Conversion From Vagal to Sympathetic Predominance With Strenuous Training in High-Performance World Class Athletes

Ferdinando Iellamo, MD; Jacopo M. Legramante, MD; Fabio Pigozzi, MD; Antonio Spataro, MD; Guido Norbiato, MD; Daniela Lucini, PhD, MD; Massimo Pagani, MD

Background—Benefits of moderate endurance training include increases in parasympathetic activity and baroreflex sensitivity (BRS) and a relative decrease in sympathetic tone. However, the effect of very intensive training load on neural cardiovascular regulation is not known. We tested the hypothesis that strenuous endurance training, like in high-performance athletes, would enhance sympathetic activation and reduce vagal inhibition.

Methods and Results—We studied the entire Italian junior national team of rowing (n=7) at increasing training loads up to 75% and 100% of maximum, the latter 20 days before the Rowing World Championship. Autoregressive power spectral analysis was used to investigate RR interval and blood pressure (BP) variabilities. BRS was assessed by the sequences method. Increasing training load up to 75% of maximum was associated with a progressive resting bradycardia and increased indexes of cardiac vagal modulation and BRS. However, at 100% training load these effects were reversed, with increases in resting heart rate, diastolic BP, low-frequency RR interval, and BP variabilities and decreases in high-frequency RR variability and BRS. Three athletes later won medals in the World Championship.

Conclusions—This study indicates that very intensive endurance training shifted the cardiovascular autonomic modulation from a parasympathetic toward a sympathetic predominance. This finding should be interpreted within the context of the substantial role played by the sympathetic nervous system in increasing cardiovascular performance at peak training. Whether the altered BP and autonomic function shown in this study might be in time hazardous to human cardiovascular system remains to be established. (Circulation. 2002;105:2719-2724.)

Key Words: exercise ■ nervous system, autonomic ■ reflex

Exercise training is a key component of cardiovascular preventive strategies, because it is strongly associated with a variety of beneficial metabolic, psychological, and neurovegetative effects.1 Concerning changes in cardiovascular autonomic regulation, it is generally believed that in cardiac patients, exercise training leads to a decrease in sympathetic activity and an increase in parasympathetic activity and baroreflex sensitivity (BRS).2–5 Investigations in cardiac patients focused on the effect of moderate-intensity endurance exercise training. In healthy young subjects, there is also consistent evidence indicating an enhanced parasympathetic activity associated with increased aerobic power,6–10 whereas inconsistent results have been reported as far as sympathetic activity7,10 and BRS11–13 are concerned. These inconsistencies might be attributable mostly to the cross-sectional nature of the studies, which are limited by some uncontrollable bias because of nontraining-related differences between groups and interindividual variability14 and to different or poor definition of the fitness level and training regimens, although differences in the methods of determining autonomic balance and BRS also might have contributed.

Conversely, despite the potential risks of strenuous exercise, to our knowledge there is no long-term, longitudinal study that has addressed specifically the effect of very intensive exercise training, such as that experienced by high-performance world class athletes on neural cardiovascular regulation. Very high athletic performances might require adaptational changes in the neural control of circulation that could be different from those brought about by moderate-intensity training in noncompetitive athletes and, even more, in cardiac patients, in whom enhancing parasympathetic activity while concomitantly reducing sympathetic activity is highly desirable.15,16 Indeed, there is some evidence to suggest that in highly trained athletes, there are, at rest, signs of enhanced parasympathetic activity that coexist with signs of cardiac sympathetic excitation at the peak of the training season.17,18

In the present investigation, we tested the hypothesis that strenuous physical training in a selected group of high-performance athletes preparing for a world-level competition alters the neural mechanisms of cardiovascular regulation in
Methods

Study Population
This study was conducted on the entire group of male athletes comprising the Italian junior national team of rowing (n=7, all 18 years of age) over the whole season preceding the Junior Rowing World Championship. All athletes were normotensive and had been previously screened for cardiovascular or metabolic diseases that could contraindicate participation in agonistic competitions. Athletes had been engaged in agonistic competitions for at least 3 years. The Italian team of rowing was selected for this study because of the very intensive endurance training sustained by these athletes. Over the whole period of the study, all athletes were living in the athletic campus of the Italian Federation of Rowing (Piediluco, Rieti, Italy) and hence shared the same daily scheduled activity and controlled diet. All athletes were nonsmokers. Each subject provided informed consent to participate in the study, and the study was approved by the medical staff of the Italian Federation of Rowing and by the Ethical Committee of the Istituto Universitario di Scienze Motorie of Roma.

Study Protocol
The study started in mid-September. In August and the first half of September, the athletes did not perform any scheduled physical activity; thus, for the purpose of this study, at this time they were taking drugs at the time of the recording sessions. The study started in mid-September. In August and the first half of September, the athletes did not perform any scheduled physical activity; thus, for the purpose of this study, at this time they were taking drugs at the time of the recording sessions. In August and the first half of September, the athletes did not perform any scheduled physical activity; thus, for the purpose of this study, at this time they were taking drugs at the time of the recording sessions. In August and the first half of September, the athletes did not perform any scheduled physical activity; thus, for the purpose of this study, at this time they were taking drugs at the time of the recording sessions. In August and the first half of September, the athletes did not perform any scheduled physical activity; thus, for the purpose of this study, at this time they were taking drugs at the time of the recording sessions. Therefore, after instrumentation, athletes underwent a maximal exercise test on the rowing ergometer (1000-m rowing test) with determination of oxygen consumption. No athlete was considered overtrained at the time of the recording sessions, based on the lack of the following signs: inability to sustain usual training program or reduced performance and the presence of symptoms, such as increased feeling of fatigue during daily training routine, sleeping disorders, apathy, or restlessness. 19 No subject was taking drugs at the time of the recording sessions.

Recorded Variables
The continuous ECG signal was obtained with a modified C5 lead, connecting the electrodes to an analog preamplifier (Marazza). Arterial blood pressure was continuously and noninvasively measured by Finapres (Ohmeda 2300 NIBP monitor). Respiratory signal was recorded with a piezoelectric thoracic belt. The 3 analogue signals were connected to an A/D board inserted in a personal computer, sampled at 300 Hz per channel, and stored on the hard disk for subsequent analyses. 20–24 These signals were used to assess autonomic function

Protocol
All of the recording sessions were performed on a Saturday afternoon (between 3:00 PM and 6:00 PM) at least 2 hours after a light lunch. Athletes did not perform strenuous physical activities in the 20 hours before recordings. The experiments were performed in a room at ambient temperature (22°C to 24°C). After instrumentation, the subjects lay supine for 15 minutes before experiments to relax in the room made dark and noiseless; thereafter, BP was measured twice, 5 minutes apart by sphygmomanometry, and the measurements were averaged. After BP measurements, continuous data acquisition was performed for 10 minutes. On each of the recording days, athletes collected an unstimulated saliva sample in the morning (8:00 AM) and afternoon (3:00 PM) for the determination of the protein-unbound, free cortisol. The saliva sample was collected directly into a plastic tube, which was immediately placed in liquid nitrogen and then stored at −80°C until cortisol assayed, which was determined by a solid-phase radioimmunoassay kit. Salivary cortisol was determined to have a measurable index of somatic and psychological stress 25–26 and impending overtraining in addition to the coach’s and physician’s reports.

Power Spectral Analysis
Details of the offline analysis have been published previously. 21–24 Briefly, the harmonic components of RR interval and BP variabilities were evaluated by the autoregressive method. Components in the frequency band from 0.03 to 0.15 Hz were considered low frequency (LF), and those in the range of 0.15 to 0.4 Hz, which is synchronous with respiration, were considered high frequency (HF). LF components of RR interval and BP variabilities are considered to be an expression of cardiac and vascular efferent sympathetic regulation, respectively, whereas the HF component of RR interval variability is considered to be an expression of cardiac vagal modulation. 20–24 Oscillations slower than 0.03 Hz were considered as very low frequency components. Spectral analysis of the respiratory signal was performed on the signal sampled once for every cardiac cycle. Respiratory spectra were used to assess the main respiratory frequency. The power density of each spectral component was calculated both in absolute values and normalized units. 21

Spontaneous Baroreflex Analysis
Details of this analysis have been previously described. 5,23–24 Briefly, the beat-by-beat time series of systolic arterial pressure (SAP) and RR interval were scanned by a computer to identify sequences of 3 or more consecutive beats in which SAP and RR 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/RR 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. 27 This method reflects mainly vagally mediated baroreceptor-cardiac responses 23 and has provided reproducible results. 28

Statistics
The significance of differences in the reported variables 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. Relations between variables were assessed by Spearman rank order correlation. Data are presented as median and interquartile range (IQ). Differences were considered statistically significant when P<0.05.

Results
Peak VO2 was 5600 mL (IQ 5200 to 5900) at baseline and 5800 mL (IQ 5300 to 6200) at the time of the highest training load (P=0.031). There was a progressive bradycardia from baseline (56 beats/min, IQ 52 to 61) up to 75% training load (50 beats/min, IQ 46 to 57, P<0.01) that was accompanied by a progressive increase in the HF component and a decrease in the LF component of RR interval variability and in the LF/HF ratio. BRS showed a nonsignificant trend toward an increase. At 100% training load, opposite changes were observed, with a relative increase in HR (61 beats/min, IQ 58 to 66, P<0.01 versus baseline and 75% training load) accompanied by a marked and significant decrease in the HF and an increase in

a direction associated with enhanced sympathetic activation and reduced vagal inhibition.
the LF component of RR interval variability and in the LF/HF ratio. BRS was also markedly decreased compared with baseline and with the values observed at 75% training load (Table 1). The decrease in BRS was in inverse relation to the increase in the LF component (normalized units [n.u.]) of RR interval variability ($r = 0.67$, $P = 0.001$).

SAP did not significantly change from baseline throughout the study, whereas DAP increased significantly at the 6th month of 75% training load and even more at 100% training load. LF$_{SAP}$ and LF$_{DAP}$ did not change significantly from baseline up to 75% training load, but both increased markedly and significantly at 100% training load (Table 2). An example from one athlete of spectral analysis of RR interval and SAP variability and of BRS at the different training loads is illustrated in the Figure.

Salivary cortisol concentration did not change throughout the study while maintaining the physiological circadian variation. Median cortisol concentration in the morning was 3.8 ng/mL at baseline, 4.8 and 3.7 ng/mL at the time of the 1st and 2nd assessment at 75% training load, and 4.5 ng/mL at 100% training load, respectively ($P = 0.72$ by ANOVA on ranks). The respective afternoon values were 1.5, 1.7, 1.7, and 1.0 ng/mL ($P = 0.72$), significantly smaller than the respective morning ones.

**Discussion**

The novel and unique finding of the present investigation is the observation of a switch from parasympathetic to sympathetic predominance in high-performance athletes at the peak of a hard training regimen for a world-level competition. In the highly selected athletes of this study, we observed a progressive bradycardia from baseline with increase in training load up to 75% of maximum, an effect associated with marked increases in the HF and (nonsignificant) decreases in the LF component of heart rate variability (HRV) and in the LF/HF ratio. These findings are in line with most of the studies performed so far and would confirm that even in top-level athletes submaximal exercise training enhances vagal and tends to decrease sympathetic cardiac modulation. Sympathetic vasomotor control also did not change from baseline, as indicated by the lack of significant variations in the LF component of BP variability.22 Also in agreement with

### TABLE 1. RR Interval, Spectrum Analysis of RR Interval Variability, and Spontaneous Baroreflex Sensitivity

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>75% (3rd Month)</th>
<th>75% (6th Month)</th>
<th>100% (9th Month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR interval, ms</td>
<td>1065 (966–1150)</td>
<td>1095 (1029–1133)*</td>
<td>1192 (1053–1317)†</td>
<td>978 (923–1044)†‡</td>
</tr>
<tr>
<td>Variance, ms$^2$</td>
<td>4356 (2257–9408)</td>
<td>4624 (2479–9403)</td>
<td>5776 (3627–18604)</td>
<td>4356 (1843–8092)</td>
</tr>
<tr>
<td>Low frequency n.u.</td>
<td>51.5 (29.1–58.9)</td>
<td>41.7 (28.1–49.9)</td>
<td>29.0 (21.7–36.1)</td>
<td>63.1 (62.1–68.3)†‡</td>
</tr>
<tr>
<td>High frequency n.u.</td>
<td>31.9 (29.6–57.6)</td>
<td>50.8 (32.4–66.2)</td>
<td>60.2 (47.2–70.4)†</td>
<td>25.9 (17.9–27.6)†‡</td>
</tr>
<tr>
<td>LF/HF</td>
<td>1.4 (0.4–2.0)</td>
<td>0.8 (0.4–1.8)</td>
<td>0.4 (0.3–0.8)</td>
<td>2.5 (2.4–3.5)†‡</td>
</tr>
<tr>
<td>Respiration, Hz</td>
<td>0.32 (0.30–0.33)</td>
<td>0.31 (0.29–0.34)</td>
<td>0.30 (0.28–0.36)</td>
<td>0.34 (0.23–0.36)</td>
</tr>
<tr>
<td>BRS, ms/mm Hg</td>
<td>26.3 (16.4–40.9)</td>
<td>32.6 (24.4–50.2)</td>
<td>32.5 (30.8–47.7)</td>
<td>15.5 (8.9–21.9)†‡</td>
</tr>
</tbody>
</table>

Values are given as median and interquartile range. 
* $P < 0.05$ vs baseline. 
† $P < 0.05$ vs 75% training load at 3rd month. 
‡ $P < 0.05$ vs 75% training load at 6th month.

### TABLE 2. Arterial BP and Spectrum Analysis of BP Variability

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>75% (3rd Month)</th>
<th>75% (6th Month)</th>
<th>100% (9th Month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAP, mm Hg</td>
<td>127 (121–130)</td>
<td>130 (126–143)</td>
<td>135 (130–148)</td>
<td>130 (125–135)</td>
</tr>
<tr>
<td>Low frequency mm Hg$^2$</td>
<td>3.2 (1.3–6.5)</td>
<td>2.4 (1.7–4.0)</td>
<td>2.4 (0.5–6.2)</td>
<td>10.2 (5.1–11.9)†‡</td>
</tr>
<tr>
<td>High frequency mm Hg$^2$</td>
<td>1.2 (0.8–1.7)</td>
<td>0.9 (0.7–2.4)</td>
<td>0.6 (0.3–2.7)</td>
<td>1.6 (1.5–2.8)</td>
</tr>
<tr>
<td>DAP, mm Hg</td>
<td>72 (65–70)</td>
<td>65 (60–77)</td>
<td>80 (76–87)†</td>
<td>85 (81–90)†</td>
</tr>
<tr>
<td>Low frequency mm Hg$^2$</td>
<td>2.4 (1.4–4.8)</td>
<td>1.7 (0.9–1.9)</td>
<td>1.1 (0.6–2.6)</td>
<td>4.5 (2.4–8.9)†‡</td>
</tr>
<tr>
<td>High frequency mm Hg$^2$</td>
<td>0.6 (0.3–1.9)</td>
<td>0.4 (0.2–0.9)</td>
<td>0.5 (0.3–1.4)</td>
<td>0.4 (0.3–0.5)</td>
</tr>
</tbody>
</table>

Values are given as median (interquartile range). 
* $P < 0.05$ vs baseline. 
† $P < 0.05$ vs 75% training volume at 3rd month. 
‡ $P < 0.05$ vs 75% training volume at 6th month.
previous studies performed in healthy subjects, BRS showed a nonsignificant trend toward an increase with long-term submaximal exercise training, at variance with the increase in BRS consistently reported after training in cardiac patients.2,5 However, when the training load approached the maximum at the time of the nearing World Championship competition, neural cardiovascular regulation showed a clear shift from vagal to sympathetic predominance, with concordant changes in hemodynamic variables and in cardiac and vascular indices of autonomic modulation. In fact, the resting relative tachycardia and the marked increase in DBP were associated with marked increases in the LF component of both HR and BP variability and in the LF/HF ratio and with a drastic decrease in the HF component of HRV and in BRS, this latter being highly related to the increase in the LFRR (n.u.). The possibility that the increased markers of sympathetic activation would represent an after-effect of the daily exercise routine17 seems unlikely, because athletes did not train vigorously from at least 20 hours before the recording sessions and no signs of enhanced sympathetic activation was detected in the recordings sessions performed with the same experimental schedule at 75% training load. In addition, an after-effect of exercise on LF/HF ratio has been demonstrated directly only in sedentary people,17 whereas markers of sympathetic cardiac modulation have been shown to be restored more rapidly after exercise in athletes.29,30 Finally, short-term overtraining in elite athletes did not alter frequency domain indices of HRV as well as plasma catecholamines.31 The absence of overtraining or stress-related bias is also suggested by the persistently unchanged salivary cortisol concentration.25,26

To our knowledge, this is the first study to evaluate the effects of heavy training on both cardiac and vascular autonomic regulation with complete noninvasive and unobtrusive methodologies during a whole training season culminating with a high-level competition in a selected group of peak performance athletes with a relatively long history of intense exercise training.

In the light of our results, we suggest that enhanced sympathetic activation and attenuated vagal inhibition could represent the neurovegetative adaptation for increasing athletic performance. Reducing the inhibitory influences of vagal mechanisms while concomitantly enhancing sympathetic activity might serve to prepare the cardiovascular system to the rapid and wide, even anticipatory, variations in heart rate, cardiac output, flow redistribution, and muscle perfusion of highly demanding competitions.32 Although the mechanisms underlying these effects were not examined as a part of this study, the fact that 3 out of the 7 athletes won a medal (1 silver and 2 bronze) in the World Championships would be in keeping with our suggestion.
Of note, power spectral analysis of short-term HRV might represent a valuable tool to assess the time course of neurovegetative cardiovascular adaptations to competitive training.

Clinical Implications
Presently, it is unclear whether resting periods after strenuous training programs restore BP and autonomic function toward basal normal levels or whether years of top-level agonistic career (and intensive training) may predispose to alterations in the neural control of circulation, possibly leading to cardiovascular derangements. Indeed, we do not know whether the altered BP and vasomotor autonomic function shown in this study might be in time hazardous to human vessels, contributing to the vascular impairment that has been reported after high-intensity physical training. Finally, it remains to be established whether the enhanced background level of sympathetic activation and reduced vagal activity might represent a condition of greater risk for threshold arrhythmias under the unique circumstances of extremely demanding training and competitions in athletes with an underlying susceptible myocardial substrate. Surprisingly, little attention has been given to functional triggers of arrhythmias in athletes. The results of this study might suggest the need for a careful evaluation of signs of excessive sympathetic activation during periods of very intensive training, particularly in athletes with risk factors for or overt cardiovascular diseases.

Limitations
The main limitation of this study is the lack of a control group. However, this would be more a theoretical than an actual methodological limitation within the framework of our investigation. Indeed, it is hard to hypothesize that very young normotensive yet untrained subjects would undergo 15-mm Hg increase in resting DAP, signs of marked sympathetic activation, and 50% decrease in BRS over a 9-month period like in this study. The ideal protocol of training/detraining with a crossover design is virtually impossible in world class athletes. Second, our results are limited to a small yet highly homogeneous group of elite athletes comprising the entire team of Italian junior rowers. A final potential limitation of this study includes the indirect method used to assess changes in autonomic function. The issue of the validity of this approach was recently addressed by experiments in humans, 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 low and high frequencies in nerve activity, RR interval, and SAP variabilities at various levels of induced pressure changes provides support to the use of LFHR and HFHR to infer the changing state of, respectively, sympathetic and vagal modulation of the sinoatrial node and of LFSAP as an index of efferent sympathetic vascular modulation. In conclusion, the results of this study indicate that heavy training in high-performance, world class athletes shifted the cardiovascular autonomic modulation from a parasympathetic toward a sympathetic predominance.

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References


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