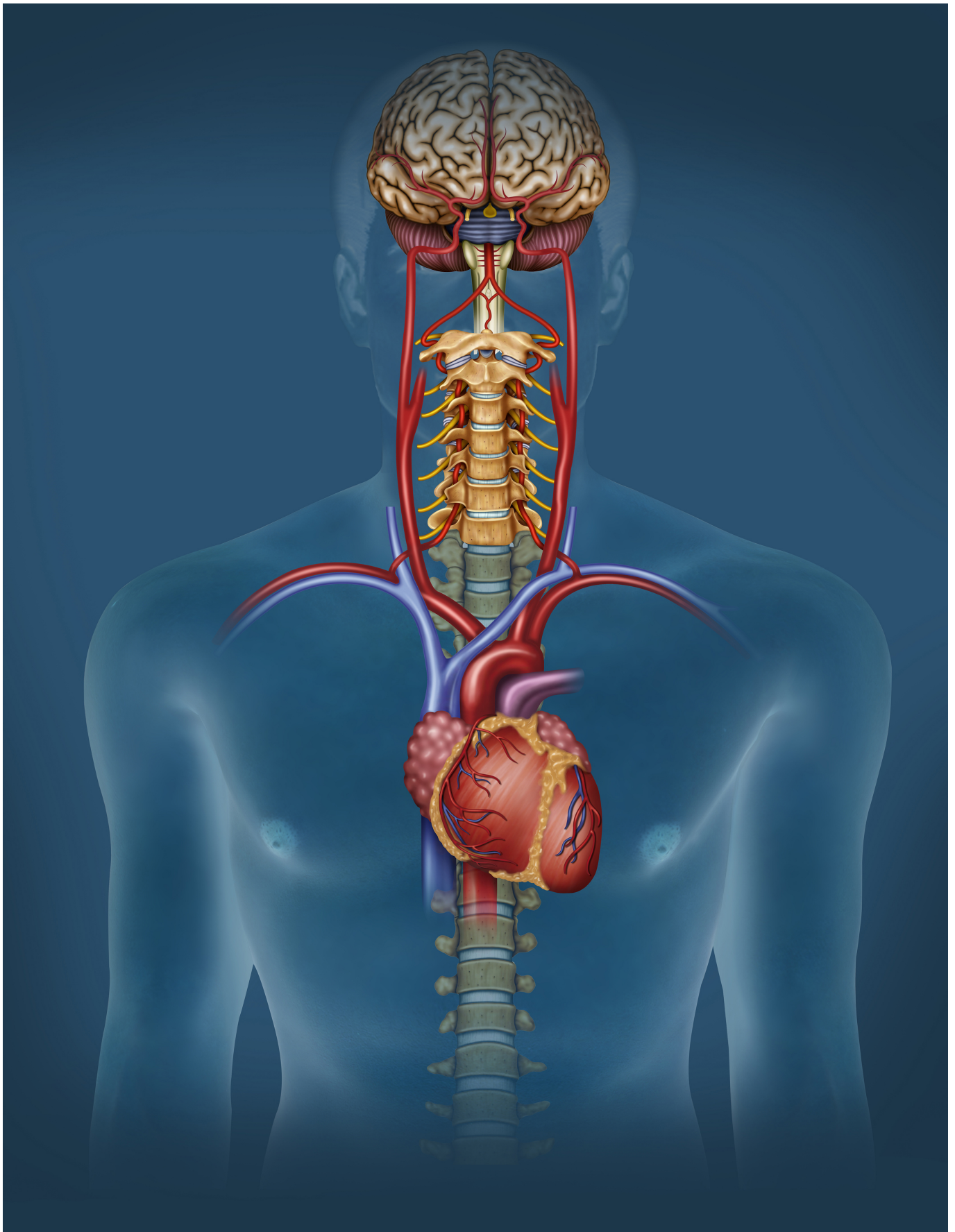


ORIGINAL ARTICLE

# Sex-specific reaction of the cardiac autonomic - nervous system to different training phases in Swiss elite runners

CARDIOLOGY / ELITE SPORTS / MONITORING / PERFORMANCE / RECOVERY / SPORTS AND TECHNOLOGY /  
SPORTS MEDICINE



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## Abstract

**Background:** Heart rate variability (HRV) as a measure of the cardiac autonomic nervous system activity (CANA) has the potential to tailor endurance training and may contribute to the prevention of overtraining. We aimed to investigate whether there are sex differences and sex-specific reactions of the CANA to different training periods (TPs) in Swiss elite runners.

**Methods:** Two HRV measurements (each 5 minutes supine and 5 minutes standing) per athlete were performed, the first during preparation period (PP) and the second during competition period (CP). Main outcome parameters were the square root of the mean squared differences of successive R-R intervals in supine position (RMSSD<sub>supine</sub>) as a time-domain marker of parasympathetic activity and the low frequency/high frequency power ratio after orthostatic challenge (LF/HF<sub>stand</sub>) as a frequency-domain marker of the sympatho-vagal balance. Average total number of training sessions per week (TSPW) as well as number of high-intensity and low-intensity TSPW was recorded.

**Results:** Fifteen female (23.5±4.2 years) and 22 male (21.8±3.2 years) elite runners were included. Females reported a higher number of low-intensity TSPW in PP while there were no sex differences in any other training parameters. Females showed a higher RMSSD<sub>supine</sub> and a lower LF/HF<sub>stand</sub> compared to their male counterparts in both training periods. Males showed a higher LF/HF<sub>stand</sub> in CP compared to PP while LF/HF<sub>stand</sub> remained unchanged in females in both periods.

**Conclusion:** Male runners showed a shift towards higher markers of sympathetic activity in CP compared to PP while these markers did not change between TPs in female runners. Compared to males, females had higher markers of parasympathetic activity and lower markers of sympathetic activity in all TPs.

## Zusammenfassung

**Hintergrund:** Die Analyse der Herzfrequenzvariabilität (HRV) ermöglicht eine Beurteilung der kardialen autonomen Nervensystemaktivität (CANA) und das Potenzial, Ausdauertrainings zu steuern und Übertraining zu verhindern. Ziel der Untersuchung war, Geschlechtsunterschiede und geschlechtsspezifische Reaktionen des CANA in verschiedenen Trainingsperioden (TPs) von Schweizer Elite Läufer zu untersuchen.

**Methoden:** Zwei HRV Messungen (jeweils 5 Minuten Rückenlage und 5 Minuten Stehen) pro Sportler wurden durchgeführt. Die erste während der Vorbereitungsphase (PP) und die zweite während Wettkampfphase (CP). Primäre Endpunkte waren Zeit-Domain-Marker der parasympathischen Aktivität (Quadratwurzel der mittleren quadratischen Unterschiede der sukzessiven R-R-Intervalle in Rückenlage, RMSSD<sub>supine</sub>) und Frequenz-Domain-Marker der

sympathovagalen Balance nach orthostatischer Belastung, Niedrig-Frequenz/Hochfrequenz Domänen Verhältnis, LF/HFstand). Durchschnittliche Trainingsstunden pro Woche (TSPW) sowie Anzahl der hochintensiven und niedrigintensiven TSPW wurden aufgezeichnet. *Ergebnisse:* Fünfzehn weiblich ( $23,5 \pm 4,2$  Jahre) und 22 männlich ( $21,8 \pm 3,2$  Jahre) Elite-Läufer wurden eingeschlossen. Frauen hatten eine höhere Anzahl von TSPW mit niedriger Intensität in der PP, ansonsten gab es keine Geschlechtsunterschiede in anderen Trainingsparametern. Frauen zeigten eine höhere RMSSDsupine und eine niedrigere LF/HFstand im Vergleich zu männlichen Läufern in beiden Trainingsperioden. Männer zeigten einen höheren LF/HFstand in der CP im Vergleich zur PP, während LF/HFstand bei Frauen unverändert blieb in beiden Perioden.

*Schlussfolgerung:* Männliche Läufer zeigten eine Verschiebung hin zu höher Marker der sympathischen Aktivität in der CP im Vergleich zur PP während diese Marker sich bei weiblichen Läufern nicht zwischen den TP unterschieden. Im Vergleich zu Männern hatten Frauen höhere Marker der parasympathischen Aktivität und niedrigere Marker der sympathischen Aktivität in allen TP.

## Introduction

The right balance between stress and recovery is a key component for successful sports performance [1]. In order to adjust training to the individual need of athletes, it is therefore highly important to monitor their stress-recovery balance. It has been suggested that analyzing HRV as a marker of the cardiac autonomic nervous system activity (CANA) could be an important tool for stress prediction in athletes [2–5]. As a first step for such a monitoring, it is important to know how HRV changes between different training periods (TPs). Endurance training is generally accepted to increase HRV markers of parasympathetic activity [6–8]. However, it has been shown that very intensive exercise training, such as performed by male world class rowers or recreational marathon runners, results in a conversion from cardiac vagal to sympathetic predominance [9,10]. During competition period (CP), track and field athletes perform more intensive training than during preparation period (PP), suggesting a potentially higher sympathetic activity in CP compared to PP.

Sex-specific effects of different training periods on HRV have been investigated in adolescent [10] and adult elite cross-country skiers [11]. It is presently unknown whether HRV parameters change between different training periods in elite runners and whether such changes would be different between sexes. Therefore, the aim of the present study was to investigate sex-specific reactions of HRV on different training stimuli during different training periods in elite runners. We hypothesized that there is a conversion from vagal to sympathetic predominance during the CP and that this conversion may be different between male and female athletes.

## Methods

### Subjects

Male and female middle- and long-distance runners competing at national level were recruited to participate in the present study. Inclusion criteria were age between 14 and 35 years and holder of a Swiss Athletics license, which allows to compete at national track and field competitions. Exclusion criteria were known cardiovascular diseases, febrile infections within the last 2 weeks prior to the examination and intensive training within the last 24 h prior to the measurements. The study was approved by the local ethics committee and all participants signed the informed consent.

### *Measurement procedures*

Two measurements per athlete were performed, the first during PP between November and March and the second during the CP between May and September. Each measurement started with a standardized questionnaire assessing training habits followed by a clinical examination including blood pressure and HRV measurement during spontaneous breathing. Every athlete was tested by the same procedure and during the same time of the day (between 5 and 8 p.m.) on both occasions.

### *Heart rate variability*

Short-term HRV recordings were performed in supine position and after an orthostatic challenge using a three channel electrocardiograph recorder from a Lifecard CF digital recorder (Lifecard CF, Del Mar Reynolds Medical Inc, Irvine, CA, USA). After a 5 min recording in supine position, athletes were verbally instructed to stand up and stand quietly for another 5 min. Data was uploaded to the Pathfinder Software (Spacelabs Healthcare, Snoqualmie, Washington, USA) to visually analyse the ECG. Measurements with less than 90% valid data were excluded from analysis. R-R intervals of the measurements were transferred to Kubios-HRV (V2.1, Department of Physics, University of Kuopio, Finland) [12] software and analyzed as recommended by the European Society of Cardiology Task Force [6]. Trend components were removed using the smoothness priors method ( $\lambda = 500$ ,  $f_c = 0.035$  Hz). Analysis was performed for 4 min segments in each supine position and standing. The segment for supine position started 4 min before standing up and the segment for standing started at the shortest R-R interval. Mean heart rate (HR), the square root of the mean squared differences of successive R-R intervals (RMSSD), low-frequency power (LF, ms<sup>2</sup>), high frequency power (HF, ms<sup>2</sup>) and LF/HF power ratio were calculated. Frequency bands were set at 0.15 to 0.4 Hz for HF and 0.04 to 0.15 Hz for LF [6]. HF and LF in normalized units (HF<sub>nu</sub> and LF<sub>nu</sub>) were not reported due to their redundancy with LF/HF power ratio [13]. Primary outcome parameters were the RMSSD in supine position as marker of vagal tone [6] and the LF/HF power ratio after orthostatic challenge (stand) as marker of sympathetic activity [14]. All signals were corrected with the automated artifact correction filter from Kubios-HRV (artifact correction was set as low as possible to eliminate artifacts).

### *Blood pressure*

Systolic and diastolic blood pressure were measured with an automated blood pressure monitor (OMRON 711, Omron, Switzerland). Two measurements were taken after 10 min in



supine position and the mean of these two measurements was calculated and used for analysis.

### *Monitoring of exercise training*

The average number of total, high-intensity and low-intensity training sessions per week (TSPW) in the last four weeks before the measurement was quantified by a standardized questionnaire.

### *Data analysis*

The data was analyzed with SPSS Statistics, Version 21 (IBM Corp. Armonk, NY, USA). Normality of the data was examined using the Kolmogorov-Smirnov test. Data is presented as mean  $\pm$  standard deviation or median (inter-quartile range). Non-parametric data were log transformed for analysis. Analysis was performed using a repeated measures ANOVA for sex, time and time-sex interaction. Paired t-tests were used to calculate time effects within sexes. Mann-Whitney U tests were used to calculate the different HRV reactions to training between middle- and long-distance runners. Female athletes were excluded from this subanalysis due to the small sample of female middle-distance runners. A p value of less than 0.05 was considered statistically significant.

## **Results**

### *Subjects*

Thirty-seven athletes were included in the final analysis, whereof 22 were male and 15 female athletes. Two European champions in mountain running and 14 athletes who qualified for international races like European Championship in Athletics participated in the present study. Athletes' characteristics are shown in Table 1. There were no significant differences between sexes except for height and body weight (Table 1).

### *Training*

Training data are illustrated in Table 2. Both female and male athletes performed significantly more high-intensity and significantly less low-intensity TSPW in CP compared to PP. There were no significant sex differences with regard to number of total TSPW, number of high-intensity or low-intensity TSPW. The only exception was the number of aerobic TSPW during PP, in which female athletes had significantly more TSPW compared to their male counterparts. No athlete exhibited symptoms of overtraining during PP or CP.

|   | Females (n=15) | Males (n=22)   | P-value |
|---|----------------|----------------|---------|
| Age   | 23.53 ± 4.17   | 21.82 ± 3.19   | 0.165   |
| Height                                      | 169.40 ± 5.07  | 179.23 ± 4.91  | 0.000   |
| Weight                                      | 57.31 ± 5.59   | 67.02 ± 5.61   | 0.000   |
| Body Mass Index (BMI)                       | 19.97 ± 1.79   | 20.84 ± 1.23   | 0.088   |
| Age categories <sup>a</sup>                 | 4.47 ± 0.74    | 4.14 ± 1.08    | 0.403   |
| Middle-distance/ Long-distance <sup>b</sup> | 4/ 11          | 13/ 9          | 0.055   |
| Systolic blood pressure                     | 105.77 ± 5.35  | 120.89 ± 10.53 | 0.000   |
| Diastolic blood pressure                    | 66.33 ± 8.36   | 73.81 ± 12.61  | 0.216   |

Values are given as mean ± standard deviation.

a: Age categories are made as used in athletics; 1= under 16 years, 2= under 18 years, 3= under 20 years;

4= under 23 years, 5 = masters athletics; for most athletes, training load and sports-specific training increase with age.

b: Middle-distance (800 m and 1500 m), Long-distance (5000 m, 10000 m, half marathon, marathon)

Table 1: Athletes characteristics.

|                     | PP          | CP          | p-value sex<br>PP | CP    | p-value time |
|---------------------|-------------|-------------|-------------------|-------|--------------|
| Total TSPW          | 6.92 ± 2.67 | 7.14 ± 2.37 | 0.052             | 0.444 | 0.293        |
| Males               | 6.27 ± 2.57 | 6.86 ± 2.25 |                   |       | 0.037        |
| Females             | 7.87 ± 2.61 | 7.53 ± 2.56 |                   |       | 0.571        |
| Low-intensity TSPW  | 5.81 ± 2.50 | 4.78 ± 2.03 | 0.029             | 0.191 | 0.000        |
| Males               | 5.09 ± 2.37 | 4.55 ± 2.26 |                   |       | 0.022        |
| Females             | 6.87 ± 2.39 | 5.13 ± 1.64 |                   |       | 0.003        |
| High-intensity TSPW | 1.11 ± 0.97 | 2.35 ± 1.16 | 0.466             | 0.792 | 0.000        |
| Males               | 1.18 ± 0.91 | 2.32 ± 0.95 |                   |       | 0.000        |
| Females             | 1.00 ± 1.07 | 2.4 ± 1.45  |                   |       | 0.004        |

PP (preparation period), CP (competition period), TSPW (training sessions per week)

Values are given as mean ± standard deviation or median (interquartile range); PP (preparation period); CP (competition period); HR (heart rate); RMSSD (square root of the mean of the squares of differences between adjacent RR intervals); LF (low frequency power); HF (high frequency power). P-value for time\*sex interaction and p-value for sex differences were calculated using repeated measures ANOVA while time effects were calculated using paired t-tests. Significance level was set at 0.05.

Table 2: Training characteristics.

Neither HR nor any HRV parameters changed between training periods when female and male athletes were analyzed together. When analyzed separately, male athletes showed a significantly higher LF/HFstand in CP compared to PP. In supine position, trends (p-values ≤ 0.09) towards a higher HR and LF/HF ratio in CP compared to PP were observed in males. After orthostatic challenge, females had a tendency towards a lower HR and men towards a lower HF in the CP compared to PP (Table 3).

Diastolic blood pressure significantly changed between the two training periods. This change only remained significant for males and not for females when analyzed sex-specifically (Table 4). Systolic blood pressure remained similar between training periods.

|                 | PP                | CP                | P-value<br>Time*sex | P-value<br>Time | P-value<br>sex |
|-----------------|-------------------|-------------------|---------------------|-----------------|----------------|
| <b>Supine</b>   |                   |                   |                     |                 |                |
| HR              | 56.31 ± 6.90      | 57.41 ± 7.82      | 0.110               | 0.371           | 0.001          |
| Males           | 58.33 ± 5.99      | 61.04 ± 6.14      |                     | 0.088           |                |
| Females         | 53.34 ± 7.27      | 52.08 ± 7.05      |                     | 0.334           |                |
| RMSSD           | 68.43 [39.30]     | 56.20 [69.21]     | 0.626               | 0.470           | 0.021          |
| Males           | 54.46 [32.11]     | 46.09 [37.49]     |                     | 0.570           |                |
| Females         | 72.65 [38.41]     | 100.85 [72.42]    |                     | 0.733           |                |
| LF              | 1633.69 [2007.37] | 1623.25 [1370.53] | 0.444               | 0.539           | 0.608          |
| Males           | 1433.98 [1751.61] | 1479.25 [1199.10] |                     | 0.506           |                |
| Females         | 2097.66 [1435.54] | 1751.81 [1239.45] |                     | 0.334           |                |
| HF              | 1296.99 [1875.98] | 1011.52 [2897.73] | 0.731               | 0.231           | 0.024          |
| Males           | 934.25 [1143.07]  | 697.44 [1120.41]  |                     | 0.223           |                |
| Females         | 2018.63 [2164.82] | 2817.11 [3626.24] |                     | 0.910           |                |
| LF/HF           | 1.33 [1.01]       | 1.30 [1.68]       | 0.151               | 0.365           | 0.003          |
| Males           | 1.42 [1.10]       | 1.79 [1.73]       |                     | 0.072           |                |
| Females         | 1.08 [1.21]       | 0.75 [0.79]       |                     | 0.281           |                |
| <b>Standing</b> |                   |                   |                     |                 |                |
| HR              | 70.62 ± 8.28      | 72.28 ± 12.59     | 0.029               | 0.458           | 0.002          |
| Males           | 71.92 ± 7.36      | 77.54 ± 12.92     |                     | 0.131           |                |
| Females         | 68.71 ± 9.40      | 64.58 ± 7.09      |                     | 0.088           |                |
| RMSSD           | 36.89 [23.30]     | 38.64 [39.80]     | 0.403               | 0.430           | 0.023          |
| Males           | 34.14 [21.00]     | 31.00 [31.11]     |                     | 0.592           |                |
| Females         | 39.24 [41.15]     | 48.66 [25.15]     |                     | 0.394           |                |
| LF              | 2414.01 [1968.33] | 2308.96 [2790.57] | 0.679               | 0.629           | 0.512          |
| Males           | 2154.05 [2137.88] | 1976.19 [3835.86] |                     | 0.306           |                |
| Females         | 2707.49 [970.35]  | 2458.23 [2266.46] |                     | 1.000           |                |
| HF              | 395.72 [649.18]   | 479.06 [801.14]   | 0.229               | 0.445           | 0.045          |
| Males           | 297.92 [529.64]   | 262.27 [523.64]   |                     | 0.067           |                |
| Females         | 424.27 [1316.35]  | 588.10 [773.73]   |                     | 0.191           |                |
| LF/HF           | 5.64 [6.24]       | 6.42 [7.51]       | 0.088               | 0.558           | 0.024          |
| Males           | 5.89 [6.07]       | 10.15 [6.94]      |                     | 0.001           |                |
| Females         | 5.62 [7.40]       | 3.75 [4.18]       |                     | 0.281           |                |

Table 3: Changes over time, time\*sex interactions and sex differences of heart rate variability parameters in supine position an after orthostatic challenge.



### *Sex differences in HR, HRV and blood pressure*

Female athletes showed significantly higher RMSSD and HF power and significantly lower HR and LF/HF power ratio in both, supine position and after orthostatic challenge while no sex difference was found for LF power (Table 2).

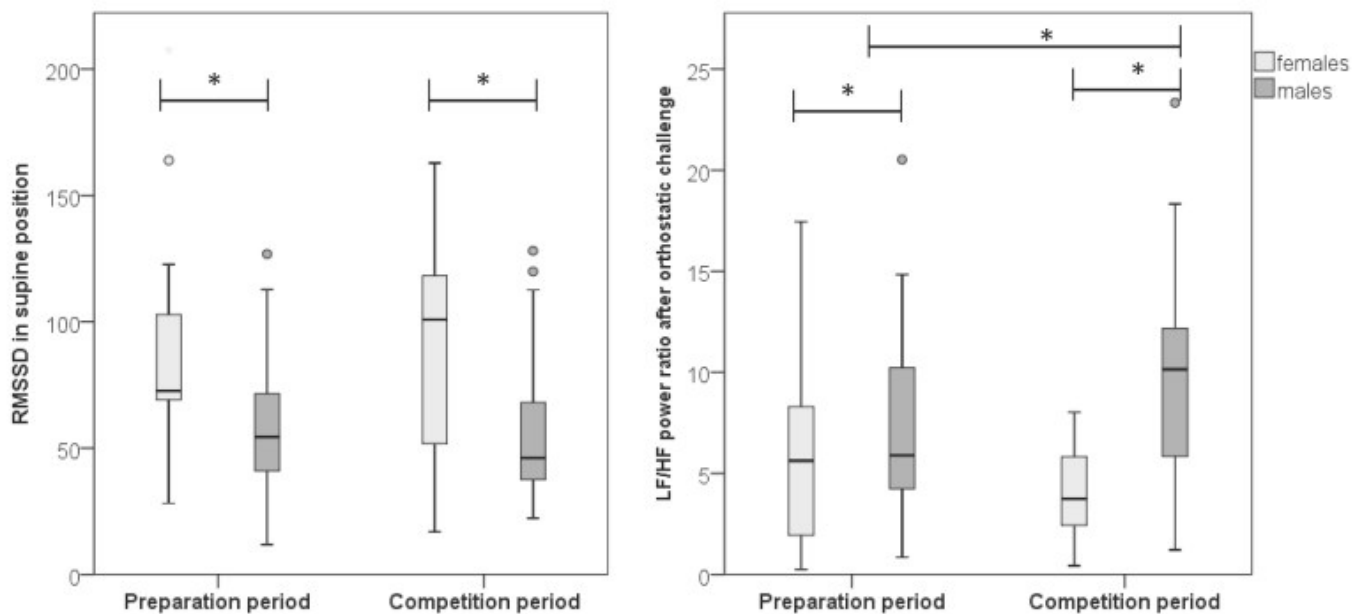
### *Time-sex interactions between training phases*

Time-sex interaction was only significant for HR after orthostatic challenge, for which male athletes showed increased while female athletes showed decreased HR in CP compared to PP. A trend ( $p=0.088$ ) was observed for LF/HFstand, with male athletes showing an increase while female athletes showed a decrease from PP to CP (Figure 1).

## **Discussion**

The main finding of the present study was a shift towards higher markers of sympathetic activity in CP compared to PP in male but not in female athletes. Moreover, as shown in other sports [11], female runners showed higher markers of parasympathetic activity and lower markers of sympathetic activity in all TPs.

CP in our athletes was more strenuous than PP due to significantly higher number of high-intensity TSPW and a slight but not significant increase in total number of TSPW in CP compared to PP in both, male and female track and field athletes (Table 2). Our results of a shift towards higher sympathetic activity in the more strenuous training phase in male athletes is therefore in agreement with studies conducted in male rowers [9] and recreational marathon runners [15]. However, such a conversion was not found in other sports such as volleyball [16] or soccer [17]. While several studies measured changes in HRV between different TPs in female and male athletes [18,19], to our knowledge, sex-specific changes between TPs have so far only been investigated in cross-country skiers.



Hedelin et al. found an increased total variability at rest and reduced LF power in the tilted position in adolescent cross-country skiers directly after the CP compared to PP [10]. However, no significant differences between HRV parameters in CP and PP were found when sex-specific analysis was performed, which may be related to the small sample size [10]. In elite cross-country skiers, HRV parameters did not change between various training periods in supine position or after orthostatic challenge, neither in female nor in male cross-country skiers [11]. We suggest that besides different study populations further reasons for the different findings may have been the different training volume and intensity distribution between cross-country skiers and runners, the different training periodization, the different training history and performance level or the sport mode itself.

Low-intensity endurance training is known to increase markers of parasympathetic activity [6–8]. Whether the significantly higher number of low-intensity trainings per week in female athletes in both training phases is protective against a conversion from vagal to sympathetic predominance in the CP remains to be elucidated. However, a greater relative decrease in low-intensity TSPW in CP compared to PP and a greater relative increase in high-intensity TSPW was found in female compared to male athletes. Therefore, differences in training intensity between PP and CP are unlikely to be the reason for the greater response in LF/HFstand found in male athletes. A more likely reason may be the higher number of long-distance and lower number of middle-distance runners in female athletes compared to their male counterparts. It may be that athletes with a longer competition time show fewer changes in HRV between different TPs. We tested this hypothesis in a subanalysis in our male participants and found an increase in LF/HFstand in CP for male middle-distance but not long-distance runners

(subanalysis for females was not conducted because only 15 were middle-distance runners). There were no differences in supine position. Future studies including a more homogeneous group of middle- and longdistance runners should test whether these results can be confirmed in a larger sample size, also including female athletes.

We found significant sex differences in all calculated HRV parameters except LFsupine and LFstand. A higher HFsupine has also previously been reported in young women compared to men (Barnett et al., 1999; Fukusaki et al., 2000) while other studies showed similar HF power between sexes (Agelink et al., 2001; Fürholz et al., 2013; Ramaekers et al., 1998). Absolute HF power and RMSSD are dependent on HR (Sacha et al., 2013; Sacha & Pluta, 2008). These conflicting results in the literature may therefore be a consequence of sex differences in HR (Fürholz et al., 2013). Consequently, the higher RMSSD and HF power in supine position and after orthostatic challenge in female compared to male athletes found in some studies may partly be a result from their lower HR in both positions.

Our results indicate the absence of sex differences in LFstand in elite runners. In response to stressors such as tilt or active orthostatic challenge, other authors reported a lower LF power in young females compared to men (Barantke et al., 2008). However, our results confirm the results of no sex difference in LFstand after orthostatic challenge in other athletes such as in adolescent [10] or elite cross-country skiers [11], indicating that sex differences in this HRV parameter may diminish with increasing training load.

The reasons for sex differences in HRV are not clear and may have different origins. For example, it has been suggested that sex differences in ANS activity may be present due to developmental differences, different sex hormones, differences in afferent receptor stimulation, in central reflex transmissions, in the efferent nervous system or in post synaptic signaling (Dart et al., 2002).

Limitations were the use of HRV measurements as an indirect method to assess the autonomic innervation of the heart. At the moment it is highly debated whether any HRV parameter reflects cardiac sympathetic activity. It is generally accepted that LF fluctuations of HRV at rest are not related to muscle sympathetic nerve activity [8]. However, when measured in an orthostatic challenge, it has been shown that LF/HF power ratio and muscle sympathetic nerve activation change in parallel [14,20], suggesting that this HRV ratio may reflect enhanced adrenergic activity as response to provoked stress. A further limitation is the use of spontaneous breathing instead of paced breathing, which may have resulted in a reduced reproducibility of frequency-domain HRV parameters, particularly those related to the LF power band [21]. Analysis in female athletes was not synchronized with their menstrual cycle. Further, this study comprises a relatively heterogeneous population of athletes from different sport clubs with different training regimen, which makes it more difficult to find changes.

## Conclusion

Male runners showed a shift towards higher markers of sympathetic activity in CP compared to PP while these markers did not change between TPs in female runners. Compared to males, females had higher markers of parasympathetic activity and lower markers of sympathetic activity in all TPs.

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## Practical implications

Our results point out the importance of sex-specific HRV analysis since the significant change in LF/HFstand between TPs for male runners would have gone undetected when only analyzing female and male athletes together. This finding may be important for study designs and analyses of future studies in this field and has also practical implication on daily training monitoring with HRV. Since no athlete included in this study experienced symptoms of overtraining, we suggest considering sex differences when monitoring stress-recovery balance in athletes for optimal training steering. Further, the fact that differences between PP and CP were only found for LF/HFstand suggests that HRV parameters measured during orthostatic challenge may be more sensitive with regard to training than HRV parameters measured in supine position.

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ATHLETES   AUTONOMIC NERVOUS SYSTEM   ENDURANCE   GENDER DIFFERENCES   ORTHOSTATIC TEST