Effects of exercise training on heart rate and QT interval in healthy young individuals: are there gender differences?

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Aims The aim of the present study was to assess the effects of exercise training on heart rate, QT interval, and on the relation between ventricular repolarization and heart rate in men and women.

Methods and results A 24 h Holter recording was obtained in 80 healthy subjects (40 males) who differed for the degree of physical activity. Trained individuals showed a lower heart rate and a higher heart rate variability than sedentary subjects, independent of the gender difference in basal heart rate. Mean 24 h QTc was similar in trained and non-trained men, while a significant difference was observed between trained and non-trained women. Exercise training reduced the QT/RR slope in both genders. This effect on the QT/RR relation was more marked in women; in fact, the gender difference in the ventricular repolarization duration at low heart rate observed in sedentary subjects was no longer present among trained individuals.

Conclusion The results of this study suggest that the cardiovascular response to exercise training may be different in men and women. Women may benefit more from interventions aimed to increase physical activity as a tool for prevention of cardiovascular morbidity and mortality.

KEYWORDS QT interval; QT/RR relationship; Heart rate variability; Gender; Exercise training

Introduction

The effects of exercise training on the heart have been widely explored.1 Experimental and human studies have shown that exercise training improves survival after myocardial infarction.2,3 This effect may be partially explained by an increase in cardiac vagal activity, which reduces the susceptibility to arrhythmias and sudden death.4 Indeed, exercise training decreases heart rate and increases heart rate variability (HRV) in healthy individuals5,6 and in patients with myocardial infarction7 or heart failure.8 A higher heart rate before and during exercise in apparently healthy persons9 and a decreased HRV are associated with a higher risk of sudden death.10

The effects of exercise training on other indices associated with a higher risk of sudden death, such as QT interval duration, have not been extensively studied. A prolonged QT interval may favour life-threatening arrhythmias and sudden death in the long QT syndrome11 after myocardial infarction12 and even in healthy individuals.13,14 Recently, Perhonen et al. have shown that also carriers of long QT syndrome gene mutations may benefit from regular exercise training.15

It has been shown that there are gender differences in heart rate, QT interval duration, and in the relation between ventricular repolarization and cardiac cycle length.16 Women, when compared with men, have a higher heart rate and a longer QT interval corrected for heart rate. A further QT interval prolongation at long cycle lengths16 and a more significant effect of QTc-prolonging drugs in women, compared with men, have been demonstrated.17 A greater alteration of ventricular repolarization duration in females when compared with their male counterparts has been also shown in response to important changes in plasma and intracellular electrolytes, such as during haemodialysis.18

The aim of the present study was to assess the effects of exercise training on heart rate, QT interval, and on the relation between ventricular repolarization and heart rate in men and women. QT interval variability and its long-term relation with RR interval, as well as the 24 h variability of
heart rate have been evaluated in a group of young trained athletes of both genders and compared with that of sedentary subjects matched for age and gender.

Methods

Study population

The study was performed in 80 apparently healthy subjects (40 males and 40 females) who differed for the degree of physical activity. Twenty men and 20 women who were currently undergoing two or more weekly exercise training sessions and were participating in at least one weekly competitive sport event were considered trained subjects. All the subjects in the trained group had been performing physical activity for several years and were already trained at the time of study recruitment. The remaining 40 subjects (20 males and 20 females) were considered sedentary since they did not practise sport. The degree of physical activity in each group was expressed as METS min/week, according to the International Physical Activity Questionnaire (IPAQ) Scoring Protocol. None of the subjects was taking drugs that could have affected QT interval.

All subjects participating in this study gave written informed consent. The local Ethical Committee approved the protocol of the study.

Twenty-four hour ECG Holter recordings

A 24 h electrocardiographic (ECG) Holter monitoring was recorded in each subject. All recordings were obtained using portable battery-operated three-channel Holter recorder (ELA Medical, Le Plessis Robinson, France). All tapes were analysed by an automatic analysis system, performing a 200 Hz A/D conversion with an 8 bit resolution. All subjects reported their daily activities and particularly the time of sleeping and of waking. Recordings were analysed separately for the 24 h period, during wakefulness and during sleep.

Heart rate variability analysis

HRV has been analysed by using time domain parameters. Mean and SD of RR intervals (SDRR) were analysed for the whole 24 h and the periods of wakefulness and sleep. Also, the coefficients of variation of RR intervals (CVRR = SD RR/mean RR × 100) have been calculated for the same periods. The SD of the averages of RR intervals in all 5 min periods (SDANN) and the percentage of RR intervals differing by more than 50 ms from the adjacent RR interval (pNN50) have also been calculated.

QT interval analysis

The digitized three-channel ECG signals were processed by the commercially available ELATEC Holter analysis software (ELA Medical), which sampled the 24 h recording into 2880 templates obtained by a given ECG index, in males compared with females. P values < 0.05 were considered significant.

Statistical analysis

Data are presented as mean (SD) and compared by means of the Student’s t-test. The analysis was also generalized by using linear regression in order to account for the amount of training as a continuous variable (IPAQ score) and in order to perform interaction tests. The interaction between training and gender allowed us to evaluate whether training had a significantly different impact, on a given ECG index, in males compared with females. P values < 0.05 were considered significant.

Results

Characteristics of the population

The characteristics of the study population are summarized in Table 1. The mean ages were 26 (4) and 29 (4) years in trained and sedentary males and 28 (5) and 27 (4) in trained and sedentary women, respectively. Age did not differ between trained and non-trained subjects. Mean weight, body mass index (BMI), and body surface index (BSI) were significantly greater in men than in women, they were not different within gender or between trained and non-trained subjects. The prevalence of cigarette smoking was similar in trained and non-trained subjects and no gender differences were observed. The prevalence of use of oestro-progestinics was similar in trained and non-trained women. Trained subjects had a higher degree of physical activity, expressed with the IPAQ score, than sedentary controls in both genders (P < 0.0001). No differences in physical activity were found between control females (CF) and control males (CM), while the score of trained females (TF) was lower than that of trained males (TM) (P = 0.001; Table 1).

Heart rate and HRV

Women, either trained or not, had on average a higher heart rate than males, as measured during 24 h, during wakefulness and sleep. In both genders the effect of training was to decrease the heart rate significantly, as shown in Figure 1 for the 24 h period. Mean (SD) values during wakefulness were 68 (6) vs. 79 (6) bpm for TM vs. CM (P < 0.001) and 75 (7) vs. 87 (6) bpm TF vs. CF (P < 0.001) and during sleep were 51 (4) vs. 59 (5) bpm TM vs. CM (P < 0.001) and 61 (6) vs. 69 (7) ms TF vs. CF (P = 0.002). The results on the effect of training were confirmed also when the data for the amount of physical activity, as measured by the IPAQ score were analysed, in a regression model.

Heart rate variability, expressed as the SD of mean 24 h RR interval, was greater in men than in women for both non-trained and trained subjects. The effect of training on this parameter was more marked in men (but the interaction was not significant, P = 0.333). Trained men showed a greater SDcR than non-trained men [203 (31) vs. 168 (28) ms, P < 0.001], and the difference was present both during wakefulness and during sleep [155 (27) vs. 127 (19) ms (P < 0.001) and 165 (41) vs. 120 (22) ms (P < 0.001)]. By contrast, trained women had similar SDcR when compared with non-trained women [157 (33) vs. 137 (37) ms], except for the sleeping hours, where again trained women showed a higher HRV than non-TFs [120 (35) vs. 89 (28) ms, P = 0.004]. The same pattern was observed when SDANN and pNN50 were considered. It has to be noted that the difference in HRV between trained and non-trained men

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control Females (CF)</th>
<th>Control Males (CM)</th>
<th>Trained Females (TF)</th>
<th>Trained Males (TM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26 (4)</td>
<td>29 (4)</td>
<td>26 (4)</td>
<td>29 (4)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
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<tr>
<td>Body Mass Index (BMI)</td>
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<tr>
<td>Body Surface Index (BSI)</td>
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<tr>
<td>Physical Activity (IPAQ score)</td>
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</tbody>
</table>

Table 1: Characteristics of the population.
could be explained by a lower mean heart rate in trained subjects, which corresponds to a higher mean RR interval. In fact, when a measure of HRV that takes into account the changes in mean heart rate (the coefficients of variation of RR intervals, CVRR) is considered, the effects of training were evident only during sleep. In this period of the analysis of Holter recordings, the difference in CVRR between trained and non-trained subjects was present in both genders [14.1 (3.7) vs. 11.8 (1.9) in males ($P = 0.019$) and 12.1 (2.8) vs. 10.0 (2.4) in females ($P = 0.018$) Figure 2].

**QT interval, QT interval variability, and QT/RR relationship**

The mean QT interval corrected for heart rate (QTc) was longer in females than in males in both trained and non-trained subjects [412 (3.7) vs. 11.8 (1.9) in males ($P = 0.019$) and 12.1 (2.8) vs. 10.0 (2.4) in females ($P = 0.018$) Figure 2].

Trained and non-trained men a difference was observed between trained and non-trained women. In fact, trained women showed a shorter QTc than sedentary women during the 24 h period [412 (16) vs. 424 (22) ms, $P = 0.045$], during wakefulness [413 (16) vs. 424 (20) ms, $P = 0.075$] and during sleep [410 (16) vs. 424 (22) ms, $P = 0.033$]. Nevertheless, the test for interaction between training and gender was not significant, $P = 0.563$.

Twenty-four hour QTc variability did not differ between men and women, both trained and non-trained, while the circadian variation of QTc was greater in men than in women both in not-trained subjects [8.2 (8.0) vs. 8.0 (9.1) ms, $P = 0.002$] and in trained subjects [11.1 (10.5) vs. 3.0 (10.0) ms, $P = 0.018$]. Exercise training did not affect the variability of QT interval or the circadian variation of QT interval.

Gender differences in the relationship between QT and RR interval were observed in both trained and non-trained subjects. In fact, the slope of the QT/RR regression line

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**Table 1** Characteristics of study subjects

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trained $n = 20$</td>
<td>Control $n = 20$</td>
</tr>
<tr>
<td>Weight, kg, mean (SD)</td>
<td>75 (6)</td>
<td>74 (7)</td>
</tr>
<tr>
<td>Height, m, mean (SD)</td>
<td>1.81 (0.04)</td>
<td>1.78 (0.06)</td>
</tr>
<tr>
<td>BMI, kg/m², mean (SD)</td>
<td>22.7 (1.5)</td>
<td>23.3 (1.9)</td>
</tr>
<tr>
<td>BSI, m², mean (SD)</td>
<td>1.95 (0.9)</td>
<td>1.92 (0.12)</td>
</tr>
<tr>
<td>IPAQ score, min/week mean, (SD)</td>
<td>3997.6 (560.9)</td>
<td>574.1 (355.0)</td>
</tr>
<tr>
<td>Cigarette smoke, n (%)</td>
<td>6 (30%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Oestrogen use, n (%)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
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**Figure 1** Box-plot representation of heart rate, by gender. The inner line indicates the median and the white square indicates the mean. The vertical segments out of the box represent the minimum and the maximum values.

**Figure 2** Box-plot representation of coefficient of variation of RR intervals (CVRR), by gender, during wakefulness and sleep. The inner line indicates the median and the white square indicates the mean; the vertical segments out of the box represent the minimum and the maximum values.
was steeper in females than in males in both groups, in agreement with previous findings.

Exercise training significantly affected the relation between QT and RR interval by reducing the QT/RR slope in both genders. In fact, both male and female trained subjects showed a lower QT/RR slope compared with non-trained subjects [0.13 (0.02) vs. 0.16 (0.02) TM vs. CM, \( P < 0.001 \), and 0.16 (0.03) vs. 0.20 (0.04) TF vs. CF, \( P < 0.001 \)] (Figure 3).

The same result is obtained also if the analysis accounts for the amount of physical activity as measured by the IPAQ score. There was a significant interaction between training and gender: the effect of training in decreasing the slope was higher in females than in males, given the same level of IPAQ score (\( P = 0.044 \) on test for interaction). When the absolute values of QT interval at fixed RR intervals were compared in trained and non-trained men and women, no gender differences in QT interval were found at short RR intervals (600 ms). By contrast, at long cardiac cycles (1000 ms) QT intervals were significantly greater in women than in men in the sedentary group [416 (15) vs. 399 (18) ms, \( P = 0.032 \)], but the gender difference was not present in the group of trained subjects.

**Discussion**

This study has demonstrated that healthy trained individuals of young age show a lower heart rate and a higher HRV than sedentary subjects, independent of the gender difference in basal heart rate.

In contrast, the effects of exercise training on QT interval were different in men and women. In fact, trained women had a shorter QT interval corrected for heart rate than sedentary females, while this difference was not observed in their male counterparts.

Also the long-term relationship between ventricular repolarization and heart rate was affected by exercise training. In trained subjects, QT interval was less prolonged at long cycle lengths than in sedentary individuals and this effect was more marked in women. As a consequence, the gender difference in ventricular repolarization duration at low heart rate observed in sedentary subjects is no longer present among trained individuals.

**Effects of training on heart rate and HRV**

Chronic exercise training produces a resting bradycardia that is thought to be partly due to enhanced vagal modulation. A meta-analysis of 13 studies on 322 subjects showed that exercise training significantly increases both RR interval and the high frequency component of the power spectrum of RR interval (HF), suggesting the role of increased vagal tone.

Our finding that the increase in HRV in trained subjects is present only during sleep is in agreement with a previous study, which showed differences between trained and untrained subjects only in the supine position. The lack of increased HRV in the standing position and during wakefulness in trained individuals may be due to a persistent sympathetic activation after exercise, lasting up to 24 h. Furthermore, it has been shown that enhanced athletic performance resulting from long-term training might depend on an increase of both parasympathetic and sympathetic modulation.

**Different effects of training on QT interval in men and women**

The effects of training on QT interval, at variance with those exerted on HRV, have not been extensively explored. A randomized, controlled intervention study of the effect of
a 6-month intensive training programme on QTc was performed in an elderly population of 229 healthy men and women, aged 60–80 years. The subjects of the intervention group trained three-four times a week at a workload of about 70% of their maximum capacity for 6 months, while the control subjects maintained their habitual activities. For women, the mean QTc interval of the intervention group was significantly reduced, while it did not change in the control group. In contrast, men of both the intervention and the control groups did not show any change in QTc. The present study performed in trained and sedentary young individuals showed that regular physical activity favourably affects QTc in women but not in men. Although the difference between trained and untrained women was relatively small, it may represent the beneficial effect on potential arrhythmic risk.

The effect on QT interval might be due to a reduced vagal activity on the heart at ventricular level induced by exercise training. Indeed, experimental studies have shown that vagal activity has important influences on refractoriness and susceptibility to ventricular arrhythmias. In adult and young animals, the experimental removal of vagal innervation to the heart induces a prolongation of the QT interval and a decrease in the threshold to induce ventricular fibrillation.

We do not have a clear explanation for the different effect of exercise training on ventricular repolarization in men and women. It is unlikely that training exerted different effects on vagal activity in men when compared with women, as heart rate and HRV were similarly affected. One possibility might be related to a higher level of training in women than in men. However, TF showed lower IPAQ scores than TM, suggesting a lower degree of weekly physical activity. Finally, we cannot exclude that sex steroid hormones may have played a role in the differential effects of training on ventricular repolarization in males and females.

Also, the relationship between QT and RR interval was differentially affected by training in men and women. A previous study performed in healthy subjects demonstrated that not only QTc on standard ECG but also the long term relation between ventricular repolarization and heart rate is affected by gender. The differences in QT interval duration between males and females are more marked at long cycle lengths and disappear at short cycle lengths, as indicated by steeper slopes of the relationship between QT and RR intervals. The present study confirmed these findings among a group of young sedentary subjects. However, in a group of trained individuals the gender difference in the duration of QT interval at long cycle lengths was no longer present. The observation of a steeper slope of the rate dependency of QT interval has been associated with a higher susceptibility to ventricular arrhythmias. Accordingly, the effect of exercise training on the relation between ventricular repolarization and heart rate in women may contribute to a potential protective effect. We do not know whether the beneficial effects of exercise training on QT interval and its relation with heart rate observed in healthy young women may be extrapolated to females with altered ventricular repolarization such as in inherited or acquired long QT syndromes or with other cardiovascular diseases.

The results of this study suggest that the cardiovascular response to exercise training may be different in men and women. Women may benefit more from interventions aimed to increase physical activity as a tool for prevention of cardiovascular morbidity and mortality. However, further studies are necessary to advance this area of knowledge for a better understanding of gender differences in cardiovascular physiology and pathophysiology.

**Limitations of the study**

Our study has some limitations that should be taken into account in the interpretation of the results.

HRV has been analysed by using 24 h Holter recording. This approach allows a long-term analysis of HR and its variability, which is particularly meaningful when the time domain parameters are considered. We cannot exclude possible effects of the frequency domain parameters of HRV, which have not been analysed in this study. As the study was not performed in a controlled environment but in individuals during their usual daily activity, the effect of respiration on HRV were not analysed. Furthermore, data on arterial blood pressure in this population are not available.

**References**


