Cardiovascular autonomic function correlates with the response to aerobic training in healthy sedentary subjects

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Hautala, Arto J., Timo H. Mäkikallio, Antti Kiviniemi, Raija T. Laukkanen, Seppo Nissilä, Heikki V. Huikuri, and Mikko P. Tulppo. Cardiovascular autonomic function correlates with the response to aerobic training in healthy sedentary subjects. Am J Physiol Heart Circ Physiol 285: H1747–H1752, 2003. First published June 19, 2003; 10.1152/ajpheart.00202.2003.—Individual responses to aerobic training vary from almost none to a 40% increase in aerobic fitness in sedentary subjects. The reasons for these differences in the training response are not well known. We hypothesized that baseline cardiovascular autonomic function may influence the training response. The study population included sedentary male subjects (n = 39, 35 ± 9 yr). The training period was 8 wk, including 6 sessions/wk at an intensity of 70–80% of the maximum heart rate for 30–60 min/session. Cardiovascular autonomic function was assessed by measuring the power spectral indexes of heart rate variability from 24-h R-R intervals recorded before and during the training period. Mean peak O2 uptake increased by 11 ± 5% during the training period (range 2–19%). The training response correlated with age (r = −0.39, P = 0.007) and with the values of the high-frequency (HF) spectral component of R-R intervals (HF power) analyzed over the 24-h recording (r = 0.46, P = 0.002) or separately during the nighttime hours (r = 0.52, P = 0.001). After adjustment for age, HF power was still associated with the training response (e.g., P = 0.001 analyzed during nighttime hours). These data show that cardiovascular autonomic function is an important determinant of the response to aerobic training among sedentary men. High vagal activity at baseline is associated with the improvement in aerobic power caused by aerobic exercise training in healthy sedentary subjects.

cardiovascular autonomic function; vagal activity; aerobic training response

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Subjects in the control group dropped out because of a lack of motivation or leg problems. The protocol was approved by the Ethics Committee of the Merikoski Rehabilitation and Research Center, and all subjects gave written informed consent.

**Protocol.** The subjects performed a graded maximal exercise test on a treadmill (Telineyhymä, Kotka, Finland) at a work rate that started at 4.5 km/h and increased in 0.5 km/h increments every 2 min until exhaustion. The subjects were encouraged to perform at maximal effort. Ventilation and gas exchange (ergospirometer, model M909, Medikro, Kuopio, Finland) were monitored continuously during the protocol. The highest value of $O_2$ uptake measured during the test (1-min collection) was taken as the peak $O_2$ uptake ($O_{2peak}$). Nineteen subjects in the training group achieved a plateau in their $O_2$ uptake in both tests. Twenty subjects did not reach a plateau in one or two tests. However, all the subjects fulfilled the criteria for $O_{2peak}$ given in the literature: respiratory exchange ratio $>1.1$ or maximum HR ($HR_{max}$) within $\pm 10$ beats of the age-appropriate reference value (8). All physical exercise and alcohol were forbidden for 48 h before the day of exercise testing.

$R$-$R$ intervals were recorded before the exercise testing over 24 h with an $R$-$R$ recorder (Polar Electro) at an accuracy of 1 ms (23) and saved in a computer for further analysis of HR variability with HEARTS software (Heart Signal, Kempele, Finland). All $R$-$R$ intervals were edited by visual inspection based on ECG portions to exclude all undesirable beats, which accounted for $<2\%$ in every subject. Measures of $R$-$R$ interval dynamics were calculated from the entire 24-h recording and also separately for the hours representing the nighttime (midnight to 6 AM) and daytime (9 AM–6 PM) hours to detect possible diurnal differences (20).

The mean HR and the standard deviation of all $R$-$R$ intervals were used as time-domain measures of HR variability. An autoregressive model was used to estimate the power spectrum densities of $R$-$R$ interval variability, and the average 24-h values were calculated from the segments of 512 $R$-$R$ intervals (9). Ultra-low-frequency (LF) power ($<0.0033$ Hz), very-LF power (0.0033–0.04 Hz), LF power (0.04–0.15 Hz), and high-frequency (HF) power (0.15–0.4 Hz) values were calculated from the entire 24-h segment. LF and HF power were also calculated from 1-h segments of the 24-h recording (using segments of 512 $R$-$R$ intervals), and the mean values of these segments were used to detect day and night HR variability values (20). The spectral values are expressed as absolute values.

**Training program.** The training period was 8 wk long, including six 30-min sessions per week for the moderate-volume training group and six 60-min sessions per week for the high-volume training group at an intensity of 70–80% of $HR_{max}$. The individual $HR_{max}$ was established on the basis of the $HR_{max}$ achieved during the $O_{2peak}$ test. The American College of Sports Medicine recommends 20–60 min of aerobic training for sedentary subjects (1). The purpose of our design was to induce a wide range of changes in aerobic fitness in sedentary subjects on the basis of American College of Sports Medicine recommendations. The training mode was walking and jogging. All the subjects wore a telemetric HR monitor (Polar Smart Edge, Polar Electro) during all the training sessions to reach and retain the correct training intensity.

**Statistical methods.** Values are means ± SD. The normal Gaussian distribution of the data was verified by the Kolmogorov-Smirnov goodness-of-fit test. The spectral values of HR

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**Table 1. Effects of training on $O_{2peak}$, maximal respiratory exchange ratio, and BMI**

<table>
<thead>
<tr>
<th></th>
<th>Moderate Training Volume $(n = 20)$</th>
<th>High Training Volume $(n = 19)$</th>
<th>Control $(n = 12)$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, yr</strong></td>
<td>36 ± 10 (23–52)</td>
<td>36 ± 8 (24–50)</td>
<td>33 ± 10</td>
</tr>
<tr>
<td><strong>Height, m</strong></td>
<td>1.81 ± 0.06</td>
<td>1.80 ± 0.05</td>
<td>1.83 ± 0.08</td>
</tr>
<tr>
<td><strong>Weight, kg</strong></td>
<td>83 ± 12</td>
<td>80 ± 9</td>
<td>80 ± 9</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>25 ± 2</td>
<td>25 ± 2</td>
<td>25 ± 2</td>
</tr>
<tr>
<td><strong>Training</strong></td>
<td>5.6 ± 0.4</td>
<td>5.7 ± 0.4</td>
<td>5.7 ± 1</td>
</tr>
<tr>
<td><strong>Intensity, %HR_{max}</strong></td>
<td>76 ± 2</td>
<td>75 ± 1</td>
<td></td>
</tr>
<tr>
<td><strong>Duration, min/session</strong></td>
<td>32 ± 3</td>
<td>361 ± 1*</td>
<td></td>
</tr>
<tr>
<td><strong>$O_{2peak}$, l/min</strong></td>
<td>3.2 ± 0.4</td>
<td>3.4 ± 0.4</td>
<td>3.4 ± 0.4</td>
</tr>
<tr>
<td><strong>ml·kg⁻¹·min⁻¹</strong></td>
<td>44 ± 5</td>
<td>47 ± 6*</td>
<td>43 ± 4</td>
</tr>
<tr>
<td><strong>$RER_{max}$</strong></td>
<td>1.10 ± 0.08</td>
<td>1.12 ± 0.06</td>
<td>1.10 ± 0.06</td>
</tr>
</tbody>
</table>

Values are means ± SD; with ranges in parentheses. $n$, no. of subjects. $O_{2peak}$, peak $O_2$ uptake; $RER_{max}$, maximal respiratory exchange ratio; BMI, body mass index; $HR_{max}$, maximum heart rate. *$P < 0.001$ vs. Post.

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variability were skewed. Therefore, the natural logarithms of the absolute values were taken to transform these data. The differences within the groups after training were analyzed by a two-factor analysis of variance with time and interventions followed by post hoc analysis (Student’s paired t-test). Pearson’s bivariate correlation analysis was performed between the baseline status of age, BMI, \( \dot{V}O_2 \text{peak} \), training response (\( \Delta \dot{V}O_2 \text{peak} \)), and different HR variability parameters. 

\( \Delta \dot{V}O_2 \text{peak} \), was adjusted for the effects of covariates using a stepwise linear regression procedure for baseline age, together with the HR variability indexes. Each HR variability parameter that correlated with the training response was tested separately in a linear regression analysis procedure because of the high correlation between the different HR variability indexes (28). When the training group was divided into quartiles according to \( \Delta \dot{V}O_2 \text{peak} \), analysis of variance was followed by post hoc analysis of Bonferroni’s t-test comparing the differences between the groups. \( P < 0.05 \) was considered statistically significant.

RESULTS

The individual training responses are shown in Fig. 1. The average increase in \( \dot{V}O_2 \text{peak} \) was 11 ± 5% (range 2–19%; Table 1). The training response did not differ between the moderate- and high-volume training groups. None of the measured variables changed within the control group during the study.

Contribution of HR variability to the training response. The training response correlated with age (\( r = -0.39, P = 0.007 \)), but not with the baseline level of \( \dot{V}O_2 \text{peak} \) or BMI (\( r = -0.06 \) and \( -0.12, \) respectively, not significant for both). Age accounted for 16% of the change as an independent predictor of the aerobic training response, and the corresponding values for \( \dot{V}O_2 \text{peak} \) and BMI were 0.4 and 1.4%. A significant correlation was observed between the training response and the baseline HF power of R-R intervals analyzed over the 24-h recording (\( r = 0.46, P = 0.002 \)) during the nighttime (\( r = 0.52, P = 0.001 \)) and daytime (\( r = 0.35, P = 0.028 \)) hours. Also, the LF power during the nighttime hours (\( r = 0.38, P = 0.018 \)) and the very-low-frequency power over 24 h (\( r = 0.34, P = 0.017 \)) were related to the training response. After adjustment for age, only HF power was associated with the training response (Fig. 2). HF power during the nighttime hours accounted for 27% (\( P = 0.001 \)) of the change as an independent predictor of the aerobic training response. The correlations between the training response and the mean HR, standard deviation of all R-R intervals, or ultra-LF power were not significant under any conditions.

Baseline HR variability indexes in quartiles according to the training response. The study group was also divided into quartiles according to the training response (17 ± 1, 11 ± 1, 8 ± 1, and 5 ± 2% increase in \( \dot{V}O_2 \text{peak} \), \( P < 0.001 \) between groups). HF power at baseline analyzed over 24 h or during the nighttime hours was higher among the group with the best training response than among the group with lower responses (Table 2). The groups did not differ from each other in terms of baseline \( \dot{V}O_2 \text{peak} \), age, and BMI (Table 2).

DISCUSSION

The main finding of this study was that 24-h HR dynamics at baseline, particularly the vagally mediated HF power spectral component, are associated with the improvement in aerobic power caused by aerobic exercise training in healthy sedentary subjects. There was a relation between the baseline HR variability...
indexes, such as the HF power spectral component, and the training response, suggesting that cardiovascular autonomic regulation is an important determinant of training response to physical exercise.

**Individual responses to aerobic training.** Large individual differences in the response to regular aerobic training have been observed after highly standardized exercise programs in healthy sedentary subjects (5, 14, 15). Consistent with the previous studies, we also found a large variation in the training response after a controlled aerobic training intervention in healthy sedentary men. The HERITAGE Family Study, based on 720 healthy sedentary subjects, summarized the contributions of age, gender, race, and baseline fitness level to the response to aerobic training. All these variables together accounted for only 11% of the variance in the response to 20 wk of standardized training. The subject’s gender was the most powerful predictor of the training response, with a contribution of 5.4%, followed by age, with a contribution of 4% (5). In our male population, age accounted for 16% of the response as an independent predictor of the aerobic training response. Our training intervention was short (8 wk) compared with that of the HERITAGE Family Study (20 wk), which may emphasize the importance of age on the short-term training response. The age range of our subjects was large (23–52 yr) compared with the age ranges in training studies performed with older healthy sedentary individuals (60–71 yr) (14) and younger subjects (21–29 yr) (15). In agreement with the previous studies, the baseline fitness level was not significantly associated with the training response in the present study.

The American College of Sports Medicine recommends that the duration of a single aerobic training session should be 20–60 min for sedentary subjects (1). In the present study, however, both modes of training (30 and 60 min/session) resulted in similar changes of aerobic fitness in sedentary subjects. Our results show that the response to an aerobic training intervention in sedentary subjects is not dependent on the volume of training but, rather, must be determined by other factors.

**Cardiovascular autonomic regulation as a determinant of training response.** The total HR variability has been shown to decrease by 80%–90% after complete vagal blockade. Therefore, vagal activity has been proposed to be the major determinant of HR variability in healthy humans (7, 29). Efferent cardiac vagal outflow has been generally proposed to contribute to the HF spectral power of HR variability (7, 28). In the present study, baseline HF power during the nighttime hours was the most powerful HR variability index associated with the future training response, accounting for 27% of the change as an independent predictor of the aerobic training response. This is an important finding, because the nighttime hours reflect a more standardized condition, and the results are less influenced by the subject’s behavioral pattern. Together, these findings support the concept that cardiac vagal activity is an important determinant of the training response in sedentary men.

**Possible mechanisms for individual cardiovascular adaptation.** The mechanisms underlying the relation between the baseline vagal activity and the training response remain speculative. In accordance with the
large interindividual variation in the training response to physical exercise, wide intersubject variation has also been observed in cardiovascular autonomic regulation in healthy subjects when measured by the HR variability indexes (20). Recent studies have shown that genetic factors may determine a large proportion (>20%) of the interindividual variation of R-R interval variability (25, 26), whereas demographic and other factors, including blood pressure, blood cholesterol, cardiac dimensions, BMI, and smoking, explain only a small proportion (~10%) of this variation in autonomic regulation (19). Similarly, it is well known that genetic background causes considerable variation in the baseline aerobic capacity and the changes in aerobic fitness after exercise training interventions (4, 21, 22). Therefore, there might be a common denominator that explains partly adaptation to aerobic training and HR variability. Genetic factors are the major candidates for this denominator.

A mechanistic link between the cardiac vagal function and the training response is also possible. In those subjects with good vagal function, the cardiovascular system may have a better capacity to adapt to various external stimuli, e.g., physical exercise. This adaptation capacity may improve overall cardiovascular performance after the regular physical training, thereby also improving the aerobic fitness. This hypothesis should be confirmed in future experimental studies.

Study limitations. In the present study, we investigated the differences in HR variability and training response only in healthy men. However, there are no significant differences in aerobic training responses between men and women (18, 27), and we decided to start with healthy men, because it may be important to understand the association between the training response and autonomic regulation in a homogeneous sample of subjects. An obvious limitation of the study is that the test subjects’ age range was relatively large, which must be taken into consideration in interpretation of the results.

Conclusion. The present observations provide novel information on the contribution of the cardiovascular autonomic function to the training response. These observations may have some practical implications. For example, measurement of autonomic function may become important in designing individual training programs. However, the present findings are still preliminary and should be confirmed in future studies with different training programs and in various populations before generalization of the results. Finally, more experimental work is needed to understand the possible mechanistic link between the cardiovascular autonomic function and the training response.

DISCLOSURES

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