Dose-response relationship of autonomic nervous system responses to individualized training impulse in marathon runners

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Manzi V, Castagna C, Padua E, Lombardo M, D’Ottavio S, Massaro M, Voltarann,i M, Iellamo F. Dose-response relationship of autonomic nervous system responses to individualized training impulse in marathon runners. Am J Physiol Heart Circ Physiol 296: H1733–H1740, 2009. First published March 27, 2009; doi:10.1152/ajpheart.00054.2009.—In athletes, exercise training induces autonomic nervous system (ANS) adaptations that could be used to monitor training status. However, the relationship between training and ANS in athletes has been investigated without regard for individual training loads. We tested the hypothesis that in long-distance athletes, changes in ANS parameters are dose-response related to individual volume/intensity training load and could predict athletic performance. A spectral analysis of heart rate (HR), systolic arterial pressure variability, and baroreflex sensitivity by the sequences technique was investigated in eight recreational athletes during a 6-mo training period culminating with a marathon. Individualized training load responses were monitored by a modified training impulse (TRIMP) method, which was determined in each athlete using the individual HR and lactate profiling determined during a treadmill test. Monthly TRIMP, steadily increased during the training period. All the ANS parameters were significantly and very highly correlated to the dose of exercise with a second-order regression model ($r^2$ ranged from 0.90 to 0.99; $P < 0.001$). Variance, high-frequency oscillations of HR variability (HRV), and baroreflex sensitivity resembled a bell-shaped curve with a minimum at the highest TRIMP, whereas low-frequency oscillations of HR and systolic arterial pressure variability and the low frequency (LF)-to-high frequency ratio resembled an U-shaped curve with a maximum at the highest TRIMP. The LF component of HRV assessed at the last recording session was significantly and inversely correlated to the time needed to complete the nearing marathon. These results suggest that in recreational athletes, ANS adaptations to exercise training are dose related on an individual basis, showing a progressive shift toward a sympathetic predominance, and that LF oscillations in HRV at peak training load could predict athletic achievement in this athlete population.

heart rate variability; baroreflex sensitivity; training load; performance; athletes

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sex- and population average-based group values for HR during the whole exercise session. The use of the mean exercise HR and the same multiplying factor does not necessarily reflect the individual demands of each training session.

To the best of our knowledge, no study has analyzed the relationship between an actually individualized training load, in terms of both volume and intensity, with ANS parameters and their relationship with performance in athletes.

In the present investigation, we tested the hypothesis that in long-distance athletes preparing for a marathon race, changes in ANS parameters are related to individual volume/intensity training load and could predict athletic performance.

To this aim, HRV has been assessed in relation to an individualized volume/intensity training load (referred to as TRIMP), as evaluated by way of a simple algorithm based on a weighting factor for each individual subject (see Methods), and applied in marathon runners.

METHODS

Subjects. Eight healthy, trained, male long-distance runners (LDRs) of recreational level (age, 40.5 ± 4 yr; height, 175.7 ± 5.4 cm; and weight, 70.0 ± 6.0 kg) with a lifelong history of physical activity volunteered to participate in the study. Inclusion criteria were the absence of clinical signs or symptoms of infection, cardiovascular disease, or metabolic disorders and a minimum weekly training distance of 50 km/wk. All subjects provided informed written consent to the experimental procedures after the possible benefits and risks of participation were explained to them. The study protocol was approved by the local Institutional Review Board and followed the guidelines laid down by the World Medical Assembly Declaration of Helsinki.

Experimental protocol. Before the beginning of the study, all the recreational LDRs abstained from running for 4 wk to avoid possible training status effects over the experimental intervention; thus, for the purpose of this study, at this time they were considered as (partially) detrained and underwent the baseline recording sessions. LDRs abstained from alcohol and caffeinated beverages and refrainmed from heavy training in the 24 h before the experimental sessions. The subjects consumed their last meal at least 3 h before the treadmill test, and a report of nutrient content was taken to ensure that a sufficient carbohydrate intake during the week before the testing was consumed. Throughout the study, all testing sessions took place at the same hour of the training sessions (afternoon) to avoid possible circadian influences on the parameters under investigation. Therefore, each athlete was investigated 8 wk apart on three subsequent occasions, according to the training periodization. The last recording was performed ~20 days before the Roma Marathon Race 2008. No one athlete was considered overtrained at the time of the recording sessions, based on the lack of the following signs: an inability to sustain the usual training program or a reduced performance and the presence of symptoms, such as increased feelings of fatigue during daily training routine, sleeping disorders, apathy, or restlessness. No subject was taking drugs at the time of the recording sessions.

Fitness assessment and training. Subject underwent two phases progressive treadmill test (Technogym Run Race 1400 HC, Gambetti, Italy) for the assessment of individual blood lactate concentration profile and maximal HR respectively, on four occasions: at the start of the study and after 8, 16, and 24 wk of training. The progressive treadmill test consisted of four to five submaximal exercise bouts at initial running speeds of 10 km/h followed by a maximal incremental test to volitional fatigue. The treadmill running velocity was increased during the submaximal test by 1 km/h every 5 min. Once the capillary blood lactate concentrations were elevated above 4 mmol/l, the treadmill speed was increased by 0.5 km/h every 30 s until exhaustion (8, 14). In the 1-min interval between each bout during the submaximal exercise test and 3 min after exhaustion in the maximal incremental test, capillary blood samples (25 μl) were taken from the earlobe and immediately analyzed to assess blood lactate concentration using an enzymolectric technique (YSI 1500 Sport, Yellow Springs Instruments, Yellow Springs, OH). Before each exercise bout, the analyzer was calibrated following the instructions of the manufacturer using standard lactate solutions of 0, 5, 15, and 30 mmol/l. HR was recorded every 5 s with a short-range telemetry system (Polar Team System, Polar Electro Oy, Kempele, Finland) during all assessments. The highest HR measured during the maximal incremental test was used as maximum reference value (HRmax). Resting HR (HRrest) was measured with subjects in a resting state (i.e., quiet room, supine position) before the treadmill test. HRrest was assumed as the lowest 5-s value of the 5-min monitoring period. Individual blood lactate concentrations versus running speeds were obtained in each subject with speeds at 2 and 4 mmol/l used as the exercise paradigm (8, 16). Blood lactate concentrations were plotted against running speeds and fractional HR elevation (ΔHR), and individual blood lactate concentration profiles (speeds at 2 and 4 mmol/l, and ΔHR values at 2.0 and 4 mmol/l) were identified via exponential interpolation (2). Recreational LDRs trained 3–5 times/wk according to the training schedule depicted in Table 1. Training mileage and intensity (i.e., the distance to be covered at selected paces) were prescribed to LDRs by an experienced marathon coach according to treadmill test results (Table 2). The speeds at selected blood lactate concentrations were used by LDRs as a training cue, and no HR feedback was provided to LDRs during training sessions. During all the training sessions, HR was assessed in each subject (Polar Team System, Polar Electro Oy), and the data were downloaded on a portable personal computer and analyzed using a dedicated software (Polar ProTrainer 5, Polar Electro Oy) and an electronic spreadsheet (Excel, Microsoft).

TRIMP calculation. The TRIMP method considers the ΔHR (HRexercise − HRrestmax/HRrestmax − HRrest) as the main exercise variable (2). The duration of any specific training session is multiplied by the average ΔHR achieved during that session. To avoid giving a disproportionate importance to long-duration activity at low ΔHR levels compared with an intense but short-duration activity, the ΔHR is weighted by a multiplying factor (y) in a way that reflects the intensity of effort. This y factor is based on the exponential rise of blood lactate levels with the fractional elevation of exercise above resting HR (2). This factor served to equate the TRIMP scores of exercises of long duration and low HR with exercises of short duration and high HR. Thus, overall, TRIMP = time (in min) × ΔHR × y, where y is a nonlinear coefficient given by the equation: y = 0.641 ± 0.92x, with e = base of the Napierian logarithms and x = ΔHR.

However, this TRIMP method as proposed by Banister et al. (2) uses the mean exercise HR during an exercise bout, and the multi-

Table 1. Training intensities and workouts

<table>
<thead>
<tr>
<th>Blood Lactate Zone</th>
<th>Blood Lactate Concentration, mmol/l</th>
<th>%Maximal Heart Rate</th>
<th>Workouts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low lactate</td>
<td>≤2</td>
<td>≤81 ± 3.9</td>
<td>Continuous running (time 70–120 min)</td>
</tr>
<tr>
<td>Lactate accommodation</td>
<td>≥2–≤4</td>
<td>81 ± 3.9–91 ± 3.6</td>
<td>Continuous running (time 60–100 min)</td>
</tr>
<tr>
<td>Lactate accumulation</td>
<td>&gt;4</td>
<td>&gt;91 ± 3.6</td>
<td>Interval training (4 × 2,000 m + 4 × 1,000 m)</td>
</tr>
</tbody>
</table>

Maximal heart rate values are means ± SE.
subject. This pseudo-integral of all activities at any time as the area under the curve represented by the HR response, the weighting factor for each subject with the best fitting method using exponential models (Fig. 1). Thus, as exercise intensity increases, the individual physiological demands of each training session. To address this issue, we introduced an individual weighting factor ($\gamma_i$) for each subject. This $\gamma_i$ reflects the profile of a typical blood lactate response curve to increasing exercise intensity. Individual $\gamma_i$ values are calculated for each subject with the best fitting method using exponential models (Fig. 1). Thus, as exercise intensity increases, as indicated by the HR response, the weighting factor $\gamma_i$ increases exponentially. Thus, overall during each training session, a TRIMP can be calculated at any time as the area under the curve represented by the pseudo-integral of all LHR data points.

**ANS assessment.** The continuous ECG signal was obtained with a modified C5 lead, connecting the electrodes to an analog preamplifier (REP 10, Marazza, Monza, Italy). The arterial BP was continuously and noninvasively measured by Finapres (Ohmeda 2300 NIBP monitor). The respiratory signal was recorded with a piezeoelastic thoracic belt. The three analog signals were connected to an analog-to-digital board inserted into a personal computer, sampled at 300 Hz per channel, and stored on the hard disk for subsequent analyses. These signals were used to assess autonomic function. All of the recording sessions were performed in the afternoon (between 3:00 PM and 6:00 PM) at least 2 h after a light lunch. The athletes did not perform strenuous physical activities in the 20 h before the recordings. The experiments were performed in a room at ambient temperature (22–24°C). After instrumentation, the subjects laid supine in a dark and noiseless room for 15 min to relax before the experiments; thereafter, their BP was measured twice, 5 min apart by sphygmomanometry, and the measurements were averaged. After the BP measurements, a continuous data acquisition was performed for 10 min.

**Power spectral analysis.** A purposely developed software (Heartscope, ver. 1.6, AMPS llc) was used to identify the peak of R wave on ECG, the systolic arterial BP (SAP) and respiratory rate (RESP). The software constructs an automatic time series of R-R intervals, SAP, and RESP, with low operator analysis interaction. The software provides calculation of the weighting factor ($\gamma$) and potentially miss in reflecting the individual cardiac cycle. Respiratory spectra were used to assess the main

Table 2. Distance covered at selected running speeds during the 24-wk training intervention

<table>
<thead>
<tr>
<th>Month</th>
<th>S2</th>
<th>S3</th>
<th>S3–S4</th>
<th>&gt;S4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>82</td>
<td>18</td>
<td>62</td>
<td>162</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>34</td>
<td>84</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>62</td>
<td>70</td>
<td>263</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>26</td>
<td>127</td>
<td>318</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>123</td>
<td>63</td>
<td>66</td>
<td>302</td>
<td></td>
</tr>
</tbody>
</table>

S2, speed at 2 mmol/l (km/h); S3, speed at 3 mmol/l (km/h); S3–S4, speed between 3 and 4 mmol/l (km/h); >S4, speed over 4 mmol/l (km/h).

respiratory frequency. The power density of each spectral component was calculated both in absolute values and NU, computed as the ratio of the absolute power of either HF or LF to the total power, less the very LF component if present, and multiplying this ratio by 100 (22). The use of NU is crucial to obtain valuable information as to the autonomic cardiac modulation, because the high interindividual variability in R-R-interval total variance and DC noise (11, 22, 23).

**Spontaneous baroreflex analysis.** Details of this analysis have been previously described. Briefly, the beat-by-beat time series of SAP and R-R interval were scanned by a computer to identify sequences of three or more consecutive beats in which SAP and R-R change in the same direction, either increasing (+RR/+SAP) or decreasing (−RR−SAP). A linear regression is applied to each individual sequence, and the mean individual slope of the SAP/R-R interval relationship, obtained by averaging all slopes computed within a given test period, is calculated and taken as a measure of the integrated baroreceptor reflex sensitivity for that period (3). This method mainly reflects vagally mediated baroreceptor cardiac responses (11) and has provided reproducible results (10).

**Statistics.** Before parametric tests were used, the assumption of normality was verified using the Shapiro-Wilk W-test. An analysis of variance (ANOVA) for repeated measures with the Newman-Keuls test was used to compare the metabolic data between different measurements. The significance of differences in the ANS parameters among the different recording sessions was evaluated by nonparametric ANOVA for repeated measures (Friedman’s test) with post hoc testing performed with the Newman-Keuls test. Data for ANS parameters were calculated as medians (and interquartile ranges). To express the dose-response relationship between the exercise stimulus and changes in cardiovascular and ANS indexes, correlations between the monthly TRIMP, and cardiovascular and ANS indexes at baseline, 8, 16, and 24 wk were estimated from a second-order regression. Pearson product-moment correlation coefficients were calculated to determine whether there was a significant relationship between various ANS indexes with the time performance obtained at the near marathon. Differences were considered statistically significant when $P \leq 0.05$. SPSS (SPSS, version 13.0.1 for Windows; Chicago, IL) was used for all statistical calculations.

**RESULTS**

All athletes completed the training program with ANS assessment. However, only six out of eight athletes successfully completed the marathon as the performance goal of the training program. One athlete did not complete the marathon because of a muscle injury after 34 km; the other one, because an intercurrent flu just before the marathon. Baseline maximal oxygen

![Fig. 1. Blood lactate concentration plotted against the fractional elevation in heart rate (HR) in a recreational long-distance runner. Exponential line provides calculation of the weighting factor ($\gamma$).](http://ajpheart.physiology.org/)

AJP-Heart Circ Physiol • VOL 296 • JUNE 2009 • www.ajpheart.org
consumption was 51.3 ± 0.8 ml·kg⁻¹·min⁻¹, indicating the high fitness level of this group of athletes. The monthly TRIMP, steadily increased during the training period. The speed at 2 and 4 mmol/l significantly increased at 8, 16, and 24 wk of training compared with baseline, indicating the high aerobic fitness level reached by this group of athletes (Table 3).

R-R interval and systolic and diastolic arterial pressure did not change significantly throughout the study as did breathing frequency (Table 4).

Spectral analysis and baroreflex function. The LF power of R-R-interval variability (in NU) showed a decrease after 8 wk and then an increase throughout the training period as did the LF-to-HF ratio. The HF component of R-R-interval variability and baroreflex sensitivity (BRS) showed a reciprocal pattern, with an increase after 8 wk and a decrease thereafter. The same occurred for the LF oscillations in SAP variability. However, the median changes in all indexes of autonomic cardiovascular regulation on the group level were not statistically significant. All the ANS parameters as well as the R-R interval were significantly and very highly correlated to the dose of exercise with a second-order regression model ($r^2$ ranged from 0.90 to 0.99; $P < 0.001$), with different and reciprocal shapes for parasympathetic and sympathetic indicators (Figs. 2 and 3).

HFNU and BRS, as well as total variance and R-R interval, resembled a bell-shaped curve with a minimum at the highest TRIMP, whereas LFNU, LF-to-HF ratio, and LFSAP resembled a U-shaped curve with a maximum at the highest TRIMP.

Notably, LFNU assessed at the last recording session was significantly and inversely correlated to the race time obtained at the nearing marathon, whereas simultaneously measured HFNU and BRS showed a significant and direct relationship with the race time (Fig. 4); that is, the higher the sympathetic indicator, the less the time spent by athletes to complete the marathon.

DISCUSSION

The main and novel findings of the present investigation are that 1) ANS adaptations to exercise training in recreational athletes are dose related on an individual basis, showing a progressive shift toward a sympathetic predominance as training load approached the maximum and that 2) LF oscillations in R-R-interval variability at a maximal training load could predict athletic achievement in this athlete population.

ANS adaptations to training. In the recreational athletes of this study, we observed a shift from vagal to sympathetic predominance on an individual basis as TRIMP, approached the maximum as indicated by the increase in the LF component of HR and BP variabilities and in the LF-to-HF ratio and by the decrease in the HR component of HRV and BRS, in keeping with previous studies suggesting that the magnitude of training load alters cardiac (12, 13, 24, 25) and vascular (12) autonomic modulation in a direction that would be consistent with a sympathetic activation. In this context, Iellamo et al. (12, 13) hypothesized that the sympathetic activation could be regarded as the neurovegetative counterpart of an optimal training status, as suggested by the excellent sports results attained by athletes at nearing high-level competitions (12). However, in those (12, 13), as in other studies, the relationship between training loads and ANS changes has been investigated without regard for individual training dose, and no direct evidence for the use of HRV parameters to predict athletic achievements was provided.

In the present investigation, we addressed these issues by using the TRIMP, method, which is an individually determined, integrated measure of responses to physical load that accounts, in a single term, for both intensity and volume effects on the physiological systems of the athletes (2). By using this method, we provided the first direct experimental evidence that the LF component of HRV, an indicator of sympathetic cardiac modulation (11, 17, 23), could be actually able to predict individual athletic achievements in LDRs, as suggested by the strong inverse relationship between LFNU at peak TRIMP, and the competition time at a nearing marathon. The increase in the LF component of HRV was accompanied by a significant decrease in markers of vagal cardiac modulation (i.e., the HF component of HRV and BRS), which were directly related to a longer competition time, supporting further the relevance of sympathetic activation to athletic achievement. Although the small sample size prevents definitive conclusions, we believe that the strong correlation ($R^2$ from 0.65 to 0.82) between individual ANS parameters at peak training load and performance makes our hypothesis tenable.

Comparisons with previous studies. Although several longitudinal studies focusing on HRV have been performed in athletes, conflicting results do exist as far as changes in the different components of HRV and BRS when training is concerned, since increases, decreases, or no changes in LF, HF, and LF-to-HF ratio of HRV and BRS have been reported (see Ref. 1 for review). The nonlinear dose-response relationship between the exercise training stimulus and the dynamic regulation of HR as well as the inadequacy to accurately define the dose of exercise, in terms of volume and intensity, may explain in part these conflicting results. Other factors to be considered for the above discrepancies are differences in athlete populations and the design of the study, that is, athletes of different sport disciplines, experiencing different training methodologies, differences in the duration of follow-up, and scheduled HRV assessments with respect to training cycles, often including only before- and after-training time points. A strength of the present investigation is the repeated measurements of ANS parameters during the training period, which could have improved our comprehension of the possible link between changes in physical fitness and changes in autonomic cardiovascular regulation. Finally, interindividual differences in response to training should also be considered (4).

Previous studies from Iwasaki et al. (14) and Okazaki et al. (18) had addressed the question of ANS adaptations to individual training load by using the TRIMP method. As in the present investigation, both these studies reported a nonlinear dose-response relationship between an endurance exercise training program and markers of ANS cardiovascular regulation, as detected by a spectral analysis of HR and BP variability. However, the results of these studies are consistent only in

Table 3. Changes in velocity at different metabolic rates during training

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>8 wk</th>
<th>16 wk</th>
<th>24 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2, km/h</td>
<td>11.1±0.68</td>
<td>13.2±0.55*</td>
<td>13.4±0.43*</td>
<td>13.9±0.55*</td>
</tr>
<tr>
<td>S4, km/h</td>
<td>14.2±0.79</td>
<td>15.5±0.95*</td>
<td>15.6±0.87*</td>
<td>16.7±0.76*</td>
</tr>
</tbody>
</table>

Values are means ± SE. *$P < 0.05$ compared with pretraining baseline.
part with our findings. In fact, although Iwasaki et al. (14)
reported a bell-shaped curve for overall HRV (i.e., SD of R-R
interval) and BRS, as in the present investigation, a bell-shaped
curve was also observed for LF oscillations in R-R interval and
BP variability with increasing TRIMP values, at variance with
our study in which a U-shaped curve has been observed for
these latter variables. On the other hand, a subsequent inves-
tigation from the same laboratory (18), performed in older
sedentary healthy subjects using the same experimental meth-
ology and design, reported a progressive decrease in R-R-
interval SD and an increase in LF oscillations of R-R-interval
variability, always described by a second-order regression
model, with increasing TRIMP values, as in the present inves-
tigation. Differences in subject populations and methodologies
may well explain these conflicting results. The aforementioned
studies (14, 18) included previously sedentary young and
elderly subjects of both sexes, whereas we studied recreational
male athletes with a lifelong history of physical activity.
Athletes practicing high-intensity physical activity from sev-
eral years represent a totally different population compared
with sedentary subjects starting a de novo short- or long-term
exercise training program, because they are already fit and
should be regarded, at least at a first sight, as unique. The high
baseline maximal oxygen consumption of our subjects, indi-
cating an high level of fitness already before starting the
training program, would be consistent with this concept. There
may also be factors not controlled for here, such as changes of
HRV during the preceding years of training that may affect
ANS adaptations to scheduled training programs in athletes.

From a methodological standpoint, we used 5-s average HR
values, which allowed us more HR values to be considered,
and individual weighting factor coefficients in calculating
TRIMP, whereas Iwasaki et al. (14) and Okazaki et al. (18)
used average-based group values for HR obtained during a
whole exercise session and standard, population-dependent
coefficients weighted equal for all subjects in their TRIMP
calculation, as proposed by Banister et al. (2). Indeed, we have
recently observed significant differences between individual-
ized TRIMP compared with the average-based TRIMP calcu-
lation in assessing fitness variations and the association with

<table>
<thead>
<tr>
<th>R-R interval, ms</th>
<th>Baseline</th>
<th>8 wk</th>
<th>16 wk</th>
<th>24 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>906 (875–995)</td>
<td>1,006 (935–1,081)</td>
<td>974 (872–1,005)</td>
<td>947 (871–1,105)</td>
</tr>
<tr>
<td>SAP, mmHg</td>
<td>116.3±1.8</td>
<td>115.0±1.9</td>
<td>113.8±2.1</td>
<td>113.1±1.6</td>
</tr>
<tr>
<td>DAP, mmHg</td>
<td>75.6±1.9</td>
<td>76.3±1.8</td>
<td>71.9±2.3</td>
<td>71.9±1.6</td>
</tr>
<tr>
<td>Respiration, Hz</td>
<td>0.27±0.01</td>
<td>0.26±0.01</td>
<td>0.28±0.01</td>
<td>0.27±0.01</td>
</tr>
</tbody>
</table>

Values are median (interquartile range) or means ± SE. SAP, systolic arterial pressure; DAP, diastolic arterial pressure. No significant differences were
detected among the different recording times.
performance, with the former being more valuable than the latter (17a). Finally and importantly, we used normalized LF and HF values and the LF-to-HF ratio to assess the dose-response relationship between HRV parameters and training load, whereas the aforementioned studies (14, 18) used absolute values. The normalization procedure is crucial to obtain information on ANS regulation from spectral analysis of HRV because of the large interindividual differences in total power and DC noise (22, 23, 28). In addition, we assessed HRV during spontaneous respiration, whereas previous data (14, 18) have been obtained during controlled respiration, which artificially influences HRV (and, as a consequence, BP variability as well) by enhancing the respiratory-related, vagal contribution to sinoatrial node modulation (17, 22), an effect observed even in those previous studies (14, 18). In agreement with our previous study (12), we observed a progressive decrease in BRS and an increase in SAP variability with the increase in the training stimulus, which is further evidence of an overall sympathetic activation with vigorous exercise training, a finding that supports our early hypothesis (12, 13). In our study, no significant differences in ANS parameters and in hemodynamics with variations in training load have been detected on a group level. The more likely explanation for the discrepancy in ANS parameters on an individual versus group level is the large interindividual difference in HR and BP variability parameters from baseline throughout the study, which prevented the detection of significant differences in median values with TRIMP, variations, despite clear trends, and the small sample size. These factors and the high level of fitness already at the start of the training period may also explain the relatively high value of the LF-to-HF ratio at baseline. The strong dose-response correlation between all ANS parameters and TRIMP over the whole training program would support this explanation. It thus appears that to adequately examine the relationship

Fig. 3. Dose-response relationship between exercise intensity/volume (monthly TRIMP) and autonomic cardiovascular indexes. LF/HF, LF-to-HF ratio in R-R-interval variability; LF_{SAP}, LF power of systolic arterial pressure variability. Entries represent median values for 8 athletes.

Fig. 4. Correlation between the time needed to complete the marathon and autonomic cardiovascular indexes assessed at the last recording time 20 days before the race. Entries are for the 6 athletes who completed the marathon.
between ANS and physical training, it is necessary to account for the relative degree of physical effort expended by each athlete.

Limitations. The main limitation of the present investigation is the small sample size, which, unfortunately, is a common characteristic of studies carried out in athletes of any class level. This limitation is compensated, in part, by the strong consistency of our data on the dose-response relationship between all ANS parameters and the training stimulus. In addition, the study lacks a control group that did not exercise. However, within the framework of the present investigation, this would be more a theoretical rather than an actual limitation. Indeed, it would be hard to hypothesize dose-response training-related changes in ANS, as those observed in our study, in subjects who do not undergo exercising training. Furthermore, there would be virtually no rationale to investigate the relationship between training-induced ANS adaptations and performance achievements in nonexercising, nonathletic individuals. It should be also outlined that the results of the present study should be regarded, at present, as inherent only to endurance training programs and could not be generalized to other athlete populations experiencing different training methodologies or to previously untrained subjects of different ages.

We should also mention that we used an indirect method to assess changes in autonomic function. Although this procedure stimulated strong debates in the literature (6, 17), nevertheless several studies have affirmed that spectral analysis of HRV is a simple way to extract the information embedded in the frequency code (17, 22, 23, 28) characterizing neural cardiovascular regulation.

Indeed, the issue of the validity of the spectral analysis approach was addressed by experiments in humans (23) in whom direct recordings of muscle sympathetic nerve activity were performed during various states of autonomic regulation, as produced by graded infusions of vasodilators and vasoconstrictors. The presence of similar, coherent oscillations at LF in nerve activity, R-R intervals, and SAP variabilities at various levels of induced pressure changes provide support for the use of LF R-R (in NU) as an index of sympathetic modulation. The lack of LF oscillations in the R-R interval (and SAP variability as well) in tetraplegic patients who lack the ability to modulate sympathetic nerve traffic to the heart and vasculature (11) provides further experimental support for the above concept.

In conclusion, the results of this study indicate that there is a curvilinear dose-response relationship between individualized training load and ANS functioning parameters and suggest that an increase in the LF component of HR variability at peak exercise training could predict, on an individual basis, athletic achievements in recreational LDRs. The combined use of TRIMP, and HRV could prove to be a valuable tool in order to tailor training programs on an individual basis to achieve the best athletic performance in endurance athletes, through a simple, noninvasive and minimally time-consuming approach. Further studies are warranted to confirm on larger numbers the predictability of athletic achievements by changes in ANS parameters with variations in training load on an individual basis.

GRANTS

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