Journal of the American College of Cardiology
© 2002 by the American College of Cardiology Foundation
Published by Elsevier Science Inc.
Vol. 39, No. 6, 2002
ISSN 0735-1097/02/$22.00
PII S0735-1097(02)01722-9

Intrinsic Sinus and Atrioventricular Node Electrophysiologic Adaptations in Endurance Athletes

Ricardo Stein, MD, ScD, Claudio M. Medeiros, MD, Guido A. Rosito, MD, ScD, Leandro I. Zimerman, MD, ScD, Jorge P. Ribeiro, MD, ScD

Porto Alegre, Brazil

OBJECTIVES In the present study, we evaluated sinus and atrioventricular (AV) node electrophysiology of endurance athletes and untrained individuals before and after autonomic pharmacologic blockade.

BACKGROUND Endurance athletes present a higher prevalence of sinus bradycardia and AV conduction abnormalities, as compared with untrained individuals. Previous data from our laboratory suggest that nonautonomic factors may be responsible for the longer AV node refractory period found in well-trained athletes.

METHODS Six aerobically trained male athletes and six healthy male individuals with similar ages and normal rest electrocardiograms were studied. Maximal oxygen uptake ($\dot{V}O_2$max) was measured by cardiopulmonary testing. The sinus cycle length (SCL), AV conduction intervals, sinus node recovery time (SNRT), Wenckebach cycle (WC) and anterograde effective refractory period (ERP) of the AV node were evaluated by invasive electrophysiologic studies at baseline, after intravenous atropine (0.04 mg/kg) and after addition of intravenous propranolol (0.2 mg/kg).

RESULTS Athletes had a significantly higher $\dot{V}O_2$max as compared with untrained individuals. The SCL was longer in athletes at baseline, after atropine and after the addition of propranolol for double-autonomic blockade. The mean maximal SNRT/SCL was longer in athletes after atropine and after propranolol. The WC and anterograde ERP of the AV node were longer in athletes at baseline, after atropine and after propranolol.

CONCLUSIONS Under double-pharmacologic blockade, we demonstrated that sinus automaticity and AV node conduction changes of endurance athletes are related to intrinsic physiology and not to autonomic influences. (J Am Coll Cardiol 2002;39:1033–8) © 2002 by the American College of Cardiology Foundation

The electrocardiogram (ECG) of endurance athletes reflects anatomic and physiologic adaptations that have been brought about by training (1,2). Sinus bradycardia and atrioventricular (AV) conduction abnormalities represent part of the spectrum of arrhythmias seen on the ECG of athletes, and most studies have attributed these findings to a relative or absolute increase in parasympathetic activity (1,2). However, the precise mechanism of these training-induced arrhythmias is still uncertain. We have recently used transesophageal atrial stimulation to evaluate aerobically trained athletes and sedentary individuals, to test the hypothesis that parasympathetic activity, as detected by heart rate variability, could be associated with changes in AV conduction (3). Athletes presented with Wenckebach AV node conduction at rates lower than those of sedentary individuals, suggesting a longer AV node refractory period. However, this could only be partially explained by increased parasympathetic activity, as detected by a time domain index of heart rate variability, suggesting that nonautonomic factors could contribute to this change in AV conduction. In the present study, we used pharmacologic blockade of the autonomic nervous system during intracavitary electrophysiologic studies to evaluate sinus node automaticity and AV node conduction in aerobically trained athletes and untrained individuals, to test the hypothesis that the altered sinus and AV electrophysiology of athletes is related to intrinsic and not autonomic adaptations.

METHODS

Study subjects and protocol. Six male runners who ran at least 50 km per week and six healthy but nonathletic men who had not participated in regular aerobic activity for at least one year were studied. During the experiments, the subjects did not ingest any food or beverage containing caffeine, and they were taking no medications. None of the participants exercised in the 24 h before the procedures. A medical history, physical examination, rest ECG and maximal exercise test were obtained to exclude pathologic conditions. For each subject, maximal oxygen uptake ($\dot{V}O_2$max) was measured by a treadmill test, and sinus automaticity and AV node conduction were evaluated by intracavitary electrical stimulation at baseline and after

From the Cardiology Division, Hospital de Clínicas de Porto Alegre, and Department of Medicine, Faculty of Medicine, Federal University of Rio Grande do Sul, Porto Alegre, Brazil. This work was supported by grants from Coordenadoria de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Brasilia, Brazil, and Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS), Porto Alegre, Brazil.

Manuscript received June 19, 2001; revised manuscript received December 7, 2001, accepted December 21, 2001.

Abbreviations and Acronyms

ANOVA = analysis of variance
AV = atrioventricular
ECG = electrocardiogram
ERP = effective refractory period
SCL = sinus cycle length
SNRT = sinus node recovery time
$\dot{V}O_2max$ = maximal oxygen uptake
WC = Wenckebach cycle

pharmacologic blockade. All subjects were informed of the risks and discomforts involved in the experiments and gave written, informed consent. In light of the results of our previous experiments (3), as well as the risks involved with the performance of invasive electrophysiologic studies in asymptomatic individuals (4), our institution's Research Committee approved the protocol for six athletes and six untrained individuals. The protocol was also approved by the Brazilian National Council for Research (CONEP, Brasilia, Brazil).

Measurement of $\dot{V}O_2max$. The subjects exercised on a motor-driven treadmill (Inbramed TK 10,200, Porto Alegre, Brazil); the 12-lead ECG was continuously monitored; and respiratory gases were analyzed by using a previously validated commercial system (Total Energy Expenditure Measurements, Aerosport, Ann Harbor, Michigan) (5). For the athletes, the exercise protocol started at a speed of 4 km/h, with additional increments of 2 km/h every 2 min until volitional fatigue. For untrained individuals, the protocol was started at a speed of 2 km/h, with additional increments of 2 km/h every 2 min until volitional fatigue.

Electrophysiologic study and pharmacologic blockade. The electrophysiologic study was performed with the subjects in the postabsorptive state. The subjects rested in the supine position for 15 min, and a 12-lead surface ECG was recorded on a Funbec (São Paulo, Brazil) electrocardiograph. The PR interval and corrected QT ($QTc = QT \cdot [\sqrt{RR}]^{-1}$) interval were measured. Correction of the QT interval was used to control for the different rest heart rates of the groups. The subjects were then continuously monitored by pulse oximetry and electrocardiography. A cannula was inserted in the antecubital vein, and 2 mg of midazolam was initially administered intravenously. Additional doses of midazolam were given throughout the procedure, if necessary for sedation. After local anesthesia of the right groin with 1% lidocaine, two sheaths were introduced percutaneously into the right femoral vein. Under fluoroscopic guidance (calculated radiation exposure of 28 to 42 mGy), two 7F, deflectable, multipolar electrode catheters were positioned against the high right atrial wall, near the region of the sinus node, and across the tricuspid valve in the area of the His bundle for recordings of intracardiac electrograms and pacing. Baseline intracardiac conduction intervals were then measured during sinus rhythm (6). Electrical stimulation of the atrium was performed with a programmable stimulator (UHS 20, Biotronik, Germany) using 2-ms, constant-current pulses at approximately twice the late diastolic threshold. Surface ECG leads and bipolar intracardiac electrograms filtered at a bandpass of 30 to 500 Hz were displayed and recorded simultaneously on a multichannel recorder (Mingograf 7, Siemens, Germany) at a paper speed of 50 or 100 mm/s.

After control recordings, the atrium was paced for 30-s periods, at constant cycle lengths of 600, 500 and 400 ms, and the rhythm was monitored to ensure complete atrial capture. At least 30 s was allowed to elapse between each successive pacing period. Measurements of sinus node recovery time (SNRT) were made using bipolar electrograms recorded from the proximal two poles of the high atrial catheter; SNRT was defined as the time from the last paced stimulus to the onset of the first deflection on the electrogram of the first sinus beat. To control for differences in sinus rate, SNRT was normalized for the spontaneous sinus cycle length (SCL) (7). At least five consecutive cycles following each pacing period and after the rhythm had returned to the control cycle length were used to calculate the mean SCL. In each individual, the longest (maximal) SNRT was determined. The Wenckebach cycle (WC) of the AV node was defined as the cycle length during incremental atrial pacing where the AV node Wenckebach phenomenon was noted. The anterograde effective refractory period (ERP) of the AV node was measured using an eight-beat drive at a cycle length equal to the SCL − 100 ms, followed by a single premature atrial stimulus introduced decrementally at 10-ms intervals. The anterograde ERP of the AV node was defined as the longest coupled premature atrial stimuli interval that failed to propagate to the His bundle (6).

Parasympathetic blockade was induced by administration of atropine, 0.04 mg/kg body weight intravenously (8,9). After a stable sinus rate had been achieved, the electrophysiologic variables described earlier were again measured. Double-autonomic blockade was then obtained by addition of 0.2 mg/kg of propranolol intravenously, and, after SCL stabilization, a final set of electrophysiologic variables was obtained again (8,9). Sheaths were pulled out; hemostasis was obtained by pressure; and the subjects rested in a recovery room for 6 h.

Statistical analyses. Data are presented as the mean ± SD. Differences between athletes and nonathletes were compared by using the Student *t* test. The effects of pharmacologic blockade on the electrophysiologic variables were compared by two-way analysis of variance (ANOVA) for repeated measures. When appropriate, multiple comparisons were made by the Student Newman-Keuls method. Based on the results of our previous study using transesophageal stimulation (3), and assuming a lower variability of the data due to sedation, we estimated that a sample size of six individuals in each group would have a statistical power of

Table 1. Physical Characteristics and Rest Electrocardiographic and Maximal Exercise Test Results of Athletes and Untrained Subjects

	Athletes (n = 6)	Untrained (n = 6)	p Value
Age (years)	29 ± 4	28 ± 5	NS
Weight (kg)	78 ± 1	77 ± 2	NS
Height (cm)	178 ± 8	178 ± 9	NS
Rest heart rate (beats/min)	52 ± 8	73 ± 7	0.001
PR interval (ms)	168 ± 15	156 ± 16	NS
Corrected QT interval (ms)	412 ± 9	398 ± 5	NS
Maximal heart rate (beats/min)	188 ± 11	191 ± 13	NS
Maximal respiratory exchange ratio	1.18 ± 0.8	1.16 ± 0.7	NS
$\dot{V}O_2$max (ml/kg per min)	65 ± 1	38 ± 4	0.001

Data are presented as the mean value ± SD.
NS = not significant; $\dot{V}O_2$max = maximal oxygen uptake.

80% to detect a 20% difference in the electrophysiologic variables, at $p = 0.05$.

RESULTS

Table 1 describes the demographic, rest ECG and exercise testing data for athletes and untrained individuals. The groups were similar in terms of age, weight and height. In athletes, the rest heart rate was significantly lower and $\dot{V}O_2$max was significantly higher. The rest ECG intervals were similar in the two groups and within the normal range for all subjects.

The mean AV conduction intervals and atrial P-wave, atrial His-bundle and ventricular His-bundle values were similar, within the normal range, and responded typically and alike during the pharmacologic interventions in athletes and nonathletes (Table 2). The mean SCLs in athletes and nonathletes were 1,030 ± 111 and 913 ± 90 ms, 737 ± 59 and 653 ± 43 ms and 831 ± 71 and 722 ± 43 ms at baseline, after parasympathetic blockade and after double-autonomic blockade, respectively (ANOVA: $p < 0.01$ for group effect; $p < 0.01$ for drug effect; $p = 0.365$ for interaction). Atropine increased and propranolol decreased the heart rate ($p < 0.05$) in similar proportions in both groups—that is, the SCL of the athletes always remained longer than the SCL of the nonathletes (Fig. 1). The mean maximal SNRT/SCL ratios in athletes and nonathletes were 1.56 ± 0.16 and 1.5 ± 0.09, 1.36 ± 0.19 and 1.26 ± 0.06 and 1.45 ± 0.09 and 1.31 ± 0.05 at baseline, after parasympathetic blockade and after double-autonomic blockade, respectively (ANOVA: $p < 0.01$ for group effect; $p < 0.01$ for drug effect; $p = 0.640$ for interaction). As expected, atropine decreased and propranolol increased ($p < 0.05$) the mean maximal SNRT/SCL ratio, but, unexpectedly, the recovery time of the athletes was significantly longer than that of the nonathletes after both parasympathetic and double-autonomic blockade, despite being expressed as a ratio of SCL (Fig. 1). The mean length of the WC of the AV node in athletes and nonathletes was 575 ± 73 and 453 ± 51 ms, 423 ± 46 and 342 ± 25 ms and 493 ± 56 and 413 ± 28 ms at baseline, after parasympathetic blockade and after double-autonomic blockade, respectively (ANOVA: $p < 0.01$ for group effect; $p < 0.01$ for drug effect; $p = 0.370$ for interaction) (Fig. 1). The mean anterograde ERP of the AV node in athletes and nonathletes was 425 ± 46 and 313 ± 44 ms, 338 ± 47 and 257 ± 26 ms and 408 ± 53 and 282 ± 43 ms at baseline, after parasympathetic blockade and after double-autonomic blockade, respectively (ANOVA: $p < 0.01$ for group effect; $p < 0.01$ for drug effect; $p = 0.690$ for interaction) (Fig. 1). As with SCL, the WC and anterograde ERP were reduced by atropine and increased by propranolol, but the values for athletes remained significantly longer than those for nonathletes.

Table 2. Electrophysiologic Intervals at Baseline, After Atropine and After Propranolol

	P-A Interval (ms)	H-A Interval (ms)	H-V Interval (ms)
Baseline			
Athletes	34 ± 9	94 ± 25	46 ± 6
Untrained	32 ± 4	93 ± 17	43 ± 6
Atropine			
Athletes	38 ± 9	76 ± 22*	45 ± 6
Untrained	33 ± 4	80 ± 15*	44 ± 6
Propranolol			
Athletes	36 ± 9	92 ± 23	46 ± 6
Untrained	32 ± 4	89 ± 15	42 ± 8

Data are presented as the mean value ± SD.
*Significantly different from baseline value, with no significant interaction.
H-A = atrial His bundle; H-V = ventricular His bundle; P-A = atrial P wave.

DISCUSSION

The rest ECGs of the well-trained endurance athlete may show certain distinguished features that are similar, in many respects, to those seen in patients with cardiovascular disease. Among the most frequent rhythm changes are sinus bradycardia and AV conduction abnormalities. Rest sinus bradycardia may be found in the great majority of endurance athletes, and borderline or first-degree AV block may be observed in 10% to 33% and second-degree Wenckebach block in 2% to 10% of long-distance runners (10). These abnormalities have been related to higher parasympathetic activity owing to their association with training and detraining, as well as their disappearance after sympathetic or vagolytic maneuvers (11).

Because of the invasive nature of electrophysiologic studies, there is little information on atrial automaticity and AV node conduction of healthy athletes. Mezzani et al. (12) performed invasive electrophysiologic studies in a group of athletes and a group of untrained individuals, all with Wolff-Parkinson-White syndrome. In that study, athletes showed a longer SCL, atrial effective and functional refractory periods and anterograde ERP of the accessory pathway; these findings were attributed to autonomic influences. In our previous study of endurance-trained athletes and untrained individuals evaluated by transesophageal stimula-

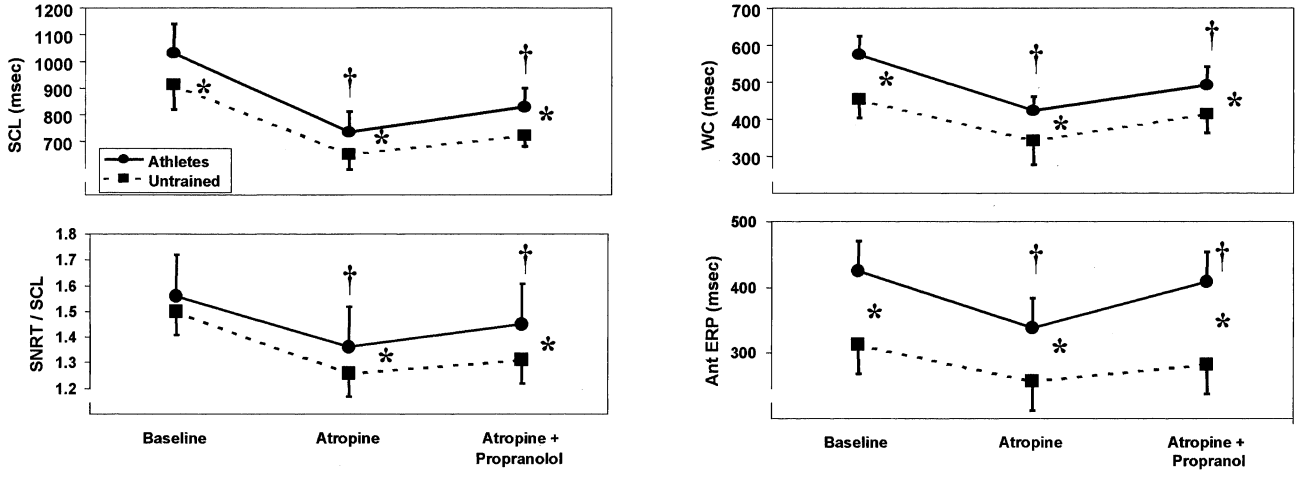

Figure 1. The sinus cycle length (SCL), maximal normalized sinus node recovery time (SNRT)/SCL ratio and Wenckebach cycle (WC) and anterograde (Ant) effective refractory period (ERP) of the atrioventricular node at baseline, after atropine and after propranolol in endurance-trained athletes **(solid circles)** and untrained individuals **(solid squares)**. Data are presented as the mean value ± SD. *Significant ($p < 0.05$) differences between athletes and untrained individuals. †Significantly different ($p < 0.05$) from previous pharmacologic intervention.

tion, only 24% of the variance in WC could be accounted for by the vagal time domain index of heart rate variability—the square root of the mean of the sum of squares of differences between adjacent RR intervals (3). Thus, we proposed that athletic training could induce intrinsic adaptations in the conduction system, which would contribute to the higher prevalence of AV conduction abnormalities in athletes. On the basis of these intriguing observations, the Research Committee of our institution approved a new protocol with pharmacologic blockade and invasive electrophysiology data acquisition. Using a cross-sectional design, in the present study we evaluated two distinct groups, in which athletes had lower rest heart rate and higher directly measured $\dot{V}O_2max$ when compared to nonathletes. We chose to use intracavitary electrophysiologic measurements under sedation to reduce the influence of psychological stress. Under these controlled conditions, we found evidence that sinus automaticity and AV node conduction of athletes at rest are determined by intrinsic electrophysiologic adaptations, rather than by autonomic influences.

Sinus automaticity in athletes. Some investigators who also used pharmacologic blockade have attributed training-induced sinus bradycardia to an imbalance of the two branches of the autonomic nervous system—that is, increased parasympathetic activity, decreased sympathetic activity or a combination of these (13). In contrast, other studies using pharmacologic blockade have proposed that alterations in the intrinsic properties of the sinus node, the so-called "nonautonomic component," were responsible for rest bradycardia of athletes (14,15). Likewise, some studies that used heart rate variability methods, which may detect vagal adaptations (16), demonstrated an increase in parasympathetic activity (17,18), although others were not able to demonstrate this effect (3,19). The effects of autonomic blockade on the SCL of our endurance athletes are consistent with the concept that long-term, training-induced rest sinus bradycardia is not caused by increased parasympathetic activity or decreased sympathetic activity, but is related to intrinsic adaptations. Indeed, atropine and propranolol caused parallel shifts in the sinus automaticity of athletes and nonathletes—that is, the incremental and decremental changes were identical. Increased parasympathetic activity would cause greater heart rate responses post-atropine and a reduction in sympathetic activity would cause lesser heart rate responses post-propranolol in athletes than in nonathletes.

The maximal SNRT/SCL of athletes was significantly longer than that of nonathletes after both parasympathetic and double-autonomic blockade, compatible with nonautonomic adaptation. This longer recovery time may reflect greater overdrive suppression, longer retrograde and anterograde sinoatrial conduction times or both. In view of the effects on AV node conduction, it is tempting to speculate about the substantial impact of these sinoatrial conductive components.

Atrioventricular node conduction in athletes. In the present study, the effects of autonomic blockade on the WC and anterograde ERP of the AV node were equal to the effects on SCL. The differences in these electrophysiologic measurements between athletes and untrained individuals were very similar in magnitude at baseline, after atropine and after propranolol, again discordant with the view of an imbalance in autonomic activity. These findings are consistent with the experiments conducted by Yamaya et al. (20), who used pharmacologic blockade in horses with AV node conduction abnormalities. Similar to the findings in horses, our data indicate that prolonged and intensive training did not disrupt the normal balance of the autonomic nervous system, and that the longer SCL and refractory period of the AV node were essentially caused by significant intrinsic electrophysiologic modifications. These findings also confirmed our previous observations (3) suggesting that the longer AV node refractory period of athletes could be

mediated mainly by nonautonomic factors, most likely induced by athletic training.

Possible mechanisms. The physiologic mechanisms by which endurance training may induce these intrinsic changes in the specialized conduction system of the heart are unknown and may be multifactorial. An altered ionic balance across the membrane (21), as well as biochemical and mechanical effects induced by dilation and hypertrophy (14,15), have been proposed as possible mechanisms. Clinical and research data indicate that active and passive changes in the mechanical environment of the heart are capable of influencing both the initiation and spread of cardiac excitation through pathways that are intrinsic to the heart—a phenomenon known as "mechanoelectric feedback" (22). One unifying explanation for the controversy about autonomic versus nonautonomic determinants of electrophysiologic adaptations in athletes could be that short-term physical training programs, such as those used in prospective studies (13,18), could induce autonomic adaptations, with a reduction in sympathetic activity and an increase in parasympathetic activity. Long-term aerobic training, accompanied by anatomic changes such as atrial and ventricular dilation, would create the mechanoelectric feedback necessary to induce intrinsic electrophysiologic adaptations, as demonstrated in the present and other cross-sectional studies (3,14,15). Interestingly, rats (23) and dogs (24) whose hearts were denervated before training did not develop intrinsic and rest bradycardia, respectively. Thus, it is likely that a functioning autonomic system is necessary for the development of electrophysiologic adaptations.

Possible clinical relevance. In the present study, we evaluated a group of well-trained athletes with rest bradycardia, but without conduction abnormalities. Thus, the demonstration of intrinsic electrophysiologic adaptations can be generalized only to other athletes with similar characteristics. However, taken together with our previous observations in another group of endurance athletes (3), we believe that intrinsic adaptations represent the electrophysiologic substrate that may facilitate the appearance of more advanced conduction abnormalities. The demonstration by Zepilli et al. (11) of a reversal in conduction abnormalities of athletes by sympathetic or vagolytic maneuvers may simply represent normal parasympathetic activity superimposed on altered intrinsic electrophysiology.

Study limitations. In this study, we assumed that the differences between athletes and untrained individuals represent physiologic adaptations in response to training. Because this is a cross-sectional study, an alternative explanation could be that the intrinsic changes represent inherited characteristics that may facilitate success or trainability. However, this is unlikely, based on the observations of previous prospective studies on sinus bradycardia (13,18) and conduction abnormalities of athletes (11). The use of pharmacologic blockade as a tool for the evaluation of autonomic and nonautonomic influences on electrophysiologic variables also has its limitations. The possible sympathomimetic effect of atropine (25), as well as its attenuated antagonism (26), could have confounded our findings. However, both of these actions, if anything, would have resulted in overestimation of parasympathetic activity, particularly in favor of the athletes (9), which we did not find in our study.

Conclusions. Our controlled intracavitary electrophysiologic studies under pharmacologic blockade demonstrate that endurance athletes with rest bradycardia and a normal ECG present with sinus automaticity and AV node conduction changes that are related to intrinsic physiology, rather than to autonomic influences.

Reprint requests and correspondence: Dr. Jorge P. Ribeiro, Cardiology Division, Hospital de Clínicas de Porto Alegre, Rua Ramiro Barcelos 2350, 90035-007, Porto Alegre, RS, Brazil. E-mail: jpribeiro@cpovo.net.

REFERENCES

1. Huston TP, Puffer JC, Rodney WM. The athletic heart syndrome. N Engl J Med 1985;313:24–32.
2. Holly RG, Shaffrath JD, Amsterdam EA. Electrocardiographic alterations associated with the hearts of athletes. Sports Med 1998;25:139–48.
3. Stein R, Moraes RS, Cavalcanti AV, Ferlin EL, Zimerman LI, Ribeiro JP. Sinus automaticity and atrioventricular conduction in athletes: contribution of autonomic regulation. Eur J Appl Physiol 2000;82:155–7.
4. Horowitz L. Risks and complications of clinical electrophysiologic studies: a prospective analysis of 1000 consecutive patients. J Am Coll Cardiol 1987;9:1261–8.
5. Novitsky S, Segal KR, Chatr-Aryamontri B, Guvakov D, Katch VL. Validity of a new portable indirect calorimeter: the AeroSport TEEM 100. Eur J Appl Physiol 1995;70:462–7.
6. Josephson ME. Clinical Cardiac Electrophysiology: Techniques and Interpretation. Philadelphia, PA: Lea & Febiger, 1993.
7. Benditt DG, Strauss HC, Scheinman MM, Behar VS, Wallace A. Analysis of secondary pauses following termination of rapid atrial pacing. Circulation 1976;54:436–41.
8. Jose AD, Taylor RR. Autonomic blockade by propranolol and atropine to study intrinsic myocardial function in man. J Clin Invest 1969;48:2019–40.
9. Ribeiro JP, Ibañez JM, Stein R. Autonomic nervous control of the heart rate response to dynamic incremental exercise: evaluation of the Rosenblueth-Simeone model. Eur J Appl Physiol 1991;62:140–4.
10. Zehender M, Meinertz T, Keul J, Just H. ECG variants and cardiac arrhythmias in athletes: clinical relevance and prognostic importance. Am Heart J 1990;6:1378–90.
11. Zeppilli P, Fenici R, Sassara M, Pirrami MM, Caselli G. Wenckebach second-degree A-V block in top-ranking athletes: an old problem revisited. Am Heart J 1980;100:281–93.
12. Mezzani A, Giovannini T, Michelucci A, et al. Effects of training on the electrophysiologic properties of atrium and accessory pathway in athletes with Wolff-Parkinson-White syndrome. Cardiology 1990;77:295–302.
13. Ekblom B, Kilbom A, Soltysiak J. Physical training, bradycardia and autonomic nervous system. Scand J Clin Lab Invest 1973;32:251–6.
14. Lewis SF, Nylander E, Gad P, Areskog NH. Non-autonomic component in bradycardia of endurance trained men at rest and during exercise. Acta Physiol Scand 1980;109:297–305.
15. Katona PG, McLean M, Dighton DH, Guz A. Sympathetic and parasympathetic cardiac control in athletes at rest. J Appl Physiol 1982;52:1652–7.

16. Polanczyk CA, Rohde LEP, Moraes RS, Ferlin EL, Leite C, Ribeiro JP. Sympathetic nervous system representation in time and frequency domain indices of heart rate variability. Eur J Appl Physiol 1998;79: 69–73.
17. Goldsmith RL, Bigger JT, Steinman RC, Fleiss JL. Comparison of 24-hour parasympathetic activity in endurance-trained and untrained young men. J Am Coll Cardiol 1992;20:552–8.
18. De Meersman RE. Respiratory sinus arrhythmia alteration following training in endurance athletes. Eur J Appl Physiol 1992;64:434–6.
19. Lazoglu AH, Glace B, Gleim GB, Coplan NL. Exercise and heart rate variability. Am Heart J 1996;131:825–7.
20. Yamaya Y, Kubo K, Amada A, Sato K. Intrinsic atrioventricular conductive function in horses with a second-degree atrioventricular block. J Vet Med Sci 1997;59:149–51.
21. Brorson L, Conradson TB, Olsson B, Varnauskas E. Right atrial monophasic action potential and effective refractory periods in relation to physical training and maximal heart rate. Cardiovasc Res 1976;10: 168–75.
22. Kohl P, Hunter P, Noble D. Stretch-induced changes in heart rate and rhythm: clinical observations, experiments and mathematical models. Prog Biophys Mol Biol 1999;71:91–138.
23. Sigvardsson K, Svanfeldt E, Kilbom A. Role of the adrenergic nervous system in the development of training-induced bradycardia. Acta Physiol Scand 1977;101:481–8.
24. Ordway GA, Charles JB, Randall DC, Billman GE, Wekstein DR. Heart rate adaptation to exercise training in cardiac-denervated dogs. J Appl Physiol 1982;52:1586–90.
25. Donald DE, Samueloff SL, Ferguson D. Mechanism of tachycardia caused by atropine in conscious dogs. Am J Physiol 1967;212:901–10.
26. Levy MN. Sympathetic–parasympathetic interactions in the heart. Circ Res 1971;29:437–45.