Parasympathetic cardiac activity is associated with cardiorespiratory fitness in overweight and obese adolescents

By: Danilo Fernandes da Silva, Josiane Aparecida Alves Bianchini, Vanessa Drieli Seron Antonini, Danielle Aparecida Munhos Hermoso, Carlos Andres Lopera, Bruno Guilherme Morais Pagan, Jessica McNeil, and Nelson Nardo Junior

Da Silva DF, Bianchini JAA, Antonini VDS, Hermoso DAM, Lopera CA, Pagan BGM, McNeil J, Nardo Junior N. Parasympathetic cardiac activity is associated with cardiorespiratory fitness in overweight and obese adolescents. Pediatric Cardiology, 2014, 35(4): 684-690. https://doi.org/10.1007/s00246-013-0838-6

Abstract:

The aim of this study was to investigate the association between cardiac parasympathetic activity and cardiorespiratory fitness, insulin, and hemodynamic profile in overweight and obese adolescent girls and boys (aged 12–16 years). Data were taken from the Multidisciplinary Obesity Treatment Program. Only post-intervention measurements are presented herein. Body composition, cardiorespiratory fitness, blood pressure, and metabolic profile (insulin and glucose profile) of adolescents were assessed. Cardiac parasympathetic activity was determined by resting heart rate variability, which was analyzed using a heart rate monitor. Greater parasympathetic cardiac activity was associated with higher levels of cardiorespiratory fitness in both girls and boys ($0.375 \leq r \leq 0.900$), while the sympathetic-vagal balance was negatively related to maximal oxygen uptake (VO_{2max}) in girls ($r = 0.478$). An association between lower parasympathetic activity and insulin resistance was noted in girls (mean of *R*–*R* intervals [RRmean] and homeostasis model assessment insulin-resistance index [HOMA-IR]: $r = -0.678$), while greater systolic blood pressure (SBP) and lower parasympathetic activity were associated in both sexes (RRmean and SBP: $r = -0.526$; high frequency [HF (nu)] and SBP: $r = -0.754$). In conclusion, autonomic nervous system activity was associated with cardiorespiratory fitness, insulin resistance, and SBP in overweight and obese adolescents. The identification of these potential relationships assists with the establishment of future long-term exercise interventions that evaluate the improvements in parasympathetic nervous system activity, in addition to metabolic profile and cardiorespiratory fitness in overweight and obese adolescents.

Keywords: heart rate variability | adolescents | obesity | metabolic profile | body composition | cardiorespiratory fitness

Article:

Introduction

The accumulation of excess fat is associated with several comorbidities, including changes in certain neurocardiac functions such as reduced autonomic nervous system parasympathetic activity [13, 27, 30].

The measurement of resting heart rate variability (rHRV) allows for the non-invasive assessment of cardiac parasympathetic function. Wolf et al. [29] demonstrated that low rHRV was associated with increased risk of death following myocardial infarction. Furthermore, Tascilar et al. [27] noted a significant association between insulin resistance and reduced heart rate variability in obese children and adolescents. Similarly, Zhou et al. [30] demonstrated a negative relationship between systolic blood pressure (SBP) and parasympathetic indices of rHRV.

A different variable that seems to be associated with rHRV is cardiorespiratory fitness. Buchheit and Gindre [3] found that greater parasympathetic activation was associated with higher maximum oxygen uptake (VO_{2max}) values in physically active, normal-weight adults. Hautala et al. [12] also noted a relationship between greater parasympathetic activation and improvements in VO_{2max} in sedentary subjects and athletes undergoing physical training. Lastly, Prado et al. [22] observed positive changes in VO_{2max} and sympathetic-vagal balance following a short-term aerobic exercise intervention (4 months) in obese children (age 10.0 ± 0.2 years). However, the relationship between parasympathetic/sympathetic activity and cardiorespiratory fitness has yet to be demonstrated in overweight and obese adolescents.

Lucini et al. [18] suggested that obesity may influence parasympathetic nervous system activity, even in a population performing supervised exercise. However, to our knowledge, the potential relationship between parasympathetic nervous system activity and cardiorespiratory fitness, insulin, and hemodynamic profile in overweight and obese adolescents remains to be elucidated. Moreover, taking into consideration the significant differences in rHRV previously observed between sexes [20, 24], potential differences in the relationship between these variables between sexes are also relevant. The identification of potential relationships can thus lead to the establishment of future long-term exercise interventions that evaluate the improvements in parasympathetic nervous system activity, in addition to metabolic profile and cardiorespiratory fitness.

The aim of this study was to investigate cardiac parasympathetic activity and its association with cardiorespiratory fitness, insulin, and hemodynamic profile in overweight and obese adolescent boys and girls. It was hypothesized that parasympathetic activity would be associated with cardiorespiratory fitness in overweight and obese adolescents. Furthermore, we also hypothesized that parasympathetic activity would be associated with insulin and hemodynamic profile in this sample.

Materials and Methods

Participants

Overweight and obese adolescents ($N = 28$) aged 12–16 years who participated in a Multidisciplinary Obesity Treatment Program (MOTP) for 1.5 years took part in this study. The details of this intervention are presented elsewhere [2]. The cross-sectional data presented herein were assessed following the completion of this multidisciplinary program.

The participants had to adhere to the following inclusion criteria: compliance of the adolescents and his/her parents/guardians in participating in the study, and aged between 10 and 18 years. The exclusion criteria were as follows: endocrine and metabolic diseases that were previously diagnosed; long-term alcohol consumption; use of glucocorticoids and psychotropics that could affect appetite regulation. Metabolic profile was only assessed in adolescents who were obese at the beginning of the intervention. The sample size for this parameter was 19 adolescents (12 girls).

The study was approved by the local Ethics Committee (protocol 463/2009) and is in accordance with the Declaration of Helsinki guidelines.

Measurements

Body Composition and Pubertal Development

Within the week following the end of the MOTP, adolescents took part in a battery of assessments, which included the measurement of body weight, height, body mass index (BMI), and waist circumference. Body weight was measured on a Welmy scale (Welmy, São Paulo, Brazil) to the nearest 0.05 kg, with the participant wearing light clothes and without shoes. Height was measured with a wall stadiometer to the nearest 0.1 cm. BMI was calculated as the weight divided by the height squared. Waist circumference was measured with a WISO tape (WISO, Santa Catarina, Brazil) to the nearest 0.1 cm.

Body composition was assessed by dual energy X-ray absorptiometry (GE Healthcare Lunar enCORE, Denver, CO, USA). Participants were tested during the afternoon. We computed relative body fat mass, central fat mass, and lean mass.

Pubertal development was assessed according to Tanner stages [26]. Adolescents who identified themselves as being in stage 1 were classified as prepubertal, stages 2 and 3 as pubertal, and stages 4 and 5 as postpubertal.

Blood Draws and Blood Pressure

We assessed blood glucose and insulin levels with blood draws. Blood draws were conducted by a nurse from an outpatient clinic during the morning following a 12-h overnight fast (Laboclin, Bahia, Brazil). Insulin resistance and sensitivity were assessed by Homeostasis Model Assessment Insulin-Resistance Index (HOMA-IR) and quantitative insulin sensibility check index (QUICKI), respectively. HOMA-IR was calculated according to the following equation: [blood fasting glucose (milligrams per deciliter) × blood insulin (in milliunits per liters)]/405

[19]. QUICKI was calculated with the following equation: 1/(log insulin + log blood glucose) [6].

Blood pressure measurements were taken on the right arm, while the participants were sitting. These measurements were obtained with an automatic sphygmomanometer (Microlife, Aargau, Switzerland) following 5–10 min of rest.

Cardiorespiratory Fitness

VO_{2max} was determined indirectly with the Leger 20-m multistage shuttle run test [16, 17]. This is a maximal test initiated with an 8.5 km/h speed, which progresses in increments of 0.5 km/h each minute until the adolescent reaches their volitional exhaustion.

An adjustment was used to determine maximal aerobic speed (MAS) obtained from the Leger 20-m multistage shuttle run test. This maximal speed was calculated as the speed of the last completed stage added to the completed fraction of the incomplete stage, calculated according to this equation: MAS = $V_{\text{complete}} + t/T$, where V_{complete} is the running speed of the last completed stage, t is the number of seconds sustained during the incomplete stage, and T is the number of seconds required to complete 1 stage (60 s) [14].

After 48 h, mean speed assessed during the 12-min Cooper test [8] was obtained during a continuous running test, as a means of determining endurance capacity. This test was carried out on a 400-m track.

Resting Heart Rate Variability

Following blood pressure measurements, rHRV was analyzed, in the sitting position, using a heart rate monitor (POLAR RS800cx, Kempele, Finland). This equipment has been previously validated for this measurement [9]. We chose not to control for respiratory rate because adolescents often have difficulty pacing their breathing with a predetermined cadence. We advised the participants to avoid the practice of any strenuous exercise, as well as the consumption of beverages containing caffeine for at least 24 h prior to this measurement. They were also asked to not consume any food for at least 2 h prior to this measurement.

R–R intervals were recorded for 10 min in a quiet room at a temperature of 23 °C between 4 pm and 5 pm. The last 5 min of each 10-min interval were used to assess rHRV variables. The data for *R–R* intervals were downloaded into a Polar Pro Trainer Software and expressed in milliseconds. Ectopic beats (deviation higher than 20 % of adjacent intervals) were identified and manually interpolated by adjacent *R–R* intervals.

The *R–R* intervals were analyzed using time-domain and frequency-domain techniques with the Kubios HRV analysis (University of Eastern Finland). In the time domain, we computed the square root of the mean of the squares of successive *R–R* interval differences (rMSSD) and the mean of *R–R* intervals (RRmean). In the frequency domain, we computed two frequency bands: low frequency (LF: 0.04–0.15 Hz) and high frequency (HF: 0.15–0.4 Hz), both in normalized units (nu). The very low frequency (VLF: 0–0.04 Hz) component is considered a dubious

measure [28] due to its uncertain physiological meaning. Thus, its interpretation was not considered in the present study. Parasympathetic cardiac activity is defined as the absolute values of HF component, rMSSD, and RRmean, resulting from respiratory sinus arrhythmia [11]. Normalized units of the LF (LFnu) and HF (HFnu) components were also computed. Furthermore, the LF:HF ratio was determined as a measure that may express sympatho-vagal balance [25, 28].

Statistical Analysis

Normality was tested using the Shapiro–Wilk test. The results of the normality test revealed that data required non-parametric tests for analysis. And so, the Mann–Whitney test was used to compare the measured variables between boys and girls. The Spearman rank test was used to determine potential correlations between insulin and hemodynamic profile, and cardiorespiratory fitness. Data were presented as medians and interquartile ranges (P75–P25). The significance level was pre-set at $P < 0.05$.

Results

Of the 28 adolescents who took part in this study, 18 (64.2 %) were girls. Of the 18 girls, 16 were in the post-pubertal sexual maturation (89.9 %) stage. Of the ten adolescent boys who were tested, eight (80 %) were in the post-pubertal sexual maturation stage. All other participants were classified in the pubertal stage. Of the 28 studied adolescents, 16 (55.2 %) were classified as overweight and 12 as obese, according to BMI cut-off points [7].

Table 1 demonstrates the mean body composition, blood pressure, metabolic profile, and cardiorespiratory fitness values for boys and girls.

Significant differences between sexes in SBP only were observed, where girls had significantly lower SBP values than boys ($P = 0.012$).

Table 2 demonstrates the median and interquartile range values for variables of time and frequency domain that define rHRV between girls and boys.

Statistical analysis revealed no significant differences between sexes for these variables. However, when rHRV indices were compared between overweight (16 adolescents) and obese (12 adolescents) adolescents, obese adolescents presented lower HF (nu), as well as higher LF (nu) and LF/HF, thus showing that sympathetic activity is greater in obese adolescents.

Tables 3 and 4 demonstrate the correlations between rHRV indices and cardiorespiratory fitness (Table 3), and insulin and hemodynamic profile (Table 4) measurements in all participants, and according to sex. According to Table 3, higher HOMA-IR was associated with lower parasympathetic activity demonstrated by the rMSSD index. For boys, SBP was positively associated with LF:HF ratio and negatively associated with HF (nu). In Table 4, we may observe that RRmean, which demonstrated parasympathetic activity was positively associated with v12km (mean velocity at 12-min Cooper test), MAS, and VO_{2max} for both sexes.

Table 1. Body composition, cardiorespiratory fitness, metabolic profile, and blood pressure values for boys and girls

Variable	Total (*N* = 28)		Girls (*N* = 18)		Boys (*N* = 10)		*P* between sexes
	Median	I_Q	Median	I_Q	Median	I_Q	
Age (years)	14	2	14	2	13.25	2	0.448
Anthropometric variables, body composition and bone mineral density							
Weight (kg)	78.6	23.3	79.3	17.6	77.5	32.25	0.869
Height (m)	1.63	0.09	1.63	0.06	1.65	0.23	0.792
BMI (kg/m^2)	27.9	5.8	28.0	6.5	26.8	5.1	0.533
WC (cm)	81.8	13.8	81.8	14.4	82.0	14.1	0.401
Body fat (%)	35.6	14.5	37.8	12.3	32.0	12.3	0.068
Lean mass (kg)	43.2	9.1	43.0	5.6	50.2	19.0	0.179
Central fat (kg)	2.4	1.5	2.5	1.4	2.1	1.3	0.533
Cardiorespiratory fitness							
v12min (km/h)	8.5	1.9	8.5	2.0	8.5	2.8	0.633
MAS (km/h)	10.5	1.6	10.4	2.1	10.5	1.3	0.774
VO_{2max} (mL/kg/min)	33.1	11.1	32.5	14.8	34.4	9.7	0.701
Insulin[a] and hemodynamic profile							
Glycemia (mg/dL)	83.0	11.0	83.0	9.8	83.0	13	0.471
Insulin (µUI/mL)	13.3	14.7	12.7	5.9	23.5	16.8	0.353
HOMA-IR	2.63	2.96	2.58	1.35	4.75	4.15	0.398
QUICKI	0.50	0.02	0.51	0.02	0.49	0.03	0.176
SBP (mmHg)	122.0	12.0	120.0	11.0	126.0	12.0	0.010
DBP (mmHg)	73.0	11.0	73.0	10.0	69.0	17.0	0.596

BMI body mass index, *DBP* diastolic blood pressure, *HOMA-IR* homeostasis model assessment insulin-resistance index, I_Q interquartile range, *MAS* maximal aerobic speed, *QUICKI* quantitative insulin sensibility check index, *SBP* systolic blood pressure, VO_{2max} maximal oxygen uptake, *v12min* mean velocity at 12 min Cooper Test, *WC* waist circumference

[a]For the insulin profile, total sample size was 19 children (7 boys and 12 girls)

Table 2. Comparison between boys and girls for the rHRV indices related to the time and frequency domains

Variable	Total (*N* = 28)		Girls (*N* = 18)		Boys (*N* = 10)		*P* (between sexes)
	Median	I_Q	Median	I_Q	Median	I_Q	
Time domain							
RRmean (ms)	710.9	179.6	740.6	204.3	697.2	139.2	0.533
rMSSD (ms)	49.0	25.0	56.3	32.5	42.7	17.8	0.213
Frequency domain							
HF (nu)	49.6	28.1	49.6	31.9	46.7	27.5	0.886
LF (nu)	50.5	28.1	50.5	31.9	53.4	27.5	0.886
LF/HF	1.0	1.3	1.0	1.6	1.2	1.3	0.886

HF high frequency, I_Q interquartile range, *LF* low frequency, *rHRV* resting heart rate variability, *RRmean* mean of *R–R* intervals, *NU* normalized units, *rMSSD* square root of the mean of the squares of successive *R–R* interval differences

Table 3. Correlations between rHRV indices and insulin and hemodynamic profiles in all participants according to sex

	RRmean (ms)	rMSSD (ms)	HF (nu)	LF (nu)	LF/HF
All participants (*N* = 19)					
Insulin (μUI/mL)	−0.298	−0.514*	−0.147	0.147	0.147
HOMA-IR	−0.237	−0.502*	−0.109	0.109	0.109
QUICKI	−0.196	0.480*	0.173	−0.173	−0.173
SBP (mmHg)	−0.321	−0.368	−0.353	0.353	0.353
DBP (mmHg)	−0.195	−0.091	−0.161	0.161	0.161
Girls (*N* = 12)					
Insulin (μUI/mL)	−0.755*	−0.713*	−0.490	−0.490	−0.490
HOMA-IR	−0.678*	−0.678*	−0.427	0.427	0.427
QUICKI	0.466	0.522	0.301	−0.301	−0.301
SBP (mmHg)	−0.526*	−0.394	−0.306	0.306	0.306
DBP (mmHg)	−0.158	−0.181	−0.027	0.027	0.027
Boys (*N* = 7)					
Insulin (μUI/mL)	0.250	−0.107	0.071	−0.071	−0.071
HOMA-IR	0.321	−0.071	−0.250	−0.250	−0.250
QUICKI	−0.393	0.143	−0.214	0.214	0.214
SBP (mmHg)	0.055	0.394	−0.754*	0.754*	0.770*
DBP (mmHg)	−0.543	0.189	−0.330	0.330	0.317

DBP diastolic blood pressure, *HF* high frequency, *HOMA-IR* homeostasis model assessment insulin-resistance index, *LF* low frequency, *rHRV* resting heart rate variability, *RRmean* mean of *R–R* intervals, *NU* normalized units, *QUICKI* quantitative insulin sensibility check index, *rMSSD* square root of the mean of the squares of successive *R–R* intervals differences, *SBP* systolic blood pressure

Table 4. Correlations between rHRV indices and cardiorespiratory fitness in all participants according to sex

	RRmean (ms)	rMSSD (ms)	HF (nu)	LF (nu)	LF/HF
All participants (*N* = 28)					
v12min (km/h)	0.663*	0.318	0.309	−0.309	−0.299
MAS (km/h)	0.635*	0.392*	0.396*	−0.396	−0.391*
VO_{2max} (mL/kg/min)	0.652*	0.416*	0.375*	−0.375*	−0.370
Girls (*N* = 18)					
v12min (km/h)	0.561*	0.163	0.368	−0.368	−0.368
MAS (km/h)	0.647*	0.347	0.459	−0.459	−0.459
VO_{2max} (mL/kg/min)	0.656*	0.365	0.478*	−0.478*	−0.478*
Boys (*N* = 10)					
v12min (km/h)	0.900*	0.467	0.226	−0.226	−0.167
MAS (km/h)	0.685*	0.248	0.164	−0.164	−0.115
VO_{2max} (mL/kg/min)	0.758*	0.430	0.055	−0.055	−0.006

HF high frequency, *LF* low frequency, *MAS* maximal aerobic speed, *RRmean* mean of *R–R* intervals, *NU* normalized units, *rHRV* resting heart rate variability, *rMSSD* square root of the mean of the squares of successive *R–R* intervals differences, VO_{2max} maximal oxygen uptake, *v12min* mean velocity at 12 min Cooper Test

Discussion

Greater parasympathetic cardiac activity (RRmean and HF (nu)) was associated with higher levels of cardiorespiratory fitness (VO_{2max}, MAS, and v12min) in both girls and boys, while sympathetic-vagal balance was negatively related to VO_{2max} in girls. Moreover, a relationship between lower parasympathetic nervous system activity (RRmean and rMSSD) and insulin resistance (HOMA-IR) was observed in girls. On the other hand, a relationship between higher SBP and lower parasympathetic nervous system activity (RRmean and HF (nu)) was noted in boys.

Better cardiorespiratory fitness seems to be associated with increased activity of the parasympathetic nervous system [3, 12]. Furthermore, physical exercise in obese children was previously associated with a reduction in sympathetic-vagal balance [10, 22]. Gutin et al. [10] observed that, after 4 months of physical detraining, rHRV decreased in obese children, reinforcing that physical exercise plays a positive role in the control of neurocardiac function, and that this role could be mediated by cardiorespiratory fitness. In addition, a hypocaloric intervention alone did not improve parasympathetic activity in obese children, while improvements in this variable were seen in those following an exercise plus diet intervention [22], suggesting that parasympathetic activity is mediated by physical exercise in this population. In the present study, rHRV indices reflecting parasympathetic activity were positively associated with variables related to cardiorespiratory fitness (e.g., MAS and VO_{2max}) in adolescents of both sexes who followed an MOTP, which included the practice of regular physical activity. Moreover, as in adults [4], little is known on the relationship between cardiac parasympathetic activity and endurance capacity in adolescents. In this study, the 12-min Cooper test, which indicates endurance capacity, was positively associated with the mean *R–R* interval in both sexes. To our knowledge, this is the first study to demonstrate this relationship in overweight and obese adolescents, thus reinforcing the findings of previous studies that demonstrated that cardiorespiratory fitness is an important protective factor against the risk of cardiovascular disease [1, 21] such as decreased parasympathetic nervous system activity.

A negative correlation between insulin and HOMA-IR with cardiac parasympathetic activity in girls was also observed in the current study, which is similar to observations by Tascilar et al. [27] and Kaufman et al. [13]. The greater amount of central fat associated with reduced cardiac parasympathetic function in girls in this study, and the association between central fat and insulin resistance previously noted [5, 23] may in part explain this relationship between cardiac parasympathetic activity and insulin resistance. The mechanisms that influence this relationship are not yet well known, and so it is not clear whether insulin resistance causes reductions in cardiac parasympathetic activity or vice versa [27].

For boys, only SBP was negatively related to cardiac parasympathetic activity and positively related to sympathetic-vagal balance. This has been previously observed by Zhou et al. [30] in adolescents of both sexes, thus suggesting that autonomic nervous system activity plays a role in blood pressure regulation; however, this role has not yet been clarified. Taken together, these findings may have important implications, since the increase in blood pressure seems to be associated with the extent of atherosclerotic lesions in coronary arteries in children and young adults. Moreover, it is speculated that the reduction in parasympathetic activity could result, in addition to insulin resistance and hypertension, in the development of metabolic syndrome [15].

This study does have certain limitations. This is a cross sectional study with a small sample size, and so the analysis does not allow us to draw cause–effect relationships. Thus, future studies would be needed to assess the changes in autonomic nervous system activity and its relation to changes in other measured parameters (e.g., cardiorespiratory fitness, body composition, and metabolic profile) longitudinally.

In conclusion, autonomic nervous system activity is associated with cardiorespiratory fitness, insulin profile, and blood pressure in overweight and obese adolescents. These associations may be different between boys and girls.

Acknowledgments

The authors thank members of Multiprofessional Nucleus of Obesity Treatment who contributed with data collection and intervention development, and the Araucaria Foundation for financial support.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

1. Aires L, Silva P, Silva G et al (2010) Intensity of physical activity, cardiorespiratory fitness, and body mass index in youth. J Phys Act Health 7(1):54–59
2. Bianchini JA, da Silva DF, Nardo CC, Carolino ID, Hernandes F, Nardo N Jr (2013) Multidisciplinary therapy reduces risk factors for metabolic syndrome in obese adolescents. Eur J Pediatr 172(2):215–221
3. Buchheit M, Gindre C (2006) Cardiac parasympathetic regulation: respective associations with cardiorespiratory fitness and training load. Am J Physiol Heart Circ Physiol 291:H451–H458
4. Buchheit M, Chivot A, Parouty J et al (2010) Monitoring endurance running performance using cardiac parasympathetic function. Eur J Appl Physiol 108:1153–1167
5. Caranti DA, de Mello MT, Prado WL et al (2007) Short- and long-term beneficial effects of a multidisciplinary therapy for the control of metabolic syndrome in obese adolescents. Metabolism 56(9):1293–1300
6. Carnier J, Sanches Pde L, da Silva PL et al (2012) Obese adolescents with eating disorders: analysis of metabolic and inflammatory states. Physiol Behav 105:175–180
7. Cole TJ, Bellizzi MC, Flegal KM et al (2000) Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 320(7244):1240–1243
8. Cooper KH (1968) A means of assessing maximal oxygen intake: correlation between field and treadmill testing. JAMA 203:201–2014

9. Gamelin FX, Berthoin S, Bosquet L (2006) Validity of the polar S810 heart rate monitor to measure RR intervals at rest. Med Sci Sports Exerc 38(5):887–893

10. Gutin B, Barbeau P, Litaker MS et al (2000) Heart rate variability in obese children: relations to total body and visceral adiposity, and changes with physical training and detraining. Obes Res 8:12–19

11. Haddad HA, Laursen PB, Ahmaidi S et al (2009) Nocturnal heart rate variability following supramaximal intermittent exercise. Int J Sports Physiol Perform 4(4):435–447

12. Hautala AJ, Kiviniemi AM, Tulppo MP (2009) Individual responses to aerobic exercise: the role of the autonomic nervous system. Neurosci Biobehav Rev 33:107–115

13. Kaufman CL, Kaiser DR, Steinberger J, Kelly AS, Dengel DR (2007) Relationships of cardiac autonomic function with metabolic abnormalities in childhood obesity. Obesity (Silver Spring) 15:1164–1171

14. Kuipers H, Verstappen FT, Keizer HA et al (1985) Variability of aerobic performance in the laboratory and its physiological correlates. Int J Sports Med 6:197–201

15. Lambert GW, Straznicky NE, Lambert EA et al (2010) Sympathetic nervous activation in obesity and the metabolic syndrome: causes, consequences and therapeutic implications. Pharmacol Ther 126(2):159–172

16. Léger LA, Lambert J (1982) A maximal multistage 20m shuttle test to predict VO2 max. Eur J Appl Physiol Occup Physiol 49:1–5

17. Leger LA, Mercier D, Gadoury C et al (1988) The multistage 20 metre shuttle run test for aerobic fitness. J Sports Sci 6(2):93–101

18. Lucini D, de Giacomi G, Tosi F et al (2012) Altered cardiovascular autonomic regulation in overweight children engaged in regular physical activity. Heart 99(6):376–381

19. Matthews DR, Hosker JP, Rudenski AS et al (1985) Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28:412–419

20. Michels N, Clays E, De Buyzere M et al (2012) Determinants and reference values of short-term heart rate variability in children. Eur J Appl Physiol 113(6):1477–1488

21. Ortega FB, Labayen I, Ruiz JR et al (2011) Improvements in fitness reduce the risk of becoming overweight across puberty. Med Sci Sports Exerc 43(10):1891–1897

22. Prado DM, Silva AG, Trombetta IC et al (2010) Exercise training associated with diet improves heart rate recovery and cardiac autonomic nervous system activity in obese children. Int J Sports Med 31:860–865

23. Roemmich JN, Clark PA, Lusk M et al (2002) Pubertal alterations in growth and body composition. VI. Pubertal insulin resistance: relation to adiposity, body fat distribution and hormone release. Int J Obes 26:701–709

24. Sato N, Miyake S (2004) Cardiovascular reactivity to mental stress: relationship with menstrual cycle and gender. J Physiol Anthropol Appl Human Sci 23:215–223

25. Soares-Miranda L, Alves AJ, Vale S et al (2011) Central fat influences cardiac autonomic function in obese and overweight girls. Pediatr Cardiol 32:924–928

26. Tanner JM (1986) Normal growth and techniques of growth assessment. Clin Endocrinol Metab 15(3):411–451

27. Tascilar ME, Yokusoglu M, Boyraz M et al (2011) Cardiac autonomic functions in obese children. J Clin Res Pediatr Endocrinol 3(2):60–64

28. Task Force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology (1996) Heart rate variability: standards of measurement, physiological interpretation, and clinical use. Eur Heart J 17:354–381

29. Wolf MM, Varigos GA, Hunt D, Sloman JG (1978) Sinus arrhythmia in acute myocardial infarction. Med J Aust 2:52–53

30. Zhou Y, Xie G, Wang J et al (2012) Cardiovascular risk factors significantly correlate with autonomic nervous system activity in children. Can J Cardiol 28(4):477–482