Autonomic dysfunction during the rest-to-exercise transition in obese children

Disfunción autonómica durante la transición reposo-ejercicio en niños obesos

Natalia Cuevas[1,2], Andrea Salamanca[2], Natalia Rodríguez-Romero[3,4], Gerardo Weisstaub[5], Ruy R. Campos[6], and Iván Rodríguez-Núñez[3,4]*

[1]Pediatric Intensive Care Unit, Hospital Exequiel González Cortés, Santiago, Chile; [2]School of Kinesiology, Faculty of Health Science, Universidad de San Sebastián, Concepcion, Chile; [3]Laboratory of Movement Physiology, Department of Kinesiology, Universidad de Concepción, Concepcion, Chile; [4]Service of Kinesiology, Science and Society Foundation, Concepcion, Chile; [5]Public Nutrition Unit, INTA, Universidad de Chile, Santiago, Chile; [6]Laboratory of Cardiovascular Physiology, Department of Fisiology, Universidade Federal de São Paulo, São Paulo, Brazil

The rising prevalence of childhood obesity is increasingly recognized as one of the most critical risk factors for the development of cardiovascular diseases (CVD)[1]. Obesity is commonly related to oxidative stress, inflammatory response, sympathetic vasomotor hyperactivity, and decreased parasympathetic modulation, leading to developing hypertension and metabolic syndrome in children by impairing beta-adrenergic signaling and insulin sensitivity[2].

The early heart rate (HR) changes are strongly related to vagal modulation during the rest-to-exercise transition. This mechanism allows resetting the arterial baroreflex to a higher operating point, which is critical for a better redistribution of the cardiac output toward the contracting muscles during exercise[3]. These mechanisms have also been shown to be impaired in individuals with cardiovascular and metabolic diseases[4]. Nonetheless, it is not clear if these physiological disturbances appear before adulthood. Besides, knowledge is scarce regarding the effects of obesity on autonomic modulation during exercise in children.

This pilot study, then, aimed to evaluate the HR response during the rest-to-exercise transition in obese and non-obese children.

This cross-sectional study selected 19 eutrophic and 19 obese children aged 8-12 years of a private school in Concepción, Chile. Children with antecedents of any chronic or acute condition before the enrollment (4 weeks) were excluded from the study. Obese and non-obese children were matched by age and sex. The study was performed at the participant's school, and all measurements were performed on the same day between 2.00 pm and 5.00 pm.

The research protocol was approved by the ethics committee of the Faculty of Medicine, University of Concepción Chile (Protocol: CEC64/2018).

Anthropometric variables were measured using a bioelectrical impedance analyzer (InBody 270) and a measurement tape (centimeters). The body mass index (BMI) was calculated as kg/m^2, and obesity was defined as a BMI between the 95th and 97th percentiles[5].

Baseline heart rate (HR) and blood pressure (BP) were measured in supine position after 10- min rest. Heart rate and RR intervals (RR) were recorded in the supine position for 10 min by a Polar H7 sensor connected to a portable HR monitor (HRM) (Polar V800, Kempele, Finland).

Table 1. General characteristics of subjects

Variables	Non-obese (n = 19)	Obese (n = 19)	p-value
Biodemographic variables			
Age, years	10.4 ± 1.7	10.6 ± 1.8	0.66
Sex, n boys (%)	13 (68.4)	12 (63.2)	0.73
Height, cm	138.8 ± 13.4	144.2 ± 12.7	0.21
Weight, kg	36.2 (27.7-42.5)[a]	55.0 (42.7-62.4)[a]	0.0001*
BMI, kg/m^2	17.7 (16.6-19.4)[a]	24.4 (23.8-27.7)[a]	< 0.0001*
% Fat mass	7.5 (4.9-9.8)[a]	18.4 (16.3-24.6)[a]	< 0.0001*
WC, cm	63.4 ± 7.8	81.2 ± 11.6	< 0.0001*
Baseline cardiovascular variables			
Rest HR. bpm	93.4 ± 18.2	88.9 ± 10.0	0.53
Rest SBP. mmHg	111.4 ± 10.3	112.6 ± 11.7	0.75
Rest DBP. mmHg	74.7 ± 8.9	73.0 ± 9.2	0.55
Rest MAP. mmHg	74.5 ± 7.7	74.0 ± 8.2	0.85
R-R interval. ms	664.1 ± 121.5	683.1 ± 73.5	0.56
rMSSD. ms	44.7 (22.5-68.3.1)[a]	35.9 (26.8-50.4)[a]	0.45
NN 50. n	56.0 (19.0-178.0)[a]	59.0 (24.8-114.3)[a]	0.69
pNN 50. %	11.7 (3.7-40.8)[a]	12.9 (5.3-26.9)[a]	0.74
LF. ms^2	747.1 (424.4-2483.2)[a]	649.4 (434.7-1155.2)[a]	0.56
LF. nu	55.6 ± 18.1	59.4 ± 15.2	0.63
HF. ms^2	517.3 (265.7-3186.8)[a]	447.8 (283.5-1001.9)[a]	0.43
HF. nu	44.2 ± 18.0	40.7 ± 15.2	0.51
LF/HF	1.3 (0.7-2.1)[a]	1.5 (1.0-2.0)[a]	0.63

BMI: body mass index; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: meanarterial pressure; FEV: forced expiratory volume; FVC: forced vital capacity; FEF: forced expiratory flow; rMSSD: the square root of the mean squared differences of successive NN intervals; SDNN: the standard deviation of the NN interval; NN_{50}: the number of interval differences of successive NN intervals greater than 50 ms; pNN_{50}: the proportion derived by dividing NN_{50} by the total number of NN intervals; LF: spectral component of low frequency; HF: spectral component of high frequency; LF/HF: rate between LFand HF. Resultsare expressed in meanand standard deviation.
[a]Results are expressed in medianand interquartile range.
*Significant differences.

For heart rate variability (HRV) analysis, a 5-min period of steady-state data with a minimum of 256 RR was only considered. Then, the RR recordings were downloaded from the manufacturer's website (Polar-Flow.com) and exported to Kubios HRV software for time and frequency domain analyses, as recommended by Rodríguez-Núñez et al[6].
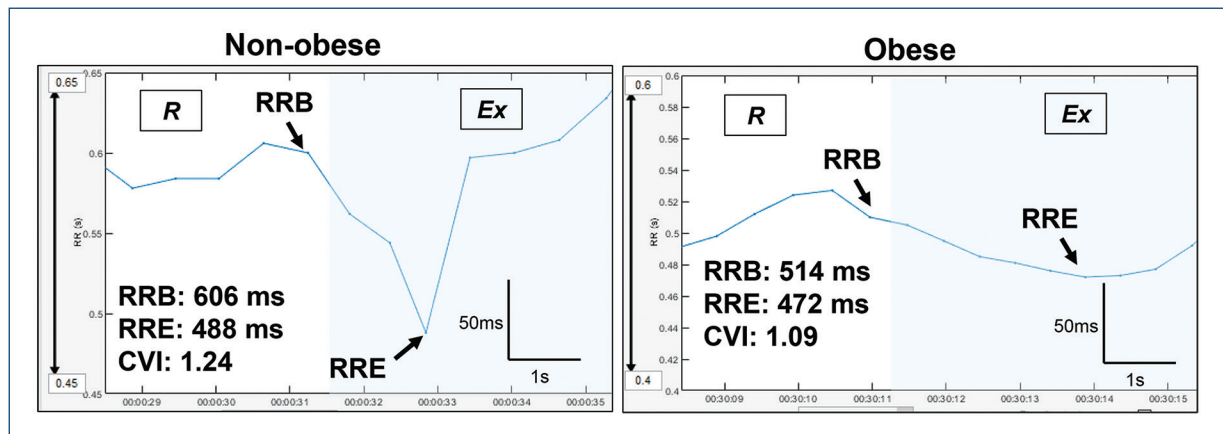
The vagal modulation in the rest-to-exercise transition was evaluated by the 4-s exercise test (4-sET), following the protocol published by Araujo et al[7]. Briefly, each participant was adequately seated on a static cycle ergometer. Once HR returned to a level similar to the basal, 4sET was performed. Volunteers were then given standardized verbal instruction regarding the procedure, which includes four-step performed at the verbal command of the examiner: (1) a quick maximal inspiratory apnea maintained for 12s, (2) at the end of the 4th s of apnea, the participant starts to pedal as fast as possible for 4 s without any resistance being added to the cycle ergometer, (3) at the end of the 8th s, leg movement is interrupted wholly and rapidly, with the subject still in apnea, and (4) finally, at the end of 12th s, the subject exhale and breathe freely again[7]. This sequence was repeated until two technically correct exercise cycles were performed.

The RR was measured during the entire test execution and then downloaded and exported to Kubios software to calculate the cardiac vagal index (CVI), which corresponds to a dimensionless variable reflecting the vagal tone loss induced by rapid response to exercise. CVI was calculated as the ratio of two RR as follow,

$$CVI = \frac{RRB}{RRE}$$ (RRB: the RR immediately before exercise; RRE: the shortest RR during exercise)[7,8].

Descriptive statistics were expressed as mean and standard deviation or median and the range between percentile 25 and 75 (interquartile range [IQr]) according to the normality of data. Then, the comparisons of quantitative variables with normal distribution were analyzed by Student t-test. The non-parametric equivalent test (U-Mann–Whitney test) was used to analyze variables with non-normal distribution. Statistical analyses were performed with Graph Pad Prism 5.0 (San Diego, USA) software. The significance level adopted was p < 0.05.

There was no statistical difference between groups in age, sex, cardiovascular parameters, and HRV indexes (Table 1). The median weight of obese children was 55,0 kg, while the weight of eutrophic children was 36,2 kg (p = 0.0001).
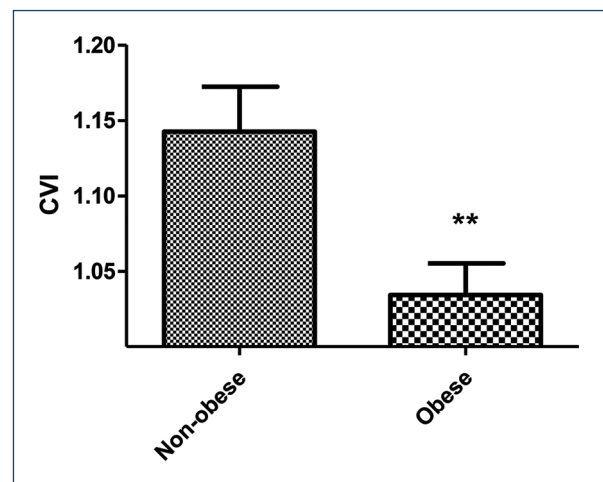
Figure 1. Tachogram of representative cases of an obese and non-obese child during the 4-s exercise test (6-s RR recording). RRB: RR interval just before the onset of exercise; RRE: The lowest RR interval during 4 s of exercise.

Regarding the autonomic modulation during exercise, obese children presented an attenuated RR change during the rest-to-exercise transition, as presented in figure 1. The value of CVI in the obese individuals was 1.03 ± 0.02 and in the non-obese ones was 1.14 ± 0.03 ($p = 0.0054$) (Fig. 2).

As the findings of this study show, obese children presented a lower mean CVI (–9.6%) than the non-obese group, which is evidence of vagal dysfunction in the rest-to-exercise transition. These findings agree with published studies examining the impact of obesity on autonomic function by HRV measurement, which showed lower parasympathetic HRV indexes on obese children than eutrophic individuals[9]. In agreement with this evidence, we also found a tendency toward lower values in the root-mean-square of differences between adjacent N-N intervals (RMSSD) (35,9 ms versus 44,7 ms) and higher values in LF/HF (1,5 versus 1,3) in obese children (Table 1).

On the other hand, it was observed that the mean CVI of both study groups was reduced compared to reference values published in the adult population[7], which suggests that age may also determine the value of CVI in childhood. In this line, some studies have informed that children exhibit a reduced parasympathetic activity, accompanied by a higher sympathetic activity than adults[10]. However, no studies have been designed to compare autonomic adaptation during exercise in children versus adults.

This study has some limitations. First, the small sample size may affect the reproducibility of the results. On the other hand, chronic respiratory disorders were the only exclusion criteria objectively verified by spirometry.

Figure 2. Mean and standard deviation of the 4-s exercise test in non-obese and obese children. CVI: Cardiac vagal index. **$Z = 2.782$; $p = 0.0054$, U Mann–Whitney test was used.

Therefore, if any study participant presented, any non-detected exclusion criteria cannot be ruled out.

Finally, we can conclude that obese children exhibited a reduced vagal response at the onset of exercise measured by 4sET. These findings contribute additional data to reinforce the importance of monitoring the autonomic nervous system in obese individuals from preadolescent age.

Funding

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

References

1. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759.
2. Qi Z, Ding S. Obesity-associated sympathetic overactivity in children and adolescents: the role of catecholamine resistance in lipid metabolism. J Pediatr Endocrinol Metab. 2016;29:113-25.
3. White DW, Raven PB. Autonomic neural control of heart rate during dynamic exercise: revisited. J Physiol. 2014;592:2491-500.
4. Grotle AK, Macefield VG, Farquhar WB, O'Leary DS, Stone AJ. Recent advances in exercise pressor reflex function in health and disease. Auton Neurosci. 2020;228:102698.
5. Health Promotion and National Center for Health Statistic. Growth Chart; 2010. Available from: https://www.cdc.gov/growthcharts
6. Rodríguez-Núñez I, Rodríguez-Romero N, Álvarez A, Zambrano L, Veiga GL, Romero F. Variabilidad del ritmo cardíaco en pediatría: aspectos metodológicos y aplicaciones clínicas. Arch Cardiol Mex. 2022;92:242-52.
7. Araújo CG, de Castro CL, Franca JF, Ramos PS. 4-Second exercise test: reference values for ages 18-81 years. Arq Bras Cardiol. 2015;104:366-74.
8. Pimentel AS, Alves EDS, Alvim RDO, Nunes RT, Costa CM, Lovisi JC, et al. Polar S810 as an alternative resource to the use of the electrocardiogram in the 4-second exercise test. Arq Bras Cardiol. 2010;94:580-4.
9. Taşçılar ME, Yokuşoğlu M, Boyraz M, Baysan O, Köz C, Dündaröz R. Cardiac autonomic functions in obese children. J Clin Res Pediatr Endocrinol 2011;3:60-4.
10. Eyre ELJ, Duncan MJ, Birch SL, Fisher JP. The influence of age and weight status on cardiac autonomic control in healthy children: a review. Auton Neurosci. 2014;186:8-21.