CLINICAL SCIENCE

Analysis of cardiac autonomic modulation in obese and eutrophic children

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INTRODUCTION: Obesity causes alterations in cardiac autonomic function. However, there are scarce and conflicting data on this function with regard to heart rate variability in obese children.

OBJECTIVE: To compare the autonomic function of obese and eutrophic children by analyzing heart rate variability.

METHODS: One hundred twenty-one children (57 male and 64 female) aged 8 to 12 years were distributed into two groups based on nutritional status [obese (n = 56) and eutrophic (ideal weight range; n = 65) according to the body mass index reference for gender and age]. For the analysis of heart rate variability, heart rates were recorded beat by beat as the children rested in the dorsal (prone) position for 20 minutes. Heart rate variability analysis was carried out using linear approaches in the domains of frequency and time. Either Student's t-test or the Mann-Whitney U-test was applied to compare variables between groups. Statistical significance was set at 5%.

RESULTS: The SDNN, RMSSD, pNN50, SD1, SD2, LF and HF indices in milliseconds squared were lower among the obese children when compared to the eutrophic group. There were no alterations in the SD1/SD2 ratio, LF/HF ratio, LF index or HF index in normalized units. There was a significant difference between groups in the RR interval (R-to-R EKG interval).

CONCLUSION: The obese children exhibited modifications in heart rate variability, characterized by a reduction in both sympathetic and parasympathetic activity. These findings stress the need for the early holistic care of obese children to avoid future complications.

KEYWORDS: Obesity; Heart rate; Sympathetic nervous system; Parasympathetic nervous system; Heart rate variability.

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INTRODUCTION

Obesity is a disorder with a multifactor etiology resulting from a complex interaction between the environment, behavior and genetic susceptibility.[1] As the prevalence of this disorder grows worldwide, obesity is increasingly considered a major public health problem.[2-4] The consequences of obesity in childhood and adolescence include arterial hypertension, atherosclerosis, dyslipidemia, diabetes, obstructive sleep apnea, alterations in the musculoskeletal system, depression and a reduction in quality of life.[5,6] Studies have also demonstrated that obesity causes alterations in the function of the autonomic nervous system (ANS) in children and adolescents.[7,8] Because the ANS controls a significant part of the internal functions of the body, this disequilibrium is an important negative factor.

One way to evaluate autonomic behavior is by heart rate variability (HRV). HRV is a simple and non-invasive indicator for the detection and investigation of possible cardiac autonomic dysfunction in a number of different medical conditions, including obesity.[9-12]

In the comparison of HRV between obese adults and those within the ideal weight range, some studies report a reduction in parasympathetic activity, and others report a reduction in both sympathetic and parasympathetic activity.[10-12] However, the literature also reports an increase in sympathetic activity.[13] Rabbia et al.[14] and Riva et al.[15] report sympathovagal dysfunction in obese adolescents, characterized by a reduction in parasympathetic activity and an increase in sympathetic activity. Guizar et al.[16] report autonomic alterations in obese adolescents, characterized by a decrease in SDNN and in total potency, as well as an increase in the LF/HF ratio.

Table 1 - General characteristics of obese and eutrophic children.

Variables	Obese	Eutrophic
Age (years)	9.98 ± 1.31 [9.63–10.33]	10.39 ± 1.42 [10.03–10.74]
Weight (kg)	63.16 ± 14.50 (60.35)[a] [59.27–67.04]	37.91 ± 7.84 (36.2)[a,*] [35.96–39.85]
Height (cm)	147.73 ± 10.45 [144.93–150.53]	147.09 ± 10.20 [144.57–149.62]
BMI (kg/m^2)	28.58 ± 3.66 (28.06)[a] [27.60–29.56]	17.33 ± 1.77 (17.05)[a,*] [16.89–17.77]

[a]Mean ± SD (median); [95% CI];
[*]significant difference between groups (Mann-Whitney U-test); BMI = body mass index

Although studies demonstrate important modifications in the autonomic control of obese adults and adolescents, there is scarce information on obese children, and the findings remain inconclusive.[17,18] Thus, the aim of the present study was to contribute knowledge on this subject by comparing the autonomic function of obese and eutrophic children through the analysis of HRV.

MATERIALS AND METHODS

Population and Sample

One hundred thirty-five children aged 8 to 12 years were evaluated. Data on the 14 children who had a greater than 5% error in RR series were excluded. The final sample was made up of 121 children (57 boys and 64 girls) divided into two groups, obese and eutrophic (within ideal weight range) based on the body mass index (BMI) reference for age and gender.[19]

The obese group was made up of 56 children (25 boys and 31 girls) who had undergone an initial evaluation to participate in a program for the treatment of childhood obesity through physical activity. The eutrophic group consisted of 65 children (32 boys and 33 girls) randomly selected from among the students of a private school, matched to the obese group for age and gender. The data were collected from January to October 2008.

Children who reported drug use or diagnosed diseases were not included in the study. Mean and standard deviation values for the age, weight, height and BMI of the subjects are displayed in Table 1.

All participants received explanations regarding the procedures and objectives of the study. Following agreement to participate, parents/guardians gave written informed consent. The study received approval from the Ethics Committee of the School of Science and Technology, FCT/UNESP, Presidente Prudente Campus, Universidade Estadual Paulista (Process n° 187/2007).

Data Collection

Data were collected under controlled temperature (21 to 23° C) and humidity (40 to 60%). The participants reported to the laboratory between 2:00 and 5:00 pm. Before beginning the experimental procedure, the participants were identified by age, gender, height, weight and BMI. Anthropometric measurements were obtained following the standard recommendations proposed by Lohman et al.[20] BMI was computed using the formula weight (kg)/height (m^2).

The heart monitor strap was placed on each subject's thorax over the distal third of the sternum. The heart rate receiver of the Polar S810i monitor (Polar Electro OY, Kempele, Finland) was placed on the wrist. This equipment has been previously validated for beat-by-beat measurements and for the use of its output in HRV analysis.[21,22]

The participants were instructed to recline in the face-up position on a bed and rest with spontaneous breathing for 20 min. For the HRV analysis, the heart rate was recorded beat by beat throughout the period at a sampling frequency of 1000 Hz. For data analysis, 1000 consecutive RR intervals were documented after digital filtering and complemented by a manual procedure for the elimination of premature ectopic heartbeats and artifacts. Only series with more than 95% sinus rhythm were included.[23] All measurements were performed by trained staff.

Analysis of Heart Rate Variability

HRV analysis was performed with linear methods in the domains of time and frequency.[9] In the time domain, the root mean square of successive differences (RMSSD), the standard deviation of normal-to-normal intervals (SDNN) and the percentage of differences between adjacent normal-to-normal intervals greater than 50 msec (pNN50) were used. The Poincaré plot was also analyzed, from which the indices of standard deviation of instantaneous beat-to-beat RR interval variability (SD1), the standard deviation of continuous long-term RR interval variability (SD2), and the SD1/SD2 ratio were extracted.

In the frequency domain, the spectral components of low frequency (LF: 0.04–0.15 Hz) and high frequency (HF: 0.15–0.40 Hz) in normalized units (LFnu and HFnu, respectively) and in milliseconds squared were used. The LF/HF ratio, which represents the relative value of each spectral component in relation to the total power minus the very low frequency component (VLF), was also used. Spectral analysis was performed using the fast Fourier transform algorithm.

The HRV analysis software program Kubios (Biosignal Analysis and Medical Image Group, Department of Physics, University of Kuopio, Finland) was used to analyze these indices.[24]

Statistical Analysis

The normality of the data was determined using the Kolmogorov-Smirnov test. Comparisons between groups were performed using either the independent Student's t-test or Mann-Whitney U-test for parametric or for non-parametric sample distribution, respectively. Statistical significance was set at 5% for all analyses, and the calculations were performed using the SPSS program, version 10.0 (SPSS Inc., Chicago, IL). The calculation of the study power, with the number of subjects analyzed and 5% significance level (two-tailed), confirmed a power higher than 80% in the detection of differences between variables.

RESULTS

Table 2 displays the values obtained for the LF and HF indices in normalized units and in milliseconds squared and the LF/HF ratio of the obese and eutrophic groups. The LF and HF (ms^2) values were significantly higher in the eutrophic group. However, there were no statistically

Table 2 - Linear index values of heart rate variability (frequency domain) of obese and eutrophic children.

Variables	Obese	Eutrophic	P
LF (ms^2)	250.4 ± 177.5 (191.0)[a] [202.84–297.95]	375.3 ± 212.7 (356.0) [322.54–427.98]	0.001*
HF (ms^2)	195.1 ± 182.5 (135.0) [146.15–243.96]	249.3 ± 159.7 (224.0) [209.67–288.85]	0.007*
LFnu (%)	59.26 ± 13.07 (58.55) [55.76–62.77]	60.57 ± 11.68 (62.10) [57.68–63.47]	0.565
HFnu (%)	40.73 ± 13.07 (41.45) [37.23–44.24]	39.43 ± 11.68 (37.90) [36.53–42.32]	0.566
LF/HF ratio	1.801 ± 1.25 (1.41) [1.47–2.14]	1.774 ± 0.91 (1.64) [1.55–2.00]	0.425

[a]Mean ± SD (median); [95% CI];
*significant difference between groups (Mann-Whitney U-test); LF: low frequency; HF: high frequency; ms: milliseconds; LFnu: low frequency in normalized units; HFnu: high frequency in normalized units

significant differences between groups in LF and HF normalized-unit values or in LF/HF ratio.

The eutrophic group presented higher values for the RR interval and the SDNN, RMSSD and pNN50 indices (Table 3). Table 4 displays the values of the SD1 and SD2 indices and the SD1/SD2 ratio. There were statistically significant differences between groups in the SD1 and SD2 indices, whereas no difference was found in the SD1/SD2 ratio.

DISCUSSION

The evaluation of the HRV indices in the present study suggests a decrease in the activity of the sympathetic and parasympathetic autonomic nervous systems in obese children. The RMSSD, pNN50 and HF indices in milliseconds squared and SD1, which indicate parasympathetic activity, were lower in the obese children than in the eutrophic children. A reduction in parasympathetic activity among obese children has also been reported by other authors.[7,18,25] The mechanisms by which vagal dysfunction is related to obesity are under debate, and it is uncertain whether this dysfunction is a consequence of obesity or facilitates their developmet.[8]

A reduction in vagal activity is associated with an increased risk for all-cause morbidity and mortality and

Table 3 - Linear index values of heart rate variability (time domain) of obese and eutrophic children.

Variables	Obese	Eutrophic	p
RR interval (ms)	652.09 ± 71.82 (657.50)* [632.85–671.33]	680.65 ± 75.44 (675.00) [661.94–699.35]	0.035[a]
SDNN	37.18 ± 26.26 (34.00) [30.14–44.21]	42.58 ± 10.48 (44.00) [39.99–45.18]	0.001[b]
RMSSD	27.45 ± 12.70 (27.80) [24.04–30.85]	31.92 ± 10.34 (32.80) [29.36–34.48]	0.038[a]
pNN50	9.65 ± 10.14 (5.95) [6.94–12.37]	12.08 ± 8.91 (12.20) [9.87–14.29]	0.0318[b]

*Mean ± SD (median); [95% CI];
[a]significant difference between groups (Student's t-test);
[b]significant difference between groups (Mann-Whitney U-test); ms: milliseconds; SDNN: standard deviation normal-to-normal intervals; RMSSD: root mean square of successive differences; pNN50: percentage of differences between adjacent normal-to-normal intervals that are greater than 50 ms

Table 4 - Mean, standard deviation, 95% confidence interval and p value for Poincaré plot of obese and eutrophic children.

Variables	Obese	Eutrophic	p
SD1	19.92 ± 9.23 [17.45–22.39]	23.24 ± 7.43 [21.40–25.08]	0.033*
SD2	52.43 ± 16.74 [47.95–56.92]	67.93 ± 16.60 [63.82–72.05]	0.001*
SD1/SD2 ratio	0.3698 ± 0.11 [0.3403–0.3993]	0.3445 ± 0.08 [0.3238–0.3652]	0.162

*Significant difference between groups (Student's t-test); SD1: standard deviation of instantaneous beat-to-beat RR interval variability; SD2: standard deviation of continuous long-term RR interval variability

for the development of several risk factors.[26] Therefore, the reduction observed in obese children may be an early sign for the prediction of the risk for cardiovascular and metabolic disease.[18]

The SDNN, SD2 and LF (ms^2) indices, which indicate global variability and sympathetic activity, were also lower among the obese children than among the eutrophic children. A reduction in sympathetic activity in obese children is also described in the literature.[18,27] The sympathetic ANS is associated with the mobilization of body energy[26] and participates in the control of glucose and fat metabolism.[27] Peterson et al.[11] report an association between the increase in body fat and hypoactivity of sympathetic and parasympathetic components of ANS. The authors state that lower sympathetic activity is related to lower energy expenditure and, consequently, to a positive energy balance and increase of body weight. According to Nagai & Moritani,[27] a causal relationship between alterations in ANS activity and obesity cannot be confirmed; however, the authors suggest that a reduction in autonomic activity may be an etiological factor in the onset and development of obesity.

The hypothalamus is a regulatory center of satiety and of the ANS. Therefore, abnormalities in the hypothalamus may cause obesity and autonomic dysfunction.[8,25] This may explain the alterations observed in the HRV indices.

Studies of ANS activity in obese children have presented conflicting results. Sekine et al.[28] analyzed HRV indices in the frequency domain and suggested that obese children exhibit higher sympathetic activity and lower parasympathetic activity than do eutrophic children. On the other hand, Nagai et al.[18] and Nagai & Moritani[27] report that obese children have both lower sympathetic and parasympathetic activity than do children within the ideal weight range. Yakinci et al.[25] performed autonomic function tests on obese children and found normal sympathetic activity and parasympathetic hypoactivity. More recently, Kaufman et al.[7] found that obese children exhibited an increase in the LF/HF ratio and a decrease in the HF index in comparison with eutrophic children.

According to Nagai et al.,[18] these discrepancies may be related to the difficulty in controlling variables such as gender, age, family history, other medical complications, diets, behavioral habits, level of physical activity and emotional stress.

The conflicting results among indices may also be attributed to methodological limitations in the evaluation of sympathetic ANS activity, due to the fact that LF and the LF/

HF ratio are not pure indices of the activity of this ANS component.[18,28] Moreover, sympathetic ANS alterations in obese children seem to be related to the duration of obesity. Rabbia et al.[14] found that the LFnu index and LF/HF ratio were higher in children classified as recently obese (< 4 years); in the intermediate obese group (4 to 7 years) and long-term obese (> 7 years) group, the LFnu was similar to the control group of children within the ideal weight range. In the present study, the duration of obesity was not investigated, so it is not possible to speculate on its effect on the sample.

The observed reduction in the sympathetic and parasympathetic components of the ANS explains the absence of statistical differences in the SD1/SD2 and LF/HF ratios as well as in the LF and HF indices in normalized units. The analysis of the RR intervals revealed significantly lower values in the obese children, indicating an increase in heart rate. Lower RR intervals in obese children have also been reported by other authors.[28,29]

One limitation of the present study is a possible bias in the selection of the sample. Although the sample size was adequate, the need to organize the groups (obese and eutrophic) through convenience sampling, which resulted in the selection of participants from a single, specific program for obese children and of controls from a single teaching institution, could limit the extrapolation of the results to the general population. However, the findings can be understood as a tendency and can certainly represent a warning with regard to problems related to obesity.

The results of the present study suggest that obese children have autonomic dysfunctions characterized by a reduction of both sympathetic and parasympathetic activity. The continuing increase in the number of obese children is alarming due to the potential risk of premature health problems.[5,6] Moreover, obese children have a high likelihood of becoming obese adults,[30] and obese adults who were once obese children have a lower treatment response than those who became obese in adulthood.[31] These concerns about the effects of obesity reinforce the need for the prevention and treatment of the condition in childhood. The importance of changes in the lifestyle of these children must be emphasized, especially with regard to eating habits and the practice of regular physical activity.

CONCLUSION

Our results suggest that obese children exhibit modifications in the ANS characterized by a reduction in sympathetic and parasympathetic activity. This finding strongly indicates the need for the early care of these children to allow them to avoid the onset of future complications.

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