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Post-exercise parasympathetic reactivation and sensibility to hypoxia

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Lausanne, 21.03.2013

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1. Introduction

Exposure to hypoxia, which is characterized by a decrease in oxygen pressure, causes an immediate compensation and adaptation in the ventilatory and cardiac systems. The individual response to hypoxia depends on the altitude and on the work intensity. However, acute response is characterized by an increase in pulmonary ventilation, heart rate and blood pressure.

In acute hypoxia, maximal exercise capacity is reduced due to a reduction in arterial oxygen content (CaO2). For example, a study has found a reduction of 50% of the maximal oxygen uptake (VO2max) during maximal exercise with a large muscle mass involvement at the simulated altitude of 5300m (1).

However, at altitudes above 4000m the reduction of VO2max is larger than what would be expected only from the reduction in the oxygen arterial content. Reduction of the arterial oxygen pressure only explains about two-third of the VO2max decrease. This implies that others mechanisms contribute to the reduction of the VO2max, like, for example, a decrease in cardiac output, an impairment of pulmonary gas exchange and changes in the distribution of blood flow (1).

It has been found that, when PaO2 is > 55 mmHg, an altitude acclimatized human has potentially a similar exercising capacity as at sea level if the exercise engages a small muscle mass; with only a minor role of PaO2 per se and an important role of the amount of flow available to perfuse the active muscle (2). The increase in local vasodilatation is a compensatory mechanism due to hypoxemia (3).

Some studies have shown that elite endurance athletes have a larger decline of VO2max compared to less trained individuals (4,5,6). This more important sensitivity of athletes to hypoxia has been related to an important decrease in arterial saturation (Sa02) and a relative hypoventilation (e.g. lower increase in ventilation) in response to hypoxia (4,5).

The change in maximal heart rate (HRmax) in acute hypoxia is still under debate. Several studies showed that HRmax does not change significantly during acute hypoxia exposure (2,4), whereas others have shown a decrease in HRmax. Differences in HRmax between trained and untrained subjects are also object of debate (6).

The autonomic nervous system (ANS) function plays an important role in the acute response to hypoxia; increase in sympathetic and decrease in parasympathetic activity is caused by the stimulation of peripheral chemoreceptors. Increase in cardiac output and in respiratory rate is a compensatory mechanism due to hypoxia.

Either resting heart rate variability (HRV), post-exercise heart rate recovery (HRR) or post-exercise HRV have been used as indirect markers of autonomic function and may offer practical and simple ways to quantifying sympatho-vagal modulation of the cardiac activity balance without invasive methods (8-12).

Pharmacological studies have shown the relationship between heart rate frequency components and sympathetic or parasympathetic activities (13). The high frequency band (HF, 0.15-0.40 Hz) corresponds to the breathing frequency (respiratory sinus arrhythmia) and it is associated with parasympathetic modulation of cardiac activity. The low frequency band (LF, 0.05-0.15 Hz) is related to arterial pressure oscillation and reflects a mixed sympathetic and parasympathetic modulation (14).

At rest or while exercising at moderate intensity in normoxic conditions, aerobically trained athletes have a greater parasympathetic activity (e.g. greater HF power density of HRV) if compared to untrained subjects (6,15,16).

Endurance training leads the sensitivity of the sympathetic nervous system to be chronically reduced and therefore causes a reduction of intrinsic heart rate and an elevated parasympathetic activity at rest and during moderate intensity efforts (17).

It has been described that acute hypoxia produces a decrease in the total spectral power with an increase in relative sympathetic tone associated with a relative decrease in parasympathetic tone during exercise (16,18).

Parasympathetic reactivation following exercise is also related to physical performance (9) and a delayed reactivation can be associated to an increased risk of sudden death and other cardio-vascular diseases (19).

Not many studies have addressed post-exercise parasympathetic reactivation in hypoxia. A recent study has found that following sub-maximal running exercise parasympathetic reactivation was impaired in normobaric hypoxia (FiO2 15.4%) if compared to normoxia. On the other hand, the effect of hypoxia on post-exercise autonomic nervous system modulation of HR was not apparent when the exercise was supra-maximal. The authors hypothesize that metaboreflex and central chemoreflex activation through post exercise metabolite accumulation is a strong determinant of parasympathetic activity restoration after exercise (15).

A progressive influence of parasympathetic activity on HR occurs with the duration of altitude exposure either via a central effect of hypoxia, by greater influence at the cardiac receptor level, or by cholinergic antagonism (20).

In our study we examined maximal exercise performance and post-exercise autonomic activity following a sub-maximal running exercise both in conditions of normoxia and of hypoxia, in elites and sub-elites ski-alpinist athletes.

Our hypothesis is that in hypoxia post-exercise sympathetic modulation of cardiac activity is greater than in normoxia, because it has been found that hypoxia is a stimulus for sympathetic activation at rest and during exercise.

Differences in post-exercise HRV and parasympathetic reactivation between elites endurance athletes and less trained athletes have never been investigated in hypoxia. Elites athletes use to have a stronger parasympathetic activity in normoxia, therefore we expect to find the same relation in hypoxia.

2.Methods

2.1. Subjects

23 healthy ski-alpinists participated at the experiment, 11 in the elite group (E, 5 males and 6 females) and 12 in the amateur group (sub elite group, SE, 6 males and 6 females). There was no difference in the mean age, weight or height (28±8 yrs., 63±7 kg, 172±5 cm for E group and 27±4 yrs., 69±11kg, 175±10 cm for SE group).

Mean VO2max in normoxia was different between E and SE ($p= 0.0001$) (61.4±8.3 ml/kg/min for E and 47.6±5.0 ml/kg/min for SE).

2.2. Experiment overview

The research protocol was performed in the laboratory of physiology of the Clinique Romande de Réadaptation de Sion. All participants gave voluntary written informed consent to take part in the experiment, which was approved by the institutional research ethics committee of Wallis. The study conformed to the recommendations of the Declaration of Helsinki.

Each subject performed two incremental tests on a treadmill, based on the Swiss Olympics guidelines, with a lag of, at least, two weeks (21).

The study was performed in a hypoxic chamber (ATS altitude, Sydney, Australia) at altitude of Sion (512 m asl) and simulated altitude of 3000 m asl (normobaric hypoxia).

The order of tests was randomly assigned, half of elite and sub-elite group started by the hypoxic test and half by the normoxic test.

After 5 min of rest, the test began with the first stage at 5.4 km/h and 2% slope for SE and with 7.2 km/h and 2% slope for E. Every 3 min the speed was increased by 1.8 km/h up to 14.4 km/h. From 14.4 km/h, the slope was increased by 2% every 3 min until exhaustion of the subject. To assess lactate blood concentration a 30 s break was inserted between the stages.

Incremental tests were followed by 5-10 min pause and 6 min of sub-maximal run at 9 km/h for the E and 7,2 km/h for the SE (in normoxia VO2 was 33.8±2.5 ml/kg/min which represents 55% of the VO2max for E and 29.5±3.8 ml/kg/min which represent 62% of the VO2max for SE).

During maximal and sub-maximal running VO2, carbon dioxide production (VCO2), ventilation (VE), HR and arterial oxygen saturation (SpO2) were measured.

Heart rate recovery (HRR) and heart rate variability (HRV) were measured over 10 min right after 6 min of sub-maximal running.

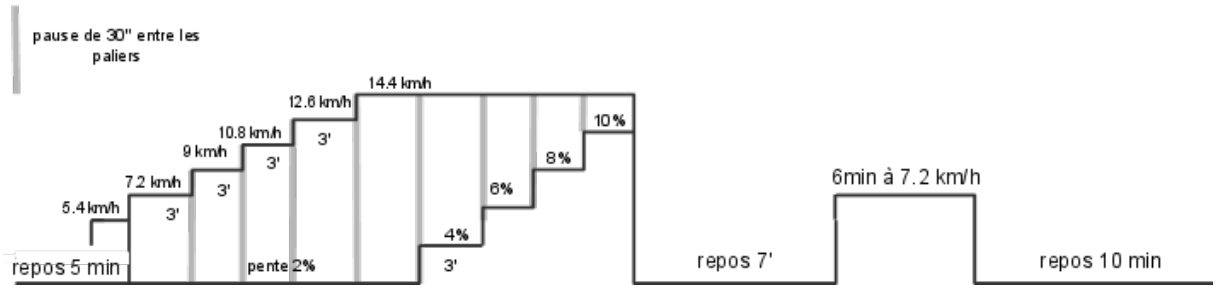

Figure 1. Incremental test on treadmill (21)

2.3. Materials

Gas exchange was assessed by indirect colorimetry (MetaMAX 3B, Cortex, Leipzig, Germany). An air-tight mask covering the nose and mouth was worn by the subjects during both the exercise and the recovery phase.

This allowed the measurement of VO2, VCO2 and VE, as well as the determination of the energy expenditure of the subject.

With an analyzer (Lactate Pro Arkray Factory Inc., Shiga, Japan) equipped with a dipstick (22) lactate blood concentration was measured. A drop of capillary blood was taken from the fingertip for measurement before exercise, at each break of 30 s between each 3 min stage, at the end of the incremental exercise, after 6 min of sub-maximal running and finally after 10 min of recovery.

SpO2 was assessed by pulse oxymeter (Wristox 3100, Nonin, USA) (23) and recorded values were 30 s averaged.

Heart rate parameters were recorded by an electrode transmitter belt fitted to the chest of each subject as instructed by the manufacturer (Suunto T6c).

2.4. HR data treatment

All R-R series recorded were extracted. Occasional irregularities of heart rhythm (extrasystol and consecutive compensative break) were visually identified and manually replaced with interpolated adjacent R-R interval values (24,25).

2.5. Post exercise HR recovery assessment

Heart rate recovery was assessed during the 10 min recovery period right after 6 min sub-maximal running. At the end of the exercise all subject immediately sat passively on a chair placed close to the treadmill. Because of the differences in HR recovery on different body posture, the time elapsed between the end of exercise and the moment the subject sat down was as short as possible.

HR recovery was calculated by 1) taking the absolute difference between the final HR at exercise completion and the HR reordered after 60 s of recovery (HRR(60s)) 2) taking the time constant of HR decay obtained by fitting the 10 min post-exercise HR recovery into a first order exponential decay curve (HHR(T)), or by 3) analyzing the first 30 s (from the 10^{th} to the 40^{th} seconds) on HHR via semi-logarithmic regression analysis (T (30s)) (24,25).

2.6. Time-varying vagal related index

During the initial 5 min of HRR, a progressive increase in the R-R interval is generally observed, however on shorter time scales (i.e. 15-60 s) the curve is partially linear with superimposed oscillations. The root mean square of successive differences in the

R-R interval was calculated for each subsequent 30 s segments of recovery (RMSSD(30s)), this represents a time-varying vagal-related index. Occasional outliers in HRV plots were smoothed by applying a median filter that replaces values with the median of the 2 adjacent values (24,25).

2.7. Short term resting HVR analysis

HVR analyses were performed on the last 5 min of the recovery period. The mean HR (HR (5-10min)), the standard deviation of normal R-R intervals (SDNN(5-10min)) and the root mean square difference of successive normal R-R intervals (RMSSD(5-10min)) were

calculated. A power frequency analysis was sequentially performed with a Fast Fourier Transform based on a non-parametric algorithm with a Welsh window after the ectopic-free data were detrended and resampled. A fixed linear resampling frequency of 1024 equally spaced points per %min period was used. The power density in the LF band (0.04-0.15 Hz) and the HF band (>0.15-0.50 Hz) were calculated for the 5 min period by integrating the spectral power density for both frequency bands. Normalized HF power (HFnu (5-10min)) was calculated as the LF/(HF+LF) ratios (24,25).

2.8. Statistical analyses

The distribution of each variable was examined with Kolmogorov-Smirnov test and Shapiro-Wilk normally test. For some data (i.e. HF and LF power density), the input values were transformed by using the natural logarithm to allow parametric statistical analyses. Differences between parameters of HR measurements and HRV recovery indices were assessed by a paired Student's t- test.

Systemic parameters and parasympathetic function indices were analyzed using two-way factors repeated-measures ANOVA (group: E vs. SE and conditions: hypoxia vs. normoxia).

Changes in time for RMSSD(30s) were analyzed with three-way factors repeated measures ANOVA (group: SE vs. E, conditions: N vs. H and time for recovery windows of 30 s).

For all analyses the level of significance was set at $p<0.05$.

3. Results

3.1. Systemic values, hypoxic conditions versus normoxia

Maximal exercise

VO2max was significantly greater ($p<0.001$) in E in both conditions (normoxia (N) and hypoxia (H)). The decrease in VO2max from N to H was larger ($p<0.001$) in E (from 61.4±8.3 to 50.3±6.9 ml/kg/min) than in SE (from 47.6±5.0 to 41.8±6.6 ml/kg/min). However, if expressed in percent of VO2max, the decrease was not significantly different (18% vs. 15%) ($p=0.164$).

As for VO2max, maximal power (Pmax) was significantly greater ($p<0.01$) in E in both conditions. The decrease in Pmax from N to H was larger ($p<0.05$) in E (from 182.2±91.1 to

115.5±70.2 W) than in SE (from 84.0±38.9 to 56.5±25.2 W). Also in this case, if expressed in percent of Pmax the decrease was not significantly different (36% vs. 30%) (p=0.437).

The maximal ventilation (VEmax) did not change neither in E (from 141.2±31.7 to 143.7±27.4 l/min) (p=0.845) nor in SE (from 122.7±28.1 to 128.3±30.5 l/min) (p=0.645) from N to H. It is to be noted that for the VEmax there was a strong inter-individual variability.

The decrease in oxygen saturation (SpO2) was larger (p=0.041) in E (-17%) than in SE (-13%).

Maximal heart rate (HRmax) remained unchanged for both groups in N vs H. (from 185±13 to 180±12 bpm for E vs. from 193±11 to 187±11bpm for SE) (p=0.360 for E and p=0.195 for SE)

Similarly, the maximal respiratory rate did not change in N vs H neither for E (from 62.3±10.8 to 61.8±12.6 1/min) (p=0.906) nor for SE (from 52.4±5.7 to 54.1±6.1 l 1/min) (p=0.514).

Sub maximal exercise

At sub-maximal intensity (9 km/h for E and 7 km/h for SE) the VO2 and the HR remained unchanged in both groups between N and H (from 33.8±2.5 to 33.7±2.9 ml/kg/min for E and from 29.5±3.8 to 29.2±3.8 ml/kg/min for SE and from 136±18 to 142±20 bpm for E and from 155±17 to 161±18 for SE in VO2 and HR respectively) (respectively p=0.100, p=0.848, p=0.468 and p=0.410).

The decrease in SpO2 was similar (p=0.140) in both groups (-14% for E and-11% for SE).

We observed a VE increase in H conditions ($p<0.001$ for E and $p<0.01$ for SE) in both groups (from 60.8±10.9 to 78.5±12.6 l/min for E and from 61.9±14.3 to 77.8±22.4 l/min for SE).

3.2. HRR-HRV- Parasympathetic reactivation:

Heart rate recovery

HHR(60s) for E was 37.5±6.2 bpm in N and 39.0±6.0 bpm in H, for SE it was 35.3±8.6 bpm in N and 36.7±5.9 bpm in H. No statistically significant difference was observed between the groups, between the conditions and between groups for condition (p=0.301, p=0.505 and p=0.998).

HHR(T) for E was 47.3±12.0 s in N and 45.8±11.9 s in H, for SE it was 54.1±24.7 s in N and 54.3±25.5 s in H, there was no statistically significant difference between the groups, between the conditions and between groups for condition (p= 0.231, p= 0.921 and p=0.894).

T(30s) for E was 169.1±41.3 s in N and 177.7±61.6 s in H, for SE it was 242.1±132.9 s in N and 210.2±68.8 s in H, there was no statistically significant difference between the groups, between the conditions and between groups for condition (p=0.059, p=0.669 and p=0.460).

Finally, the HR (5-10min) for E was 90.0±13.4 bpm in N and 95.1±13.9 bpm in H, for SE it was 103.6±9.4 bpm in N and 107.9±16.1 bpm in H. In this case a statistically significant difference (p= 0.003) between the two groups was observed, whereas no statistically significant difference between the conditions and between groups for condition could be determined (p= 0.249, p=0.959) (Fig 2).

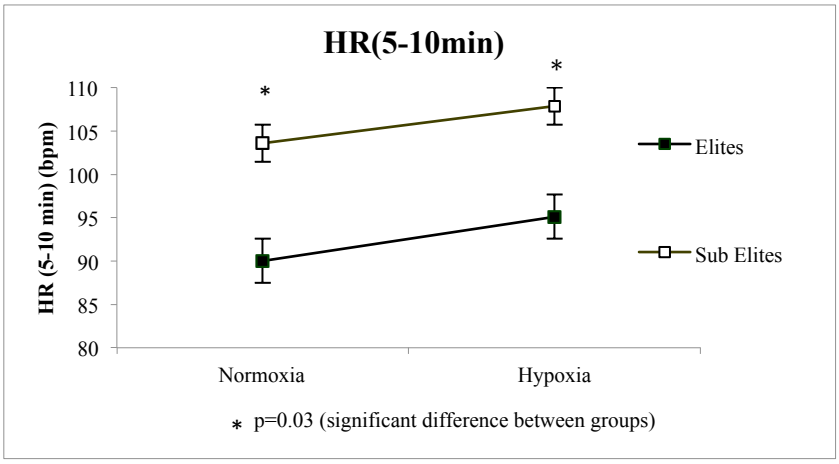

Figure 2. Mean heart rate (±SD) in the 5-10 minutes of recovery phase in both conditions

Heart rate variability

SDNN(5-10min) for E was 2.9±0.6 ms in N and 2.8±0.8 ms in H, for SE it was 3.8±1.6 ms in N and 3.5±1.2 ms in H, there was a statistically significant difference between the two groups (p= 0.048) whereas no statistically significant difference was observed between the two conditions and between groups for condition (p= 0.478, p=0.716) (Fig 3).

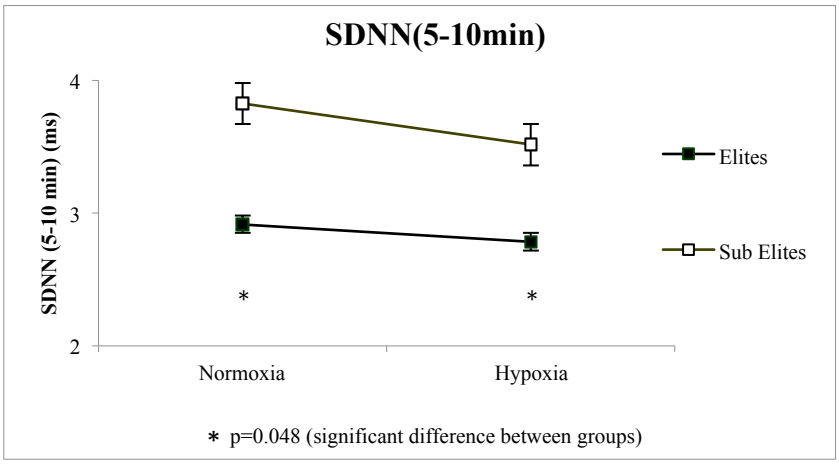

Figure 3. Mean SDNN (±SD) in the 5-10 minutes of recovery phase in both conditions

RMSSD (5-10min) for E was 9.8±3.9 ms in N and 8.3±4.0 ms in H, for SE it was 7.3±2.9 ms in N and 7.5±5.6 ms in H. There was no statistically significant difference between the groups, between the conditions and between groups for condition (p=0.142, p=0.611 and p=0.546).

LF/HF ratio (5-10min) for E was 7.9±5.6 in N and 4.9±5.9 in H, for SE it was 9.9±4.6 in N and 9.6±6.5 in H there was no statistically significant difference between the groups, between the conditions and between groups for condition (p=0.060, p=0.378 and p=0.442).
LFnu (5-10min) for E was 83.7±10.3 ms^2 in N and 72.4±14.7 ms^2 in H, for SE it was 89.5±3.8 ms^2 in N and 87.4±6.9 ms^2 in H, there was a statistically significant difference between the two groups ($p<0.001$) and between the two conditions (p=0.028) but no statistically significant difference between groups for condition (p=0.105).

HFnu (5-10min) for E was 16.3±10.3 ms^2 in N and 27.6±14.7 ms^2 in H, for SE it was 10.5±3.8 ms^2 in N and 12.6±6.9 ms^2 in H, there was a statistically significant difference between the two groups ($p<0.001$) and between the two conditions (p=0.028), but no statistically significant difference between groups for condition was observed (p=0.105) (Fig 4).

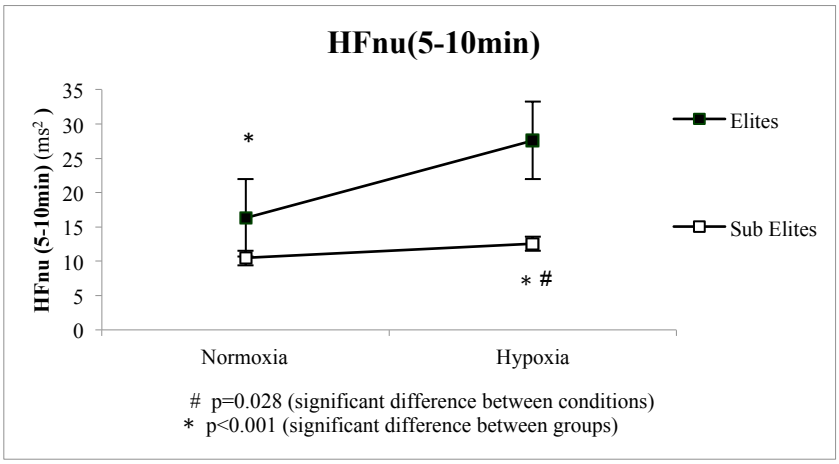

Figure 4. Mean HFnu (±SD) in the 5-10 minutes of recovery phase in both conditions

Before the sub-maximal exercise, at rest, HFnu in N was 12±12.9 ms^2 for E and 4.2±2.2 ms^2 for SE, in H it was 13.9±9.2 ms^2 for E and 11.1±5.5 ms^2 for SE. There was a statistically significant difference between the two groups (p= 0.035), whereas the difference between the two conditions was not statistically significant (p=0.082) (Fig 5).

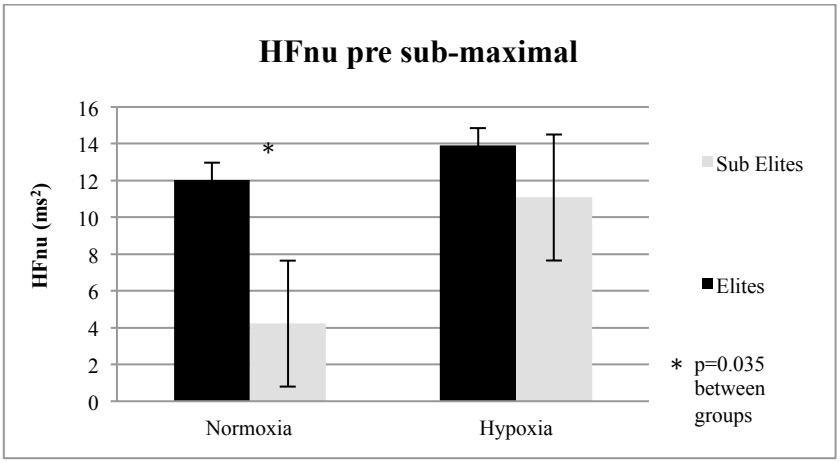

Figure 5. HFnu (±SD) pre-submaximal measured at rest before the exercise

Parasympathetic reactivation

Figure 6 shows the average time trend of RMSSD(30s) for both groups in both conditions. There is a statistically significant difference between groups (p<0.001) but no statistically significant difference between conditions (p=0.087). There is a statistically significant interaction between groups and conditions (p=0.019), RMSSD(30s) is greater for E in H than in N whereas there is no difference for SE. The significant interaction between group and condition shows that there is a different evolution of RMSSD(30s) between the two groups.

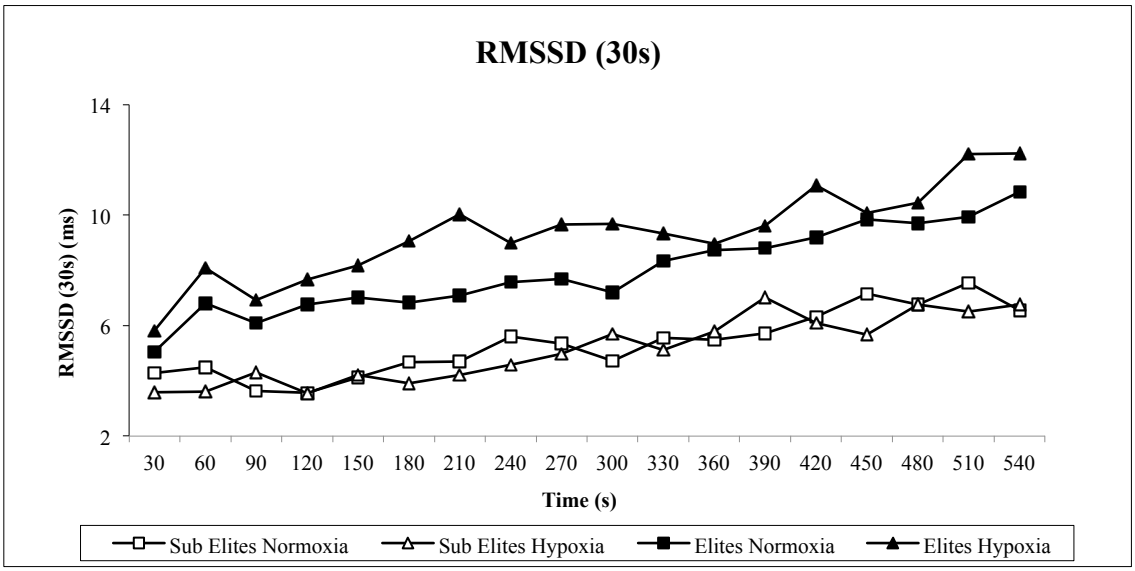

Figure 6. RMSSD30s in the recovery phase.

3.3. Correlations

The Pmax measured in N and in H were highly correlated. The subjects with a greater Pmax in N also have a greater Pmax in H (Fig 7).

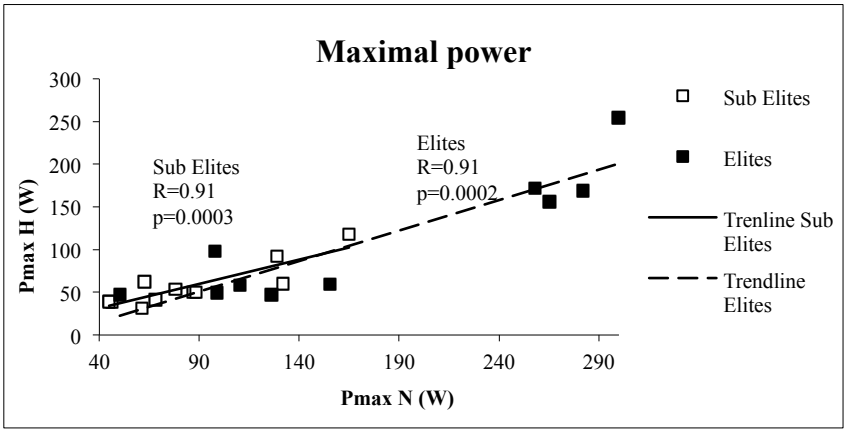

Figure 7. Relationship between maximal power in normoxia and in hypoxia

The Pmax in H is related to VE max in H (Fig 8).

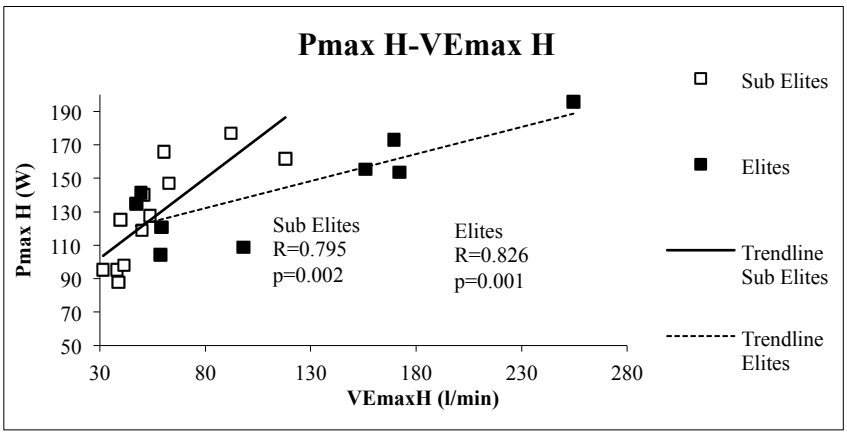

Figure 8. Correlation between maximal power in hypoxia and maximal ventilation in hypoxia

Decrease in VO2max from N to H was correlated with the difference of minimal SpO2 between N to H (Fig 9).

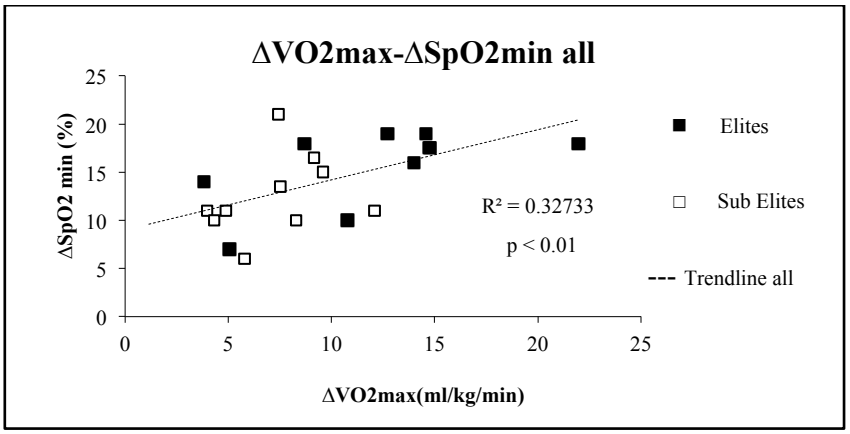

Figure 9. Correlation between difference of VO2max hypoxia-normoxia and difference of saturation hypoxia normoxia pooling all the subjects together

Considering all the subjects together, HFnu(5-10min) was correlated with the difference SpO2 between the end of the exercise and the end of recovery period (magnitude of re-saturation) (Fig 10).

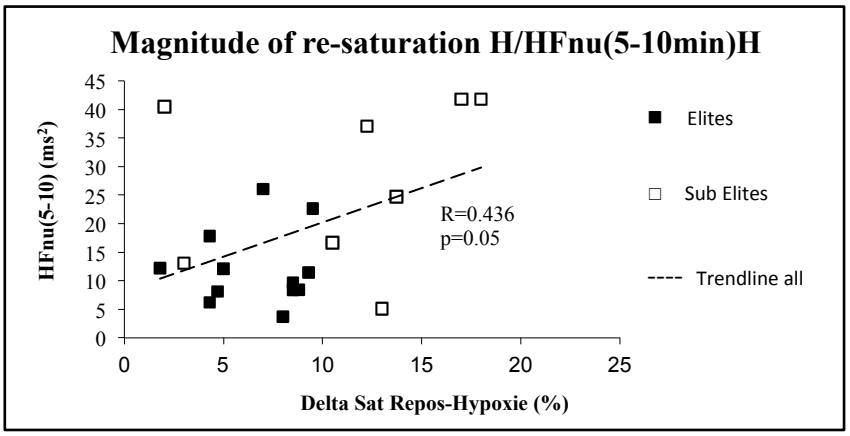

Figure 10. Relationship between the HFnu measured during the last 5 min of the recovery period and the difference in SpO2 between the end of exercise and the end of recovery

4.Discussion

4.1. Systemic values

As expected VO2max and Pmax decreases in hypoxia (4,26-28). In absolute values the loss of power was larger in the elite group. This has been reported in others studies, supporting the

hypothesis that highly trained endurance athletes suffer more severe gas exchange impairments (28).

The correlation between the difference of arterial oxygen saturation and the loss of VO2max allows to partially explain the loss in VO2max by the hypoxemia, which is larger in elite athletes.

The subjects with a greater VO2max in normoxia have a greater impairment in arterial oxygen saturation, which leads to a greater loss in VO2 max in hypoxia.

Pmax H is correlated to VEmax H. Subjects with a greater hypoxic ventilatory drive (greater increase in VE) have better performances at high altitude.

The decrease in SpO2 was larger in the elites group but this was not correlated with a more important increase in respiratory rate, which may be explained by a better tolerance to hypoxemia in endurance-trained athletes.

Greater tolerance to hypoxia (i.e. lower increase of respiratory rate, VE and HR in response to hypoxia) can be favorable to athletes at low altitude but, at high altitude, it's a predictor of a worse adaptation.

Ventilatory response to hypoxia has been used to predict the individual sensitivity to hypoxia.: this parameter is given by the ratio between the difference of ventilation and the difference of saturation between hypoxia and normoxia. There is an important inter-individuals variability, but subjects with a lower ventilatory response tend to have more difficulty of adaptation to the altitude and to suffer of more acute mountain sickness. Peripheral chemoreceptors sensibility determines the intensity of the respiratory response (5).

In the HRmax no difference was found between 512m asl and 3000m asl. In acute hypoxia HRmax reduction is still under debate (20). In our study the sample size was not large enough to compare these results.

4.2HRR-HRV- Parasympathetic reactivation

Heart rate recovery (HRR) following 6min sub-maximal exercise does not show significant differences between groups or conditions, there was an important inter-individuals variability in both groups. A recent study about the effects of acute hypoxia on post-exercise parasympathetic reactivation (15) has found reduced HRR(60s) but an unchanged HRR(T) following sub-maximal exercise in hypoxia conditions. The authors make three hypothesis to

explain these discrepancies 1) they are due at the fact that the variables span different time frames, 2) they may be caused by different mathematical entities or 3) they may be the result of different underlying mechanisms. The authors of the study, on the other hand, did not find any difference in HRR between hypoxia and normoxia following supra-maximal exercise: the different effect on HRR given by sub-maximal and supra-maximal exercise may show an important influence of post-exercise metabolite accumulation (which is a stimulus for chemoreceptors and metaboreflex through changes in plasmatic pH) on post-exercise parasympathetic activity restoration (15). Others papers shown a possible relationship between hypoxemia and HRR(60s) in unhealthy subjects (carotid atherosclerosis and diabetic patients with a high rate of scintigraphic images of myocardial ischemia), but not in healthy individuals. (29, 30,31)
Important inter-individual variability associated with relative small size of groups can explain why we don't find significant difference between the two conditions.

At rest, we found a significant difference between the two groups (E vs. SE) on HVR indices (HFnu, LFnu) but we did not find any effect related to the condition (H vs. N). These results agree with the belief that altitude should generally exceed 3500 meters to have an effect on cardiac parasympathetic activity at rest (15,29).
As shows in several studies, at rest in normoxia more trained subjects have a greater parasympathetic tone compared to less trained ones (6,9,15,16).
Elites athletes, during exercise in normoxia, have a greater parasympathetic tone if compared to sub elites subjects for the same intensity of exercise. Measurement of HRV parameters has been used to assess and predict the impact of aerobic training on endurance running performance (9).
Following sub-maximal running exercise it was observed that parasympathetic reactivation is impaired in normobaric hypoxia if compared to normoxia, but the difference was not observed when the exercise was supra-maximal (15).
In this study we analyzed heart rate frequency component in the second 5 min period of a 10 min recovery phase following a sub-maximal running exercise (6 min run). In the sub-elite group we did not find any significant difference between hypoxia and normoxia. In the elites group, on the other hand, high frequency components (which are associated with parasympathetic modulation of the cardiac activity) was increased in hypoxia.
If we consider all the 23 subjects together, HFnu(5-10min) was correlated with the difference of arterial oxygen saturation between the end of the recovery and the end of the exercise

(magnitude of re-saturation). Elite group has also a greater desaturation in hypoxia (desaturation is correlated to the decrease in VO2max in hypoxia). RMSSD(30s) shows an increased parasympathetic reactivation only in E.

We can suppose that post-exercise re-saturation (which is greater in E) is a stimulus for the parasympathetic system and this can partially explain the difference in sympatho-vagal balance in the second part of the recovery. This is not in contradiction with the studies that show a greater sympathetic modulation of cardiac activity just after an exercise in hypoxia (15). Modulation of autonomic nervous system can play a role in the differences of adaptation to hypoxia between groups.

5. Conclusions

For the cardiovascular values, in agreement with the mentioned studies, we find a reduction of the maximal performance parameters in hypoxia (VO2max, maximal power) with a greater decrease for elites athletes. This means that also elites ski-alpinist athletes, who are chronically exposed to high altitude conditions, are more sensible to hypoxia than less trained subjects, like for other endurance-trained athletes.

Regarding the post-exercise period a key finding is that the parasympathetic modulation (RMSSD(30) and HFnu(5-10)) was increased in hypoxia if compared to normoxia in the elites group only. This was statistically correlated with the post-exercise re-saturation, which was greater for elites.

These findings are partially in contrast with the initial hypothesis of a relative increase in sympathetic/decreased parasympathetic modulation of cardiac activity in hypoxia, others studies with larger groups are needed to confirm this result.

Autonomic nervous system has an important role in hypoxia adaptation and the differences in autonomic modulation of cardiac activity between elites and sub elites athletes may play a role in the individual' differences of performance at high altitude. Post-exercise heart rate variability analyses seem to be a useful tool to evaluate autonomic nervous system modulation of cardiac activity in hypoxia: this technique has been only seldom addressed in scientific studies.

6. Limitation of the study

The main limitation in this study is the sample size of the groups, which was not large enough to compare data with important inter-individuals variability. Autonomic modulation of cardiac activity is influenced by many variables and to assess the effect of hypoxia on the two groups the sample size was too small. Although P values were often close to be significant, the standard deviation was also large. On the other hand, during this study we had the opportunity to test ski-alpinist that are among the best athletes in Switzerland and this was the deciding factor that determined the size of the two groups.

Another factor that might affect the results of the study is that the two samples are composed by both males and females. Menstrual cycle phase has an influence in hemodynamic regulatory systems via the hormonal plasma concentration. In a future study it would be interesting to study the effect of the menstrual cycle phase on the HRV.

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