either maintaining or increasing of BP (38). In healthy untrained subjects of a wide age range (6-83 yr) moderate altitude of 2950 m induced small but significant increase of BP (71). Alterations in cardiovascular parameters: icreased BP and heart rate, and acute reduction in cerebral regional oxygen saturation were found to occur only after exercise load at approximately 3000 m altitude in unacclimatized subjects (63).

Adaptation to high altitude hypoxia at 4800 m induced no effect on systolic BP (71). Chronic hypoxia at 5050 m resulted in higher resting systolic and diastolic BP that could be related to increased activity of the Sympathetic Nervous System (SNS) (25).

Reported results focussed on the effect of hypoxia in military pilots and healthy subjects indicated that cardiovascular and respiratory parameters are reliable and significant indicators for studying of the effect of hypoxia and for the determination of the acute hypoxic tolerance. Acute hypoxic exposure at 5000 m at rest affects the sympathetic and parasympathetic cardiac control but results showed that the response pattern is not fully determined. To our knowledge the research on the effect of hypoxic exposure on autonomic cardiovascular function in healthy subjects is not extensive as the research sources on that topic is relatively insufficient. The observed trends of changes in hypoxic response of the autonomic cardiac control are: sympathetic dominance with parasympathetic withdrawal; vagal withdrawal; preserved sympatho-vagal interaction. Contrary to these results Koizumi, Terui., Kollai (1983) and Koizumi, McBrooks (1984) revealed in response to chemoreflex activation induced by the decreased PaO2 in animals, non-reciprocal pattern of autonomic cardiovascular control of co-activation of both sympathetic and vagal activities, followed by reciprocal response with prevailing vagal control over sympathetic concerning the sinus node. Hypoxic tachycardiac response and increased BP in humans are considered to be modulated by the autonomic function and present similar pattern of change as autonomic cardiac control: increased activity in the medullary sympathetic centers and/or parasympathetic withdrawal. Vagal dominance over sympathetic one on heart rate response to hypoxia was also observed (21; 23). Examination of the autonomic cardiac activity by HRV components under hypoxic exposure would elucidate the response pattern of autonomic control, and its causality for predisposition of cardiovascular collapse. Determination of the influence of hypoxia on the HRV components, resp. autonomic cardiac activity and clarifying of the dependence of SaO_2 and BP on HRV would promote for prognozing of the pilot's resistance to hypoxia. Effect of hypoxia on the ANS cardiac function is important to diagnoze the early symptoms of cardiovascular pre-collapse and collapse, and to detect subjects predisposed to Decompression Illness, and to determine pilot's resistance to hypoxia based on autonomic cardiovascular response pattern examined by HRV.

The aim of the present study is to examine the effect of the hypoxic hypoxia on the autonomic cardiovascular response pattern and to determine the prognosis of resistance to hypoxia in military pilots.

METHOD

Subjects

21 male military pilots employed by the Bulgarian Military Air Force whose age ranged from 21 to 42 years (mean age, X±SD: 39.85±9.12) were examined.

Criteria for exclusion included: systolic BP>130 mm Hg; diastolic BP>85 mm HG; body mass index>25 kg/m2; smoking; using medications; cholesterolaemia; diabetes; and a history or evidence of cardioavascular, respiratory, renal, hepatic, gastrointestinal or systemic disease.

Procedure

Military pilots were exposed to hypoxia in hypobaric chamber.Tolerance to hypoxic hypoxia is one of the flying physical examinations for controlling of the physiological training and performance of military pilots. Simulated altitude of 5000 m was accomplished by vertical speed ascent of 20 m/sec. The parameters of the pressure in barochamber were: barometric pressure at an altitude of 5000 m - 405.4 mm Hg, an oxygen partial pressure in inspired air - 84.8 mmHg. Hypoxic exposure was maintained during 30 minutes. Water vapour saturation partial pressure - 47 mm Hg, and carbon dioxide partial pressure - 40 mm Hg were constant during exposure.

Cardiovascular: heart rate variability measures, heart rate, systolic and diastolic blood pressure (BP), and respiratoty parameters: SaO_2 were examined from 10 min periods in sitting position before (pre-hypoxic) and after (post-hypoxic) exposure to hypoxic hypoxia. HRV data were obtained from I bipolar standard ECG lead. Heart rate was computed by continuous recording of II standard ECG lead (Nehb). Systolic and diastolic BP was recorded continuously by sphygmomanometer. Arterial oxygen saturation was recoreded continuously by plethysmographic signal from the left finger.

Heart Rate Variability

Computerized method for analyzing of HRV was applied (11; 45). A portable electronic device was used to transform ECG signal into R-R intervals and to transmit R-R intervals to IBM compatible PC for on-line processing. ECG signal was transformed to R-R intervals by AC convertor (QRS detector and timer, resolution time 2224 samples per second). This sampling rate gives a variation of 0.48 msec in locating the peak of R-wave and results in a minimum accuracy of 99.55 % in computing heart rate up to 140 beats/min.Time-domain and frequency-domain HRV measures, and HRV derived indices were analyzed:

1. Time-domain HRV measures:

X (mean R-R interval) (msec), resp. mean heart rate (beats/min); Short-Term Variability (STV) (msec) (reflecting respiratory oscillations in heart rate variations); Long-Term Variability (LTV) (msec) (reflecting baroreceptory- and thermoregulatory influences on heart rate variations); Time-Domain Index (TDI) (arb. un.) (assessing sympathetic/parasympathetic influences on histogram R-R intervals distribution).

2. Frequency-domain HRV measures:

Spectral power of the R-R intervals in the Temperature band (0.01-0.05 Hz) (P_T) (ms^2) (sympathetically mediated); spectral power of the R-R intervals in the Traube-Hering-Mayer band (0.06-0.14 Hz) (P_{THM}) (ms^2) (sympathetically and parasympathetically mediated); spectral power of the R-R intervals in the Respiratory Sinus Arrhythmia (RSA) band (0.15-0.5 Hz) (P_{RSA}) (ms^2) (parasympathetically mediated); Frequency-Domain Index (FDI) (P_T/P_{RSA}) (arb. un.) (reflecting sympathetic/parasympathetic ratio). Spectral powers of the R-R intervals in the respective frequency bands were calculated using Fast Fourier Transform.

3. HRV-derived indices:

Physical Stress (PS) (arb. un.) (mathematical algorithm based on difference between measured and age-referent values derived from the time-domain HRV measures); Mental Stress (MS) (arb. un.) (mathematical algorithm based on difference between measured and age-referent values derived from the frequency-domain HRV measures); Functional Age (FA) (yr) (mathematical algorithm computing difference beween measured and age-referent values of autonomic activity derived from the frequency-domain HRV measures); Health Risk (%) (mathematical algorithm derived from PS, MS-coefficients and number of premature heart beats).

Computerized system Schiller AG - type Cardioswiss CM - 8 was used to monitor heart rate (beats/min), systolic and diastolic BP (mm Hg) and arterial oxygen saturation (SaO_2) (%) before, during and after hypoxic exposure.

To be comparable to HRV values mean values of heart rate, SaO_2, and systolic and diastolic BP were computed in pre-hypoxic and post-hypoxic exposure.

Analysis of Data

HRV measures, HRV-derived indices, heart rate, SaO_2 and systolic and diastolic BP are expressed as means standard deviations. Means of HRV measures, HRV-derived indices, heart rate, SaO_2,and systolic and diastolic BP in pre- and post-hypoxic exposure were compared by paired-samples t-test. To determine correlations between SaO_2, heart rate, systolic and diastolic BP, and HRV measures correlation analysis was applied. Step-wise method of multiple linear regression analysis (using SaO_2, heart rate, systolic and diastolic BP as independent variables, and the HRV measures

as dependent variables) was performed for determining the dependence of SaO_2, systolic and diastolic BP, heart rate on HRV measures and for defining the resistance to hypoxia. A p value lesser than 0.05 was considered statistically significant.

RESULTS

I. Effect of Hypoxic Hypoxia on: Autonomic Cardiovascular Control Examined by HRV measures; Heart Rate; SaO_2; Systolic and Diastolic BP

To examine the effect of hypoxic hypoxia on cardiac and respiratory function, HRV, SaO_2, heart rate, systolic and diastolic BP parameters were compared between pre- and post-hypoxic exposure by paired-samples t-test. Mean values of cardiovascular and respiratory parameters are presented in Table 1.

Table 1. Means (X ± SD) and p-values of time- and frequency-domain HRV measures, HRV-derived indices, heart rate, systolic and diastolic blood pressure and arterial oxygen saturation in pre-hypoxic and post-hypoxic exposure

Variables	Pre-hypoxic exposure X ± SD	Post-hypoxic exposure X ± SD	p-value
Heart rate (beats/min)	83.10 ± 9.73	81.60 ± 13.62	n.s.
STV (msec)	42.11 ± 1.91	49.39 ± 1.63	0.026
LTV (msec)	33.11 ± 1.96	39.06 ± 1.19	0.038
TDI (arb.un.)	36.67 ± 1.95	42.11 ± 1.46	0.048
mean -R-R (X) (msec)	789.94 ± 99.02	818.89 ± 117. 65	0.05
$P_{(T)}$ (ms^2)	6.04 ± 0.67	10.74 ± 1.34	n.s.
$P_{(THM)}$ (ms^2)	8.54 ± 0.18	11.45 ± 0.82	0.003
$P_{(RSA)}$ (ms^2)	6.34 ± 0.14	9.16 ± 0.59	0.03
FDI (arb.un.)	27.34 ± 1.51	33.69 ± 1.08	0.008
PS (arb.un.)	0.71 ± 0.09	0.14 ± 0.01	n.s.
MS (arb.un.)	0.38 ± 0.03	0.57 ± 0.05	n.s.
HR (%)	52.83 ± 8.20	45.72 ± 6.94	n.s.
FA (yr)	41.94 ± 1.72	42.61 ± 1.82	n.s.
systolic BP (mmHg)	127.45 ± 10.54	122.30 ±13.33	n.s.
diastolic BP (mmHg)	78.75 ± 10.12	74.60 ± 9.93	0.033
SaO_2 (%)	97.10 ± 1.07	94.05 ± 4.96	0.009

Significant effect of hypoxic exposure was observed for HRV measures, SaO_2 and diastolic BP. Hypoxia induced significant decrease of diastolic BP and SaO_2. Hypoxia resulted also in significant increase of mean values of the mean R-R interval (X), STV, P_{RSA}, P_{THM}, LTV,TDI ad FDI. Fig. 1, Fig. 2, Fig. 3 and Fig. 4 illustrate differences in mean values of: mean R-R interval (X), STV and LTV; P_{RSA} and P_{THM}; diastolic BP; SaO_2 in pre-hypoxic and post-hypoxic exposure.

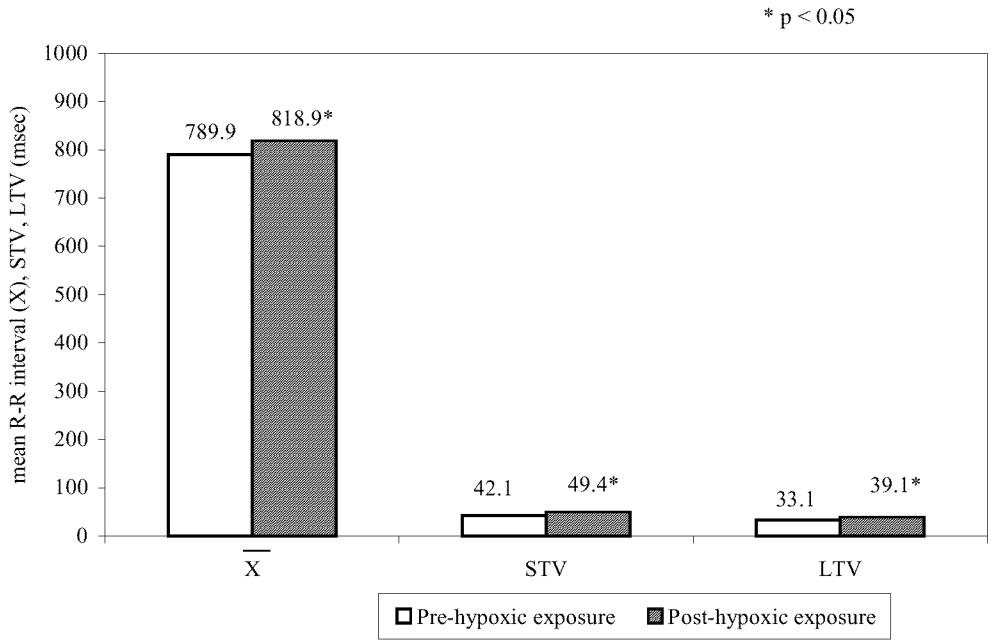

Fig. 1. Mean values of the mean R-R interval (X) (msec), STV (msec) and LTV (msec) in pre-hypoxic and post-hypoxic exposure

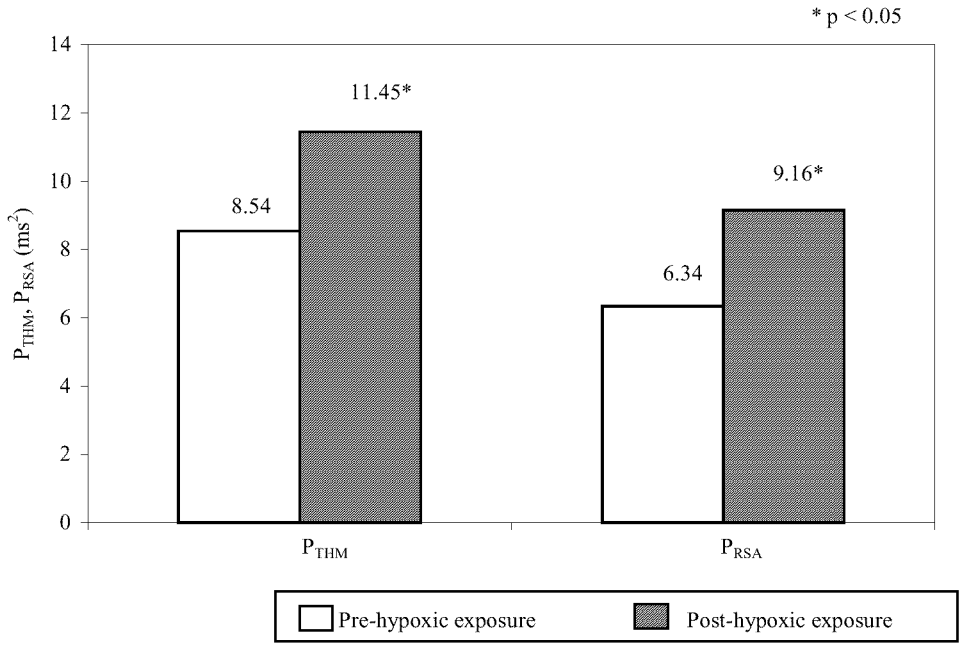

Fig. 2 Mean values of the P_{THM} and P_{RSA} (ms^2) in pre-hypoxic and post-hypoxic exposure

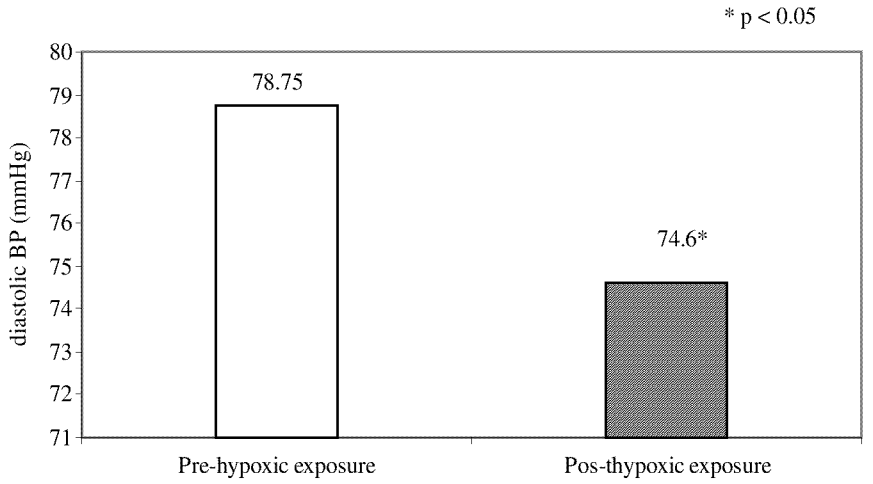

Fig. 3 Mean values of the diastolic BP (mmHg) in pre-hypoxic and post-hypoxic exposure

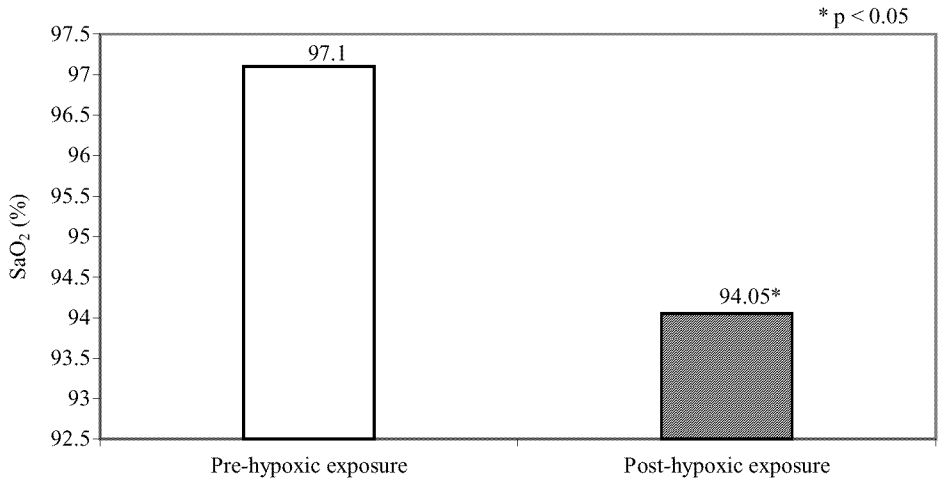

Fig. 4 Mean values of the SaO_2 (%) in pre-hypoxic and post-hypoxic exposure

II. Effect of Hypoxic Hypoxia on Association between Autonomic Cardiovascular Control Examined by HRV, and SaO_2 and diastolic BP

Effect of the response to hypoxia on the association between autonomic cardiovascular control examined by HRV, and heart rate, SaO_2, and systolic and diastolic BP parameters was determined differentially by correlation and step-wise method for multiple linear regression analysis. Results of both analyses revealed dependence only of SaO_2 and diastolic BP on the autonomic cardiovascular control.

1. Correlations of SaO_2 with HRV

1.1. Prehypoxic correlations:

- Significant positive correlations of SaO_2 with time-domain HRV measures: Mean R-R interval (X) ($r = 0.63$, $p < 0.005$); STV ($r = 0.49$, $p < 0.05$); LTV ($r= 0.55$, $p < 0.01$); TDI ($r = 0.55$, $p < 0.01$)

- Significant negative correlations of SaO_2 with HRV-derived indices: FA ($r = -0.58$, $p < 0.01$); HR ($r = 0.51$, $p < 0.05$)
- Significant negative correlation of SaO_2 with heart rate ($r = -0.59$, $p < 0.01$)

1.2. Posthypoxic correlations:

- Significant negative correlation of SaO_2 with P_{RSA} ($r = -0.54$, $p < 0.01$).

2. Correlations of diastolic BP with HRV

Significant correlations of diastolic BP with HRV were observed only in posthypoxic exposure.

- Significant negative correlation of diastolic BP with frequency-domain HRV measure: P_{THM} ($r = -0.46$, $p < 0.05$); FDI ($r = -0.51$, $p < 0.05$).
- Significant negative correlations of diastolic BP with time-domain HRV measures: STV ($r = -0.50$, $p < 0.05$); TDI ($r = -0.50$, $p < 0.05$).
- Significant positive correlation of diastolic BP with HRV-derived index: HR ($r = 0.56$; $p < 0.01$)

Correlation coefficients of SaO_2 and diastolic BP with HRV measures in pre- and post-hypoxic exposure are presented in Fig. 5 and Fig. 6.

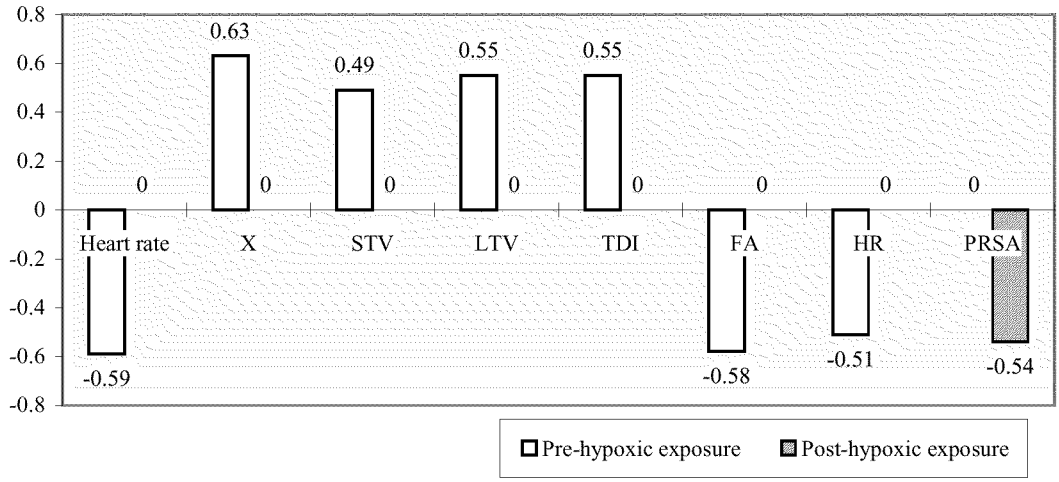

Fig. 5 Correlation coefficients of the SaO_2 with HRV measures in pre-hypoxic and post-hypoxic exposure

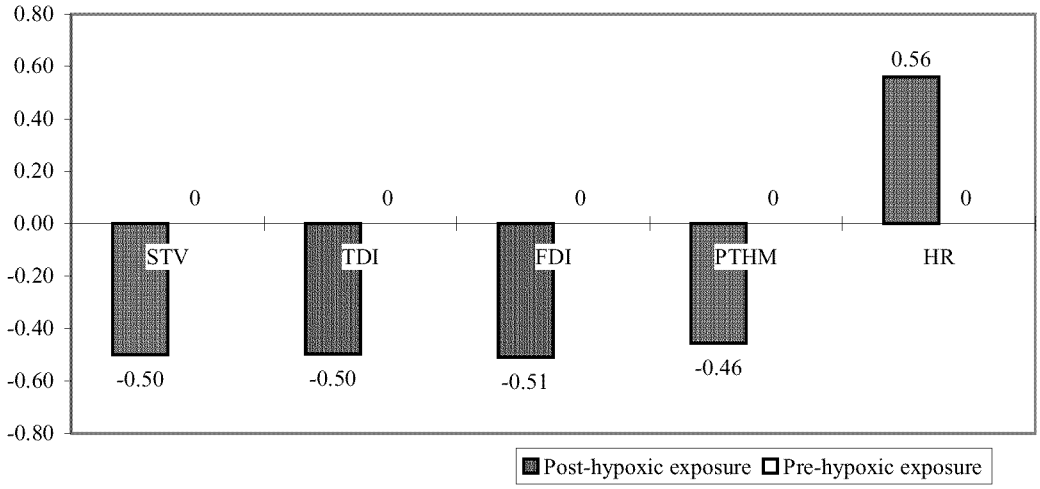

Fig. 6 Correlation coefficients of diastolic BP with HRV measures in pre-hypoxic and post-hypoxic exposure

Correlation of some paired identical measures in pre- and post-hypoxic exposure did not show statistical significance although is normally expected to present high correlation:

- Time-domain HRV measures: STV ($r = 0.43$, $p = 0.07$); LTV ($r = 0.15$, $p = 0.54$); TDI ($r = 0.44$, $p = 0.07$)
- Frequency-domain HRV measure: P_T ($r = - 0.03$, $p = 0.90$)
- HRV-derived index: HR ($r = 0.27$, $p = 0.27$)
- SaO_2: ($r = 0.34$, $p = 0.15$).

The rest of correlations between paired identical measures were significant.

3. Dependences of SaO_2 and diastolic BP on HRV

Dependences of SaO_2 and diastolic BP on HRV were observed only in posthypoxic exposure. The following dependences were observed:

- Slow extent of increasing of the spectral power of R-R intervals in the Traube - Hering - Mayer band with declining of the diastolic BP
- Moderate increasing of the spectral power of the R-R intervals in the Respiratory Sinus Arrhythmia band with declining of SaO_2.

Regression equations describing dependences of SaO_2 and diastolic BP on HRV are presented in Table 2.

Table 2. Regression equations of dependence of SaO_2 and diastolic BP on HRV measures in post-hypoxic exposure

$\mathbf{P_{THM}} = 23{,}927 - 0{,}171^* \times$ diastolic BP
$\mathbf{P_{RSA}} = 42{,}336 - 0{,}376^* \times SaO_2$

$^*p < 0.05$

III. Prognozing of the Resistance to Hypoxic Hypoxia by Cardiovascular and Respiratory Parameters

Prognozing of the resistance to hypoxia by cardiovascular and respiratory parameters was performed in post-hypoxic level based on definite values of the same variables in pre-hypoxic condition. Our results revealed that prognosis of resistance to hypoxia could be determined by P_T and PS:

- Post-hypoxic value of the spectral power of the R-R intervals in the Temperature band considered to be sympathetically mediated defined resistance to hypoxia by pre-hypoxic level of SaO_2 and diastolic BP
- Post-hypoxic level of the physical stress, resp. physical training predicted the resistance to hypoxia by pre-hypoxic level of P_T and systolic BP

Regression equations determining the prognosis of the resistance to hypoxia are presented in Table 3.

Table 3. Regression equations for prognozing of the resistance to hypoxia

$\mathbf{P_T}$ (post-hypoxic exposure) = -705.92 + 7.82* x $\mathbf{SaO_2}$ (pre-hypoxic exposure) - 0.54* x **diastolic BP** (pre-hypoxic exposure)
PS (post-hypoxic exposure) = -3.05 - 0.362* x $\mathbf{P_T}$ (pre-hypoxic exposure)+ 0.04* x **systolic BP** (pre-hypoxic exposure)

$^* p < 0.05$

DISCUSSION

Hypoxic Tolerance

Our results of exposure to moderate hypoxia in comparing of pre-hypoxic and post-hypoxic exposure demonstrated that military pilots were tolerant to hypoxia. Mean values of the heart rate, systolic and diastolic BP in pre- and post-hypoxic exposure corresponded to referents computed by the method of percentiles for both exposures (26). Hypoxic tolerance was supported by the evidence that in post-hypoxic exposure pilots did not reveal symptoms of cardiovascular pre-collapse or collapse.

Effect of Hypoxia on Autonomic Cardiovascular Control

We investigated the effect of hypoxic hypoxia caused by decreased partial oxygen pressure in inspired air (PaO2). Decreased PaO2 is a stimulus for activation of the peripheral chemoreceptors. In our study more likely mechanism for the integrated reflex cardiovascular and respiratory responses was chemoreceptors activation. Chemoreflex responses on cardiovascular and respiratory function were considered to be mediated via autonomic function (14; 39).

In post-hypoxic exposure we observed a pattern towards increased both sympathetic and parasympathetic activities with prevailing relative dominance of the vagal cardiac activity over sympathetic one on the control of heart rate variations revealed by significant increase of the mean value of R-R intervals. Vagally mediated P_{RSA} and STV measures both reflecting rhythmic heart rate variations associated with the respiratoty phases were increased after exposure to hypoxia. RSA is considered as a measure of cardiac vagal tone (31; 51). Our evidence of increased vagal cardiac control in post-hypoxic exposure was supported also by significant dependence of the SaO_2 on P_{RSA} observed only after exposure to hypoxia. Increased vagal activity reflected by the P_{RSA} could be predicted by minimal declining of the SaO_2.

Studies of Simon, Taha, Dempsey, Skatrud, Iber (1995) of respiratory modulation of hypoxic tachycardiac response, and of Grossman and Wientjes (1986) of association between respiration, RSA and cardiac vagal control suggested the centrally acting mediated brainstem rhythm to be responsible for the respiratory modulation of the parasympathetic efferent traffic to the sinus node. This model could be referred to the observed by us result of an association between vagally mediated P_{RSA} and SaO_2 with a certain approximation as we examined indirect measure of the respiratory function: SaO_2.

In post-hypoxic exposure also we observed parallelly to elevated vagal activity slight indirect trend for increased sympathetic cardiac activity. After exposure to hypoxia mean values of the considered sympathetically and vagally mediated P_{THM}, LTV, FDI and TDI were increased. Evidence for significant effect of hypoxia on autonomic cardiac activities were lack of correlations between some paired identical measures of HRV: sympathetically mediated P_T; sympathico-vagally mediated LTV, TDI, HR, and of SaO_2 in pre- and post-hypoxic conditions which in normal conditions are characterized with high significant correlation. Relatively most affected by hypoxic exposure was the sympathetic activity reflected by the P_T ($r = - 0.03$; $p = 0.90$).

To a certain degree indirect evidence for relatively increased sympathetic cardiac activity was the dependence of diastolic BP on P_{THM}. We hypothesized relative sympathetic increase as this band of the HRV spectra (P_{THM}-band) was considered sympathetically and vagally mediated (2; 42; 50). In post-hypoxic exposure decreased values of diastolic BP were associated with an increased P_{THM} response. Our study revealed an association between rhythmical fluctuations of arterial BP due to vasomotor variations synchronous with the respiration: Traube-Hering waves, and due to rhythmical variations in the activity of the vasomotor center: Mayer waves that were observed in other studies (39; 52). Increased discharge from chemoreceptors might contribute for the specific Mayer waves (19). Mayer waves were slow oscillations in the arterial pressure. When arterial pressure shows even a slight trend to decline hypoxia stimulates chemoreceptors. Arterial pressure increases as a response to stimulation which improves oxygen supplying of chemoreceptors. Specific 0.1 Hz rhythm of HRV spectra was considered sympathetically mediated, and activated from alterations of blood pressure and oxygen saturation (29). This sympathetically mediated rhythm was to a certain degree responsible for the observed by us dependence of diastolic BP on P_{THM}. Sympathetically mediated 0.1 Hz rhythm was not subject of our study. Further investigation could be performed to reveal response of the 0.1 Hz rhythm to hypoxia to determine the association of the 0.1 Hz rhythm with SaO_2 changes.

We observed activation of both sympathetic and parasympathetic cardiac activities caused by exposure to hypoxic hypoxia but the response pattern was relative dominance of vagal activity over sympathetic one on the control of heart rate variations. Studies investigating the change of the autonomic cardiac control under hypoxia are scarced and results are controversial. Our result is consistent with the results of Koizumi and McBrooks (1984) and Koizumi, Terui, Kollai (1983) evidencing that the activation of the chemoreflex in response to changes in PaO2 or PaCO2 induced non-reciprocal pattern of co-activation of sympathetic and parasympathetic cardiac activity followed by reciprocal response with prevailed vagal control over sympathetic on the sinus node. As the studies of Koizumi and McBrooks (1984) and Koizumi, Terui, Kollai (1983) were performed on animals and as there are to our knowledge only two studies of increased parasympathetic heart rate response to hypoxia (21; 23), the result of our study of pattern of co-activation of sympathetic and vagal cardiac activities with prevailing relative dominance of the vagal activity over sympathetic on

heart rate variations, induced by 30 minutes continuous exposure of hypoxic hypoxia in barochamber, needs further continuation to determine specific effect of hypoxia on autonomic cardiovascular control.

Our study confirmed an integrated response to hypoxia result of the activation of chemoreceptor reflex mechanism modulating the respective cardiovascular and respiratory responses via autonomic function, observed in the studies of Sheffield and Heimbach (1996), and of Berne and Levy (1990).

Prognozing of the Resistance to Hypoxia

Prognosis of the resistance to hypoxia of military pilots was determined by HRV measures: P_T and PS. These measures of the autonomic cardiovascular control possessed pronounced prognostic significance for determining of the resistance to hypoxia. Results indicated clearly that post-hypoxic sympathetic activity (P_T) could be predicted by pre-hypoxic level of the percent arterial oxygen saturation and diastolic BP. Strong predictor for the post-hypoxic level of physical fitness, resp. physical stress (PS) was pre-hypoxic level of the sympathetic activity (P_T) and systolic BP. Regression equations for determining of the resistance to hypoxia are valid only for the definite intervals of changes of the independent variables. To our knowledge an attempt for prognozing of resistance to hypoxia by these variables up to now is not reported.

In summary our results of acute simulated hypoxic hypoxia in military pilots demonstrated:

1. Military pilots were tolerant to hypoxia. Mean values of the heart rate, systolic and diastolic BP in pre- and post-hypoxic exposure corresponded to referents computed by the method of percentiles for both exposures. Hypoxic tolerance was supported by the evidence that they did not reveal post-hypoxic symptoms of cardiovascular pre-collapse and collapse.
2. In post-hypoxic exposure we observed a pattern towards increased both sympathetic and parasympathetic cardiac activities with prevailing relative dominance of the vagal cardiac activity over sympathetic one on the control of heart rate variations revealed by significant increase of the mean value of R-R intervals. Our result is consistent with the results of Koizumi and McBrooks (1984), and Koizumi, Terui, Kollai (1983) evidencing that the chemoreflex activation in response to reduction of the PaO2 caused non-reciprocal pattern of co-activation of sympathetic and parasympathetic cardiac activity followed by reciprocal response with prevailed vagal control over sympathetic on the sinus node.
3. Our study confirmed an integrated response to hypoxia result of the activation of chemoreceptor reflex mechanism modulating the respective cardiovascular and respiratory responses via autonomic function, observed in the studies of Sheffield and Heimbach (1996), and of Berne and Levy (1990). Our evidence of increased vagal cardiac control in post-hypoxic exposure was supported by significant dependence of the arterial oxygen saturation on P_{RSA} observed only after exposure to hypoxia. To a certain degree indirect evidence for relatively increased sympathetic cardiac activity in post-hypoxic exposure was the dependence of diastolic BP on P_{THM}.
4. Prognosis of resistance to hypoxia of military pilots was determined by P_T and PS. These measures of the autonomic cardiovascular control possessed pronounced prognostic significance for determining of the resistance to hypoxia. Results indicated clearly that post-hypoxic sympathetic activity (P_T) could be predicted by pre-hypoxic level of the percent arterial oxygen saturation and diastolic BP. Strong predictor for the post-hypoxic level of the physical fitness, resp. physical stress (PS) was pre-hypoxic level of the sympathetic activity (P_T) and systolic BP. To our knowledge an attempt for prognozing of resistance to hypoxia by these variables up to now is not reported.

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