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Cardiac autonomic dysfunction in anabolic steroid users

A. S. Maior[1], A. R. Carvalho[2], S. R. Marques-Neto[3], P. Menezes[4], P. P. Soares[5], J. H. M. Nascimento[3]

[1]School of Physical Education and Sports, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, [2]Laboratory of Respiration Physiology, Carlos Chagas Filho Biophysics Institute, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, [3]Cardiac Electrophysiology Laboratory, Carlos Chagas Filho Biophysics Institute, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, [4]Post-graduate Physical Education Program, EEFD, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, [5]Physiology and Pharmacology Department, Fluminense Federal University, Niteroi, Brazil
Corresponding author: Alex Souto Maior, Federal University of Rio de Janeiro, School of Physical Education and Sports, Av. Marechal Djalma Ribeiro, 25, apt. 103, Recreio dos Bandeirantes, Rio de Janeiro, RJ 22790-790, Brazil. Tel: +55 21 249 86017, Fax: +55 21 249 86017, E-mail: alex.bioengenharia@gmail.com

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This study aimed to evaluate if androgenic-anabolic steroids (AAS) abuse may induce cardiac autonomic dysfunction in recreational trained subjects. Twenty-two men were volunteered for the study. The AAS group ($n = 11$) utilized AAS at mean dosage of 410 ± 78.6 mg/week. All of them were submitted to submaximal exercise testing using an Astrand–Rhyming protocol. Electrocardiogram (ECG) and respired gas analysis were monitored at rest, during, and post-effort. Mean values of VO_2, VCO_2, and V_E were higher in AAS group only at rest. The heart rate variability variables were calculated from ECG using MATLAB-based algorithms. At rest, AAS group showed lower values of the standard deviation of R-R intervals, the proportion of adjacent R-R intervals differing by more than 50 ms (pNN50), the root mean square of successive differences (RMSSD), and the total, the low-frequency (LF) and the high-frequency (HF) spectral power, as compared to Control group. After submaximal exercise testing, pNN50, RMSSD, and HF were lower, and the LF/HF ratio was higher in AAS group when compared to control group. Thus, the use of supraphysiological doses of AAS seems to induce dysfunction in tonic cardiac autonomic regulation in recreational trained subjects.

Testosterone is an androgenic-anabolic hormone synthesized in the Leydig cells in men and theca cells in women. Testosterone and other androgenic-anabolic steroids (AAS) stimulate the commitment of pluripotent mesenchymal stem cell toward myogenic lineage rather than adipogenic lineage, hence increase the size of both type I and type II muscle fibers (Bhasin et al., 2003; Singh et al., 2003). On the other hand, synthetic AAS are testosterone analogs developed to maximize anabolic and minimize androgenic activity (Schanzer, 1996). The illicit AAS use is widespread among athletes aiming to optimize strength and to gain muscle mass (Sullivan et al., 1998; Urhausen et al., 2003) and also among recreational athletes with aesthetic purpose (Hartgens & Kuipers, 2004).

Chronic use of supraphysiological doses of AAS promotes adverse effects that include suppression of the hypothalamic-pituitary-gonadal axis. Besides, AAS can promote mood and behavior disorders, hepatic dysfunction with oral androgens, insulin resistance, glucose intolerance, acne, and gynecomastia (Barrett-Connor et al., 1999; Livingstone & Collison, 2002; Hartgens & Kuipers, 2004). Several reports have associated the use of AAS with cardiac risk, probably due to development of dislipidemia, hypertension, cardiac hypertrophy, myocardial fibrosis, myocardial ischemia and infarct, heart failure, cardiac autonomic dysfunction, cardiac arrhythmias, and sudden death (Hartgens et al., 2004; Di Paolo et al., 2007; Fineschi et al., 2007).

In a previous study using rat model of AAS abuse, we showed that chronic administration of supraphysiological doses of AAS impairs the tonic cardiac autonomic regulation in this model (Pereira-Junior et al., 2006). Other study suggested alteration in the reflex control of heart rate that was seen at different stanozolol doses (Beutel et al., 2005). Impairment of the autonomic cardiac regulation has been associated to increased incidence of cardiac arrhythmias and the analysis of heart rate variability (HRV) has been used as a tool for non-invasive assessment of cardiac autonomic balance in physiological and pathological conditions (Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology, 1996; Eckberg, 1997; Perini & Veicsteinas, 2003; Montano et al., 2009).

Despite of the cardiovascular adverse effects of high doses of AAS, few studies have used HRV analysis to assess cardiac autonomic dysfunction risk associated to

AAS abuse. In the present study, we evaluated the hypothesis that AAS abuse may induce cardiac autonomic dysfunction in recreational trained subjects.

Methods

Subjects

Twenty-two male subjects regularly engaged in strength training (mean 6 days per week) and low aerobic training (mean 2 days per week) at gyms in Niteroi city (Rio de Janeiro state, Brazil) completed this study. All subjects answered an 18-question survey to determine their profile characteristics, and signed a written informed consent. Anonymity was expressly guaranteed. All subjects were considered healthy on the basis of history, physical examination, and normal resting electrocardiogram (ECG). All subjects were nonsmokers, non-alcohol users, non-illicit drug users (cocaine, marijuana, and heroine), nonusers of psychotropic drugs, and asymptomatic for cardiovascular, respiratory, and metabolic disease. Exclusion criteria were refusal to participate in the research, atrial fibrillation, significant valvular heart disease, coronary artery disease, systemic hypertension (blood pressure higher than 140×90 mmHg or the use of antihypertensive medication), and metabolic disease.

Eleven subjects (mean age, 27.3 ± 4.5 years; mean height, 174 ± 5.5 cm; mean weight, 85.1 ± 6.8 kg; mean body mass index, 28 ± 2.5 kg/m^2) were included in the AAS group. Subjects in the AAS group were individuals currently using anabolic steroids for up to 5 years. The self-administration regimen was cyclical, having mean cycle duration of 6.7 ± 1.1 weeks, mean AAS dosage of 410 ± 78.6 mg/week, and an average of two cycles per year and interval between cycles of 6 months. The AAS users reported using two or more drugs in each cycle. The most common orally self-administered drugs were oxymetholone and stanozolol, and the injectable steroids were nandrolone, stanozolol, and propionate of testosterone. The control group consisted of 11 individuals (mean age, 24.7 ± 3.6 years; mean height, 178.5 ± 6.5 cm; mean weight, 81.7 ± 7.6 kg; mean body mass index, 25.6 ± 1.7 kg/m^2) who had never used AAS or analogous compounds. Serum testosterone, estradiol, follicle-stimulating hormone and luteinizing hormone were measured to confirm AAS usage, according to Maior et al. (2010).

The experimental protocol was in accordance to the declaration of Helsinki and was approved by the local board (CMM/HUAP n° 023/08). No clinical problems occurred during the study.

Submaximal exercise testing

All testing was performed between 1:00 and 15:00 hours. Subjects received a light lunch 2 h before the test. Coffee, tea, and alcohol intake was prohibited for 12 h beforehand and subjects avoided formal and strenuous exercise for 48 h before testing. Tests were performed on a cycloergometer (Monark 828 E, Stockholm, Sweden) to a given submaximal workload using the Astrand–Rhyming protocol (Astrand & Ryhming, 1954). The heart rate (HR) was continuously monitored in supine position for 10 min at rest, and after exercise using a 12-lead ECG monitor system (CONTEC, model 8000D, New York, USA). ECG records were also taken during exercises.

The test was preceded by a 3-min warm-up with a workload of 50 W at a pedal speed of 50 rpm. After warm-up, the workload was maintained between 100 and 130 W until the HR reached a steady state, usually in 6 or 7 min (130–140 beats/min, with less than 5 beats/min of difference between the rates in the 5th and 6th minute or in the 6th and 7th minute). Subjects were allowed sufficient practice during preliminary testing to become familiar with the cycloergometer. Ambient air temperature was 22 to 24 °C. The Borg exertion score (scale from 6 to 20) was used to assess the rating of perceived exertion during continuous exercise.

Respired gas analysis

The measurement of gas exchange is an important tool for assessing the cardiac risk and aerobic functional capacity in submaximal exercise testing. Measurements of oxygen consumption (VO_2), carbon dioxide production (VCO_2), and minute ventilation (V_E) were done at each three complete respiratory cycles using a portable metabolic testing system (Medical Graphics VO-2000, Saint Louis, MO, USA). The VO_2 mask and equipment were fastened to the subject after being positioned for the submaximal exercise. A face mask (Hans Rudolph V Mask™, Shawnee, OH, USA) covered the mouth and nose and was attached to a bidirectional digital flowmeter and fastened to the subject with a mesh hairnet and Velcro straps. The respired gas analysis began by assessing the subject at rest for 5 min. To establish a resting state, the following variables were considered: resting VO_2 at 3.5 mL/kg/min, minute ventilation (V_E) between 8 and 15 L/min, and the respiratory quotient (RQ) between 0.75 and 0.85 (Gibbons et al., 2002). The ventilatory equivalent for carbon dioxide (V_E/VCO_2) and oxygen (V_E/VO_2) were determined at rest, during exercise, and after exercise testing. Before each test, the gas analyzer system was calibrated, according to the manufacturer guidelines.

ECG recording and HRV analysis

ECG was continuously recorded at a sampling rate of 1 kHz with 12-bit resolution using a 12-lead ECG monitor system (CONTEC, model 8000D). All data were stored and analyzed off-line. Heart rate and the R-R time series were extracted from 10-min ECG tracings (V5 lead), recorded at rest and after submaximal exercise testing, using an R-R detection algorithm (MATLAB 7.0, The MathWorks, Inc, Natick, MA, USA). ECG recording occurred under spontaneous voluntary ventilation, at rest (average breathing rate of 10 breaths/min in the control group and of 18 breaths/min in the AAS group) and after submaximal exercise testing (average breathing rate of 21 breaths/min in the control group and 32 breaths/min in the AAS group). The ECG tracing was manually inspected and edited for any ectopic beats. Both the ectopic and the post-extra-systolic beats were deleted and replaced by interpolated adjacent R-R interval values (Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology, 1996).

The following time domain of HRV variables were analyzed: R-R, the mean of all normal R-R intervals during the 10-min recording; SDNN, the standard deviation of normal R-R intervals; NN50, the number of interval differences of successive NN intervals greater than 50 ms; pNN50, the percentage of normal R-R intervals that differ by more than 50 ms; and RMSSD, the square root of the mean of the mean squared differences of successive R-R intervals (Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology, 1996).

For frequency-domain analysis, R-R intervals time series were resampled to equal intervals by spline cubic interpolation method at 2 Hz, and data were detrended by removing the mean value and the linear trend. Fast Fourier transformation was used for calculating the power spectrum (Welch's periodogram was employed to assess the 1024-point spectra with a Hanning window and 50% overlap). Spectral power was obtained by integrating the power spectrum density function in the very low-frequency (VLF: 0.0033 and 0.04 Hz.), the low-frequency (LF: 0.04–0.15 Hz), and the high-frequency (HF: 0.15–0.40 Hz) bands. The spectral power was also computed in normalized units for the HF [HFnu = HF/(total power – VLF) × 100] and LF [LFnu = LF/(total power –

Table 1. Exercise test variables of AAS users and control subjects

Variable	Control ($n = 11$)	AAS ($n = 11$)	P-value
$VO_{2\ rest}$ (mL/kg/min)	3.6 ± 0.7	4.4 ± 0.3	0.04
$VO_{2\ peak}$ (mL/kg/min)	23.9 ± 1.4	26.8 ± 2.4	0.3126
$VCO_{2\ rest}$ (mL/kg/min)	2.6 ± 0.2	4.0 ± 0.3	0.006
$VCO_{2\ peak}$ (mL/kg/min)	23.7 ± 1.3	28.7 ± 2.7	0.1372
$V_{E\ rest}$ (L/min)	5.9 ± 0.5	10.1 ± 1.5	0.01
$V_{E\ peak}$ (L/min)	43.9 ± 3.0	53.7 ± 4.6	0.09
$V_E/VO_{2\ rest}$	30.3 ± 1.8	31.6 ± 1.7	0.5394
$V_E/VO_{2\ peak}$	22.9 ± 1.8	23.7 ± 0.4	0.6848
$V_E/VCO_{2\ rest}$	33.2 ± 1.1	32.6 ± 0.7	0.7503
$V_E/VCO_{2\ peak}$	22.7 ± 0.8	22.4 ± 0.7	0.7815

Values are expressed as mean ± SEM.
VO_2, oxygen consumption; VCO_2, carbon dioxide production; V_E, minute ventilation; V_E/VO_2, ventilatory equivalent for oxygen; V_E/VCO_2, ventilatory equivalent for carbon dioxide.

VLF) × 100], and the autonomic balance evaluated by the LF/HF (Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology, 1996).

Statistical analysis

Data are expressed as mean ± SEM. To compare resting and postexercise HRV data in control and AAS groups, a repeated measures two-way analysis of variance, with Bonferroni post-hoc test was used. Comparisons between groups for gas analysis variables were performed with unpaired Student t-test. The correlation between time and frequency-domain parameters of HRV was assessed by Pearson's correlation coefficient. A P-value < 0.05 was considered significant. All statistical analyses were performed using GraphPad Prism 5.0 (GraphPad Software Inc., San Diego, CA, USA).

Results

Respiratory data from the exercise test are presented in Table 1. At rest, mean values of VO_2, VCO_2, and V_E were higher in AAS group, but no significant difference between groups was noted for V_E, VO_2, and VCO_2 at the end of submaximal exercise. There was no significant difference between groups for SpO^2, V_E/VO_2, and V_E/VCO_2 before and at the peak of moderate exercise.

The heart rate showed significant difference between groups at rest (control: 60 ± 2.8 bpm; AAS: 68.5 ± 1.7 bpm; $P < 0.05$), but not during effort (control: 148 ± 1.1 bpm; AAS: 148.1 ± 2.4 bpm; $P = 0.9704$). The estimated percentage of maximum heart rate did not present significant difference between groups (control: 66.7 ± 1.0 %; AAS: 67.5 ± 1.8 %; $P = 0.7319$).

Figure 1 shows the time course of R-R interval and RMSSD during the first 5 min of postexercise recovery period. The mean value of RMSSD, measured at rest (Control: 79.7 ± 6.96 ms; AAS: 38.7 ± 5.99 ms; $P < 0.01$) and at 10 min of recovery after the exercise (Control: 45.2 ± 5.81 ms; AAS: 15.1 ± 1.37 ms; $P < 0.01$) was significantly lower in the AAS group than in the Control group. The R-R interval of AAS group was

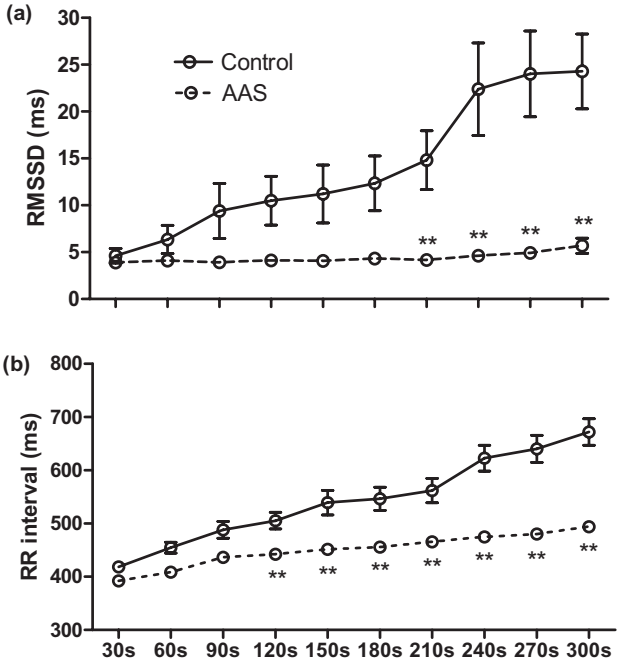

Fig. 1. Postexercise recovery of RMSSD and R-R interval. Data from the first 5 min after submaximal exercise testing. Values are expressed as mean ± SEM. $^{**}P < 0.01$ vs control group.

significantly shorter when compared to Control group, at rest and during the first 5-min of postexercise period. Figure 2 shows resting and postexercise mean values of SDNN, pNN50, and NN50 for both groups. At rest, AAS group exhibited lower SDNN, pNN50, and NN50 ($\Delta\% = 41\%$, 62%, and 58%, respectively) than control group. After exercise testing, pNN50 ($\Delta\% = 87\%$) and NN50 ($\Delta\% = 82\%$) remained lower in AAS group, but SDNN was similar to that in the control group. Figure 3 shows representative tachograms from a control and an AAS-user subject, at rest and after submaximal exercise test.

Figure 4 shows LF, HF, total power, and LF/HF ratio for the two groups, at rest and after submaximal exercise testing. AAS users had lower resting LF power ($\Delta\% = 59\%$; $P < 0.01$) and total power ($\Delta\% = 62\%$; $P < 0.001$) than the control group. In contrast, no significant difference between groups was noted for LF and total power measured after exercise (Fig. 4a,c). The HF power at rest ($\Delta\% = 69\%$; $P < 0.001$) and after submaximal exercise test ($\Delta\% = 91\%$; $P < 0.05$) exhibited lower mean values in the AAS group when compared to control group (Fig. 4b). Figure 4d shows that LF/HF ratio was higher in AAS group only after submaximal exercise test ($\Delta\% = 60\%$; $P < 0.001$). The intra-group analysis showed that postexercise values of total power, LF power, and HF power were significantly reduced in both groups when compared to baseline values. But postexercise LF/HF ratio was significantly higher than at rest for both groups.

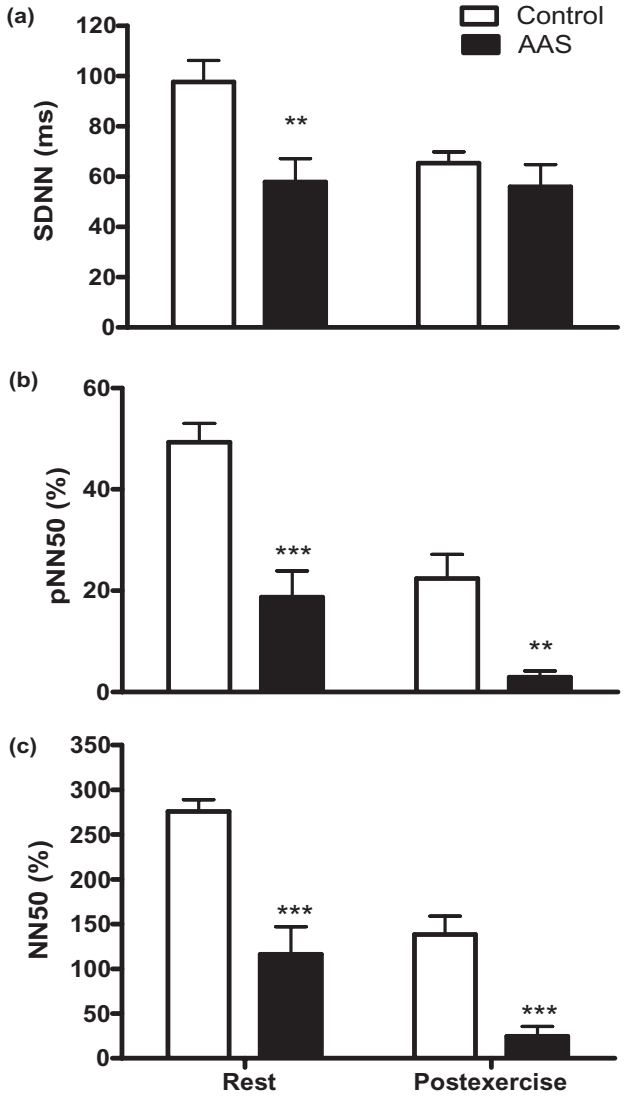

Fig. 2. Time-domain heart rate variability indexes at rest and after cessation of exercise. Values are expressed as mean ± SEM. $^{**}P < 0.01$ and $^{***}P < 0.001$ vs Control group.

AAS group showed an HF_{nu} significantly lower after effort than the control group (control: 18 ± 3.8 nu; AAS: 3.1 ± 0.7 nu; $P < 0.01$). In contrast, the LF_{nu} did not differ significantly between groups at rest (control: 31.7 ± 3.3 nu; AAS: 40.2 ± 3.8 nu; $P = 0.1102$) and after submaximal exercise testing (control: 24.6 ± 3.1 nu; AAS: 18.5 ± 5.4 nu; $P = 0.3411$). Representative examples of the spectral analysis of R-R interval variability during rest and after submaximal exercise testing are shown in Fig. 5.

Discussion

The major finding of the present study was that chronic administration of high doses of AAS may be associated to cardiac autonomic dysfunction by sympathetic dominance and reduced vagal modulation of heart rate. High doses of anabolic steroid can lead to cardiovascular abnormalities, thus contributing to the development of ventricular arrhythmias and sudden death (Di Paolo et al., 2007; Fineschi et al., 2007).

We did not observe significant difference between groups for respired gas analysis after submaximal exercise. In contrast, significant changes were observed at rest for V_E, VO_2, and VCO_2 in AAS group when compared to the control group. Besides the well-known action of androgens in increasing the basal metabolic rate (Lewis & McCullagh, 1942), it is possible that the conversion of androgens to estradiol (via aromatase) in regions of central nervous system, as hypoglossal nucleus, ventrolateral nucleus of tractus solitarius, and spinal respiratory motoneurons, contributes to increase the central chemoreflex sensibility, thereby augmenting ventilation response (Behan & Wenninger, 2008).

In the present work, the time-domain HRV variables RMSSD, pNN50, and NN50 were lower in AAS group compared to the control group, at rest and after submaximal exercise testing. The lower values of pNN50 and NN50 in the AAS group suggest parasympathetic cardiac dysfunction. However, the RMSSD index has better statistical properties for assessing parasympathetic activity than NN50 and pNN50 (Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology, 1996). The RMSSD has been used as a better index of cardiac parasympathetic control since it is uncontaminated by sympathetically mediated HRV (Berntson et al., 2005). Accordingly, the RMSSD measured during the first 5 min of recovery after exercise has been used as an index of parasympathetic reactivation (Goldberger et al., 2006). In our study, the RMSSD of non-AAS users, measured during the post-effort recovery period, increased progressively during the first 5-min after the exercise testing, whereas the RMSSD of AAS users did not change significantly, suggesting an impairment in the postexercise parasympathetic reactivation. Additionally, R-R interval of subjects using AAS rose discretely in the post-effort period compared to control subjects, showing a minor post-effort recovery of rate heart in AAS users. Since the decrease of heart rate recovery following exercise is a marker of slower reactivation of cardiac parasympathetic regulation (Billman, 2009), these results suggest a decrease in cardiac parasympathetic activity, more evident in the period immediately after submaximal exercise. Indeed, abnormal heart rate recovery after exercise testing is considered a powerful and independent predictor of death risk (Cole et al., 1999).

The mean SDNN value in AAS group was lower only at rest. This result is in accordance with previous findings of our laboratory that showed parasympathetic cardiac dysfunction in rats treated with supraphysiological doses of nandrolone decanoate during 10 weeks, as expressed by reduction in pNN5 and RMSSD, but without significant change in the SDNN value (Pereira-

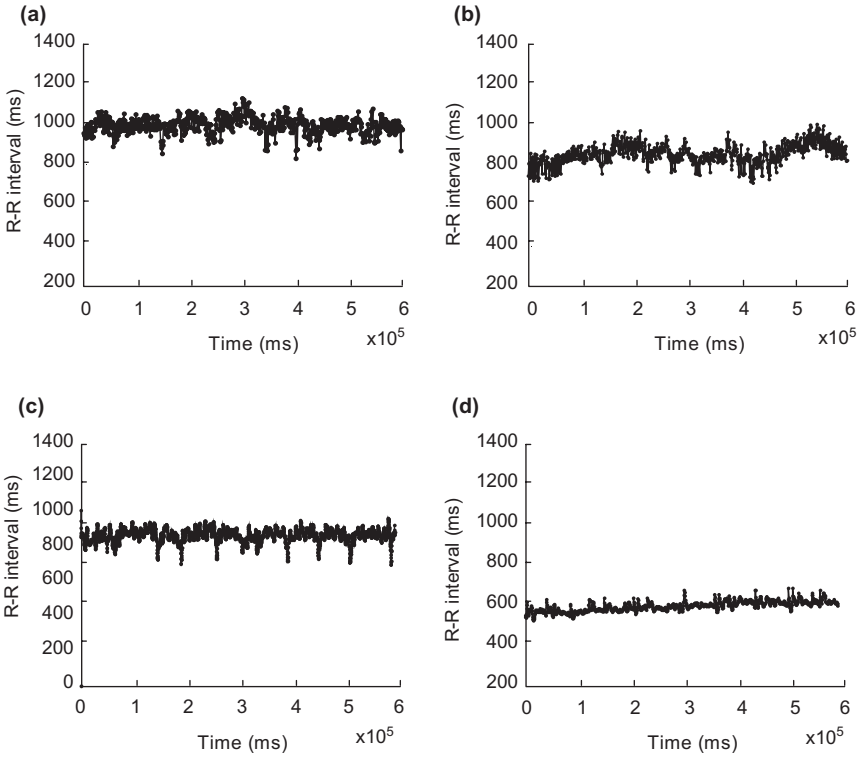

Fig. 3. Representative tachograms of R-R interval from two subjects. R-R intervals extracted from V5-lead recording at rest [(a) non-AAS user; (c) AAS user] and after submaximal exercise testing [(b) non-AAS user; (d) AAS user].

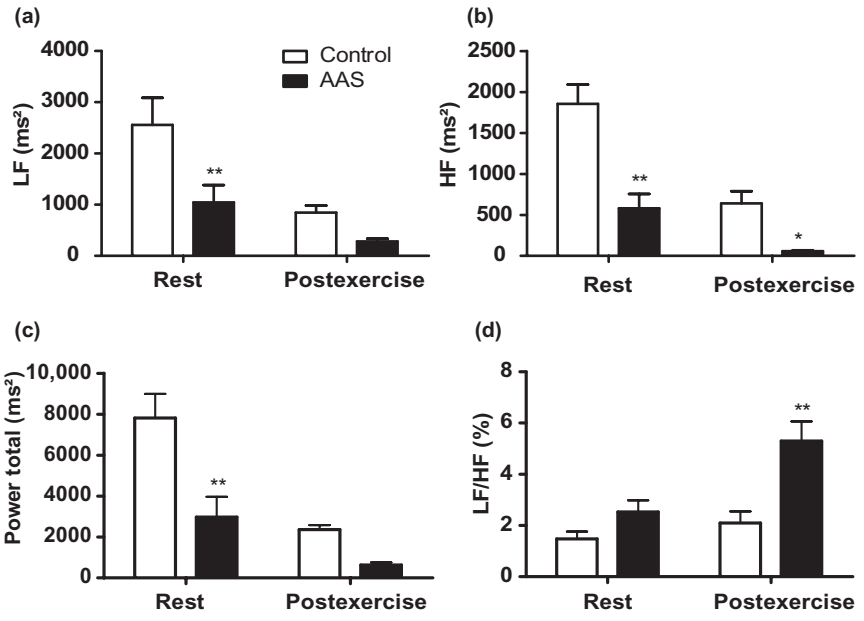

Fig. 4. Frequency-domain heart rate variability indexes at rest and after cessation of exercise. Values are expressed as mean ± SEM. $*P < 0.05$ and $**P < 0.001$ vs Control group.

Junior et al., 2006). Some studies suggest that SDNN lower than 70 ms is a marker of increased risk of cardiac disease, when combined with a low baroreflex sensibility and low ejection fraction (La Rovere et al., 1998). Other studies have associated the decrease of SDNN value with left ventricular dysfunction and development of high blood pressure (Casolo et al., 1992; Schroeder et al., 2003). Thus, supraphysiological doses of AAS seem to

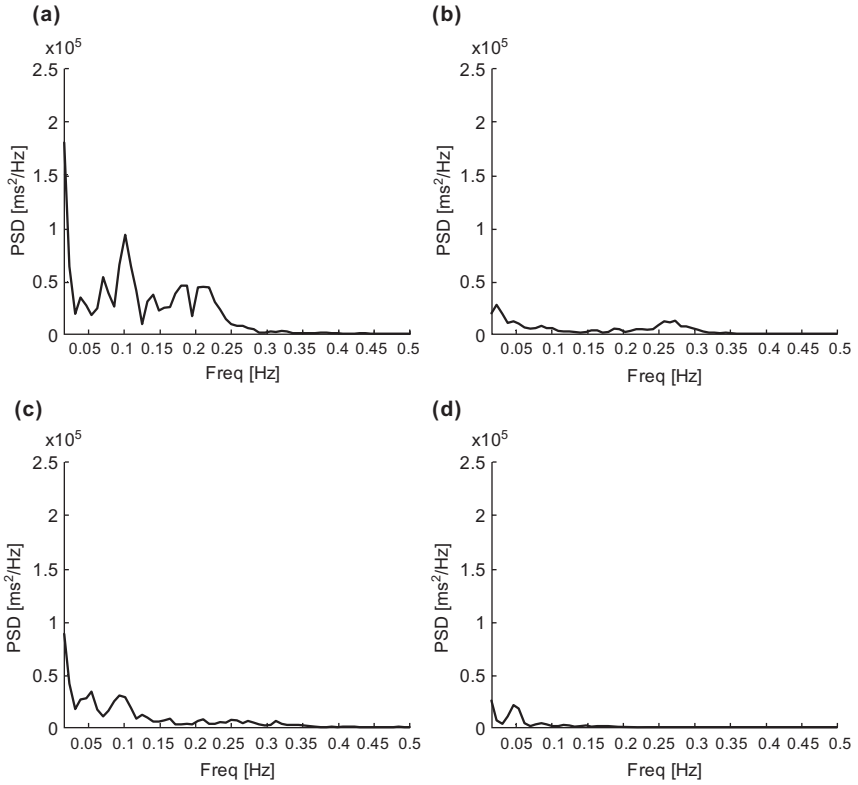

Fig. 5. Representative power spectrum distribution of heart rate variability from two subjects. R-R intervals extracted from V5-lead recording during rest [(a) non-AASuser; (c) AAS-user] and after submaximal exercise testing [(b): non-AAS user; (d) AAS user]. PSD, power spectral density.

induce an autonomic dysfunction that reflects in a reduction of the variability of R-R intervals and in a lower SDNN.

In our study, the AAS group showed a lower HF power at rest and after submaximal exercise, when compared to the control group. The HF power is strongly influenced by the efferent vagal activity (Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology, 1996), and the decrease of HF power after submaximal exercise has been associated to delayed parasympathetic reactivation (Goldberger et al., 2006; Borresen & Lambert, 2008). The analysis of spectral components could be improved by normalization of their values by the total power (Perini & Veicsteinas, 2003), since the total power index in the frequency-domain HRV analysis reflects the overall variability of the signal and its value may change in different conditions. Thus, the observation of lower normalized HF (HF_{nu}) in AAS group, after submaximal exercise, confirms a possible delayed parasympathetic reactivation in AAS users, since the HF_{nu} index reflects exclusively oscillations in the vagal component (Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology, 1996; Montano et al., 2009; Piccirillo et al., 2009).

The LF power at rest was lower in AAS users compared to non-AAS users. However, after submaximal exercise, this index did not differ significantly between the groups, even when the normalized values of LF are compared. The LF power component is an index that reflects fluctuations mediated by both cardiac vagal and sympathetic nerves (Perini & Veicsteinas, 2003). Some studies suggest that the sympathetic activity contributes to LF value approximately 15% more than the vagal activity (Eckberg, 1997; Montano et al., 2009; Piccirillo et al., 2009). In this context, the lower LF power of AAS group could be influenced by the lower level of parasympathetic activity, as shown by the lower HF_{nu} in AAS users.

In relation to LF/HF ratio, we observed significant increase of this index after submaximal exercise in AAS group. A higher LF/HF ratio suggests increased sympathetic or decreased parasympathetic drive to the heart (Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology, 1996; Eckberg, 1997; Perini & Veicsteinas, 2003). Thus, the higher LF/HF ratio and the significant reduction of HF power after submaximal exercise seem to reflect a sympathovagal imbalance, with sympathetic dominance and reduced vagal modulation. Both are associated to higher susceptibility to malignant ventricular arrhythmias and sudden death (Schuchert et al., 2005; Brown & Brown, 2007).

The mechanism underlying the cardiac autonomic dysfunction in AAS-abusing subjects remains unknown.

Previous studies have reported that androgens can cross the blood–brain barrier (Kindlundh et al., 2004; Kicman, 2008) and bind to androgen receptors in different brain regions (Sheridan & Weaker, 1982; Simerly et al., 1990; Penatti et al., 2009). Androgens may also be aromatized to estrogens and bind to estrogen receptors (Penatti et al., 2009). AAS affect GABAergic transmission in the hypothalamus and other brain areas by modulation of $GABA_A$ receptor function (Henderson et al., 2006). Thus, one might speculate that AAS alter the parasympathetic modulation mediated by central GABA and other mechanisms, by binding to androgen receptors in the hypothalamus and brain stem regions that control the tonic and reflex response of cardiovascular system. Indeed, it is well known that chronic use of high doses of AAS induces psychiatric effects, including aggressive behavior, and psychosis (Basaria, 2010), and suppress the hypothalamic-pituitary-gonadal axis (MacIndoe et al., 1997; Clark & Henderson, 2003). Additionally, we can suggest that AAS-induced cardiac electrical remodeling contributes to the observed changes in cardiac autonomic responses (Nascimento & Medei, 2011).

In conclusion, the results of the current study suggest that use of supraphysiological doses of AAS can induce dysfunction in tonic cardiac autonomic regulation at rest and after moderated exercise. Thus, the AAS group showed delayed parasympathetic reactivation after cessation of submaximal exercise. Therefore, this study provides a contraindication to AAS use, especially in those at increased risk of cardiovascular event. It is believed that future research using HRV and respiratory frequency analysis will be accomplished to investigate the mechanisms of supraphysiological doses of AAS in the induction of cardiac autonomic dysfunction.

Perspectives

The results of this study agree with previous findings in the animal model of AAS abuse (Beutel et al., 2005; Pereira-Junior et al., 2006). The implications of these findings are that the chronic use of AAS has adverse effects on the cardiac autonomic regulation of recreational athletes. Therefore, AAS abuse may reduce exercise capacity and predispose these subjects to higher risk of cardiac outcome. Our study is limited by the small sample size and gender, so further research should be extended to a larger AAS user population and both genders. In this study, subjects were allowed for spontaneous voluntary ventilation during ECG recording. For better precision of HRV analysis, future work should evaluate the subjects under controlled respiratory frequency, because modulation of heart rate is synchronous with respiration and can change HRV power spectra both in low-(0.03 Hz) and high-(0.50 Hz)) frequency regions (Poyhonen et al., 2004).

Key words: heart rate variability, androgenic-anabolic steroids, submaximal exercise testing.

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