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The Influence of Obesity in the Autonomic Nervous System Activity in School-Aged Children in Northern Portugal: A Cross-Sectional Study

A Influência da Obesidade na Atividade do Sistema Nervoso Central em Crianças em Idade Escolar no Norte de Portugal: Um Estudo Transversal

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ABSTRACT

Introduction: Obesity is one of the most prevalent chronic diseases in childhood, being an important public health issue. Excessive weight has been associated with autonomic dysfunction but the evidence in children is scarce. Therefore, the aim of this study was to assess the effect of overweight and obesity on the autonomic nervous system activity, in children.

Material and Methods: Data from a cross-sectional study of 1602 children, aged 7 to 12 years, was used and 858 children were included in the analysis. Body mass index was calculated and classified according to criteria of the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) and the International Obesity Task Force (IOTF). Body composition was characterized by bioelectrical impedance. Linear regression models were used to determine the association between body mass index, body composition and the autonomic nervous system activity, assessed by pupillometry.

Results: Average dilation velocity was higher among children with obesity, according to the CDC and percentage of body fat criteria (β = 0.053, 95% CI = 0.005 to 0.101 and β = 0.063, 95% CI = 0.016 to 0.109, respectively). The same trend was observed for WHO and IOTF criteria (β = 0.045, 95% CI = -0.001 to 0.091, and β = 0.055, 95% CI = -0.001 to 0.111, respectively). CDC and WHO body mass index z-scores were also positively associated with the values of average dilation velocity (rs = 0.030, *p* = 0.048; and rs = 0.027, *p* = 0.042, respectively).

Conclusion: Our findings suggest an association between body mass and changes in the autonomic activity, Moreover, this study provides proof of concept for interventions targeting the prevention/treatment of obesity in children that may offer some benefit in re-establishing the balance of the autonomic nervous system, and subsequently preventing the consequences associated with the autonomic nervous system dysfunction.

Keywords: Autonomic Nervous System/physiopathology; Child; Obesity/physiopathology; Pediatric Obesity; Portugal

RESUMO

Introdução: A obesidade é uma das doenças crónicas mais prevalentes na infância. O peso excessivo tem sido associado à disfunção autonómica, mas as evidências em crianças são escassas. Este estudo teve como objetivo avaliar o efeito da pré-obesidade e obesidade na atividade do sistema nervoso autónomo, em crianças.

Material e Métodos: Foram utilizados dados de um estudo transversal com 1602 crianças, sendo que 858 foram incluídas na análise. O índice de massa corporal foi calculado e classificado de acordo com a Organização Mundial da Saúde (OMS), Centro de Controlo e Prevenção de Doenças dos Estados Unidos (CDC) e a *Task Force* Internacional para a Obesidade (IOTF). A composição corporal foi caracterizada por impedância bioelétrica. Modelos de regressão linear foram usados para determinar a associação entre o índice de massa corporal, a composição corporal e a atividade do sistema nervoso autónomo, avaliada por pupilometria.

Resultados: A velocidade média de dilatação foi maior entre crianças com obesidade, segundo os critérios do CDC e percentagem de gordura corporal (β = 0,053, IC 95% = 0,005 a 0,101 e β = 0,063, IC 95% = 0,016 a 0,109, respetivamente). Igual tendência foi observada para os critérios da OMS e IOTF (β = 0,045, IC 95% = -0,001 a 0,091 e β = 0,055, IC 95% = -0,001 a 0,111, respetivamente). Os *z-scores* de índice de massa corporal do CDC e OMS também se associaram positivamente aos valores da velocidade média de dilatação (rs = 0,030, *p* = 0,048; e rs = 0,027, *p* = 0,042, respetivamente).

Conclusão: Os resultados sugerem uma associação entre a massa corporal e alterações na atividade do sistema nervoso autónomo Este estudo fornece prova de conceito para intervenções direcionadas à prevenção/tratamento da obesidade em crianças, podendo favorecer o restabelecimento do equilíbrio do sistema nervoso autónomo e, assim, prevenir as consequências associadas à sua disfunção.

Palavras-chave: Criança; Obesidade/fisiopatologia; Obesidade Pediátrica; Portugal; Sistema Nervoso Autónomo/fisiopatologia

INTRODUCTION

Childhood obesity is a growing public health problem. In 2016, there were 340 million obese children and adolescents worldwide.[1] It affects multiple low- and middle-income countries, especially in urban areas.[2] Childhood obesity affects children in numerous aspects of their emotional health and social life, by decreasing their quality of life, self-esteem and academic performance[2]; it also has a negative impact on their physical health, predisposing them to a greater number of comorbidities that classically would only appear in adulthood.[3,4] As such, it is of great importance to explore the mechanisms leading to its manifestation in order to develop prevention strategies and to decrease the incidence

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rate worldwide.

Recent studies have highlighted the role of the autonomic nervous system (ANS) dysfunction on weight gain and obesity development.[5,6] The ANS is comprised of two branches, the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS), each of them with opposing functions.[7,8] Several mechanisms to maintain body homeostasis are involved with the ANS, including the control of food intake and weight regulation.[7,9] Although autonomic dysfunction may be involved in the pathogenesis of obesity, the excessive weight may also lead to changes in ANS function.[6,9] People with obesity showed a sympathetic dominance and a parasympathetic withdrawal.[6,10,11] Additionally, chronic overeating in obese people may promote sympathetic activation, which increases energy expenditure and thus normalizes body weight.[12] This activation of the SNS may occur as a homeostatic mechanism to prevent fat accumulation by stimulating lipolysis.[10,13] Even though previous studies reported the role of ANS in adult obesity,[9,14] the evidence of this association in childhood is scarce. Additionally, the majority of the studies have evaluated the autonomic function through the heart rate variability (HRV), providing information on the cardiac autonomic function.[15] However, recent studies recognised pupillometry as a useful, simple, non-invasive and valuable method to assess the autonomic function.[16,17] Therefore, the aim of this study was to assess the effect of obesity on the ANS activity in school-aged children.

MATERIAL AND METHODS

Setting and design

This study included participants from a cross-sectional study. Twenty out of the 53 primary schools in the city of Porto, Portugal, were randomly selected.[18] A total of 1602 children, aged between 7 and 12 years, were invited to participate. Of those, 686 failed to provide the signed parental informed consent form and 58 refused to perform the assessments. These last 58 children had significantly higher BMI z-score values than the included children, but no differences regarding age, sex, parental education, respiratory symptoms and asthma prevalence. Therefore, data from 858 children (50.6% boys), corresponding to a participation rate of 53.6%, were analysed.

The study was approved by the University Health Ethics Committee and informed consent was obtained from each children's legal guardians.

Participants and assessments

A self-administered ISAAC (International Study of Asthma and Allergies of Childhood)-based questionnaire was filled out by the children's guardians regarding demographic, social and behavioural information, as well as questions about respiratory/allergic health. The level of parental education was used as a proxy for socioeconomic status and it was recorded as the number of successfully completed years of formal education, which was categorized into three groups: less than 9 years; between 10 years and 12 years; and more than 13 years. Sleep duration was estimated based on the question "How many hours does your child sleep, on average, most days of the week?". Physical activity was defined based on a positive answer to the question "Does your child partake in any sports activity outside of the normal school-period, at least once a week?". Dietary intake was assessed from a single 24-hour recall questionnaire[19] administered to the participants, from which total energy intake was estimated using the Food Processor®, (ESHA Research, USA) software. Participants were questioned accurately about their food and drinks consumption, consuming time and place and food brands. Asthma was defined based on the medical diagnosis of asthma, symptoms over the past 12 months and/or at least 12% and over 200 mL increase in FEV1 after bronchodilation, as previously described by Silva *et al*.[20]

Clinical assessments and anthropometry were performed by a research nurse. Weight (kg) was measured using a digital scale (Tanita™ BC-418 Segmental Body Analyzer). Height (cm) was measured using a portable stadiometer. Body mass index (BMI) was calculated by using the ratio of weight/height^2 (kg/m^2) and classified into different categories (underweight, normal weight, overweight and obesity) according to age- and sex-specific percentiles determined by the World Health Organization (WHO),[21] the Centers for Disease Control and Prevention (CDC)[22] and the International Obesity Task Force (IOTF).[23] Underweight and normal weight categories were merged into the same category (underweight and normal weight category) due to the lower prevalence of underweighted children. Bioelectrical impedance analysis was performed to characterize body composition. Body fat percentage was classified according to sex-specific centile curves for body fat in children[24] and categorized into three categories (under fat and normal fat; overfat; and obese). Different criteria were used to categorize the BMI, since the establishment of different cut-offs is generally statistical rather than based on risk or the degree of body fatness. As a result, different definitions often do not give the same results.

A portable infrared PLR-200 pupillometer (NeurOptics PLR-200™Pupillometer, NeurOptics Inc.,CA) was used to perform pupillometry. The participants had to spend at least 15 minutes in a quiet and semi-dark room, for the pupil to adjust to the low lighting level. Then they were instructed to focus, with the eye that was not being tested, on a small object three meters away, keeping their eyes wide open and head straight during targeting and measurement. The

tested eye was briefly illuminated by light-emitting diodes with a single light stimulus having a peak wavelength of 180 nm. In case of blinking, the measure was repeated. A light response curve of the pupil was recorded for each child. Each participant had recorded its pupil diameter before (initial) and at constriction peak (final), in millimetres; the relative constriction amplitude, in percentage; the maximum constriction velocity (MCV), the average constriction and dilation velocities (ACV and ADV, respectively), in mm/s; and the total time taken by the pupil to recover to 75% of the initial resting pupil size after it reached the constriction peak (T75), in seconds. No side-to-side differences were observed in the pupil responses, so all pupillary data reported were from one eye. Pupillometry is a non-invasive and simple technique that provides data from both branches of the ANS.[17] The SNS controls pupil dilation and the PNS controls pupil constriction[17]; therefore, ADV and T75 are measures of sympathetic activity and pupil diameter, MCV, ACV and constriction amplitude are measures of parasympathetic activity.

Statistical analyses

Statistical analysis was performed using the IBM® SPSS™ Statistics version 26.0.0.0 for Windows and Microsoft Office Excel® (see detailed information on statistical analyses in supplementary material). Distribution of continuous variables were analysed for normality check by the Kolmogorov-Smirnov test. Since non-Gaussian distributions were observed, non-parametric tests were performed for descriptive statistics (median and 25th and 75th percentile). The Mann-Whitney test was used to compare continuous variables between the girls and the boys. The chi-square test was used to evaluate the differences between sex and categorical variables. The Kruskall-Wallis test was used to perform the post-hoc test and study the relationship between body mass categories and ADV measures. Significant differences were reported when the α-value was less than 5% ($p < 0.05$). Linear regression models were performed to determine the association between the body mass criteria and pupillometry parameters, using linear coefficients (β) and its respective 95% confidence interval (CI). Two models were considered for the analysis: model 0, the null model and model 1, adjusted for age, sex, parental education, physical activity, energy intake, sleep duration and asthma.

RESULTS

The prevalence of overweight ranged between 15.1% and 20.4%, according to the CDC and the WHO, respectively. The prevalence of obesity varied between 7.5% (IOTF) and 16.2% (percentage of body fat criteria), and no statistically significant differences were found between girls and boys (Table 1). The amplitude and maximum velocity of constriction were significantly higher in boys compared to girls (36.0% *vs* 35.0%, $p = 0.011$; and 5.38 *vs* 5.24 mm/s, $p = 0.011$, respectively). However, no statistically significant gender differences were found for the remaining pupillometry parameters (Table 1).

Statistically significant differences were found between the ADV and all the body mass criteria [Appendix 1, Table S1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/17144/15177)]. ADV was significantly higher in children with obesity compared to children with underweight/under fat and normal weight/normal fat (Fig. 1). There were no statistically significant differences between parameters related to PNS, T75 and the body mass criteria [Appendix 1, Table S1 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/17144/15177)].

An increase in BMI and percentage of body fat was associated with an increase in ADV, regardless of the used criteria [model 0, Appendix 1, Table S2 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/17144/15177)]. After adjustment for age, sex, parental education, physical activity, sleep duration, energy intake and asthma, a similar result was observed for BMI defined according to the CDC and percentage of body fat criteria and ADV. An increase in BMI and percentage of body fat was associated with higher ADV values (β = 0.053, 95% CI = 0.005 to 0.101, for CDC; and β = 0.063, 95% CI = 0.016 to 0.109, for the percentage of body fat). Although non-significant, the same trend was observed for BMI according to WHO and IOTF criteria and ADV (β = 0.045, 95% CI = -0.001 to 0.091, and β = 0.055, 95% CI = -0.001 to 0.111, respectively) (Fig. 2).

Additionally, CDC and WHO BMI z-scores were positively associated with the values of ADV (rs = 0.030, $p = 0.048$; and rs = 0.027, $p = 0.042$, respectively) [Appendix 1, Table S3 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/17144/15177)]. There were no statistically significant associations between the remaining parameters related to PNS, T75 and body mass criteria [Appendix1, Table S2 and Table S3 (Appendix 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/17144/15177)].

DISCUSSION

Our findings suggested an association between body mass and changes in the autonomic activity, namely with a sympathetic dysautonomia, in school-aged children. The average dilation velocity (ADV) was significantly higher in children with obesity compared to children with underweight/under fat and normal weight/normal fat, regardless of the criteria used.

Our study has a few limitations:

- The cross-sectional design does not allow us to establish a causal relationship.
- The use of BMI may be a limitation, since it depends only on body weight, regardless of body composition,[25] and does not allow distinction between fat mass and fat-free mass.[26] Nonetheless, the majority of people with high BMI have an excessive body fat.[27]
- The use of bioelectrical impedance analysis (BIA) in children and the measurement of the percentage of body fat to classify them may be a limitation.

Table 1 – Characteristics of the participants

Characteristics	Total	Girls	Boys	*p*-value
Age, y [mean (SD)]	8.76 (0.80)	8.77 (0.78)	8.75 (0.81)	0.648
Parental education, n (%)				0.345
0 - 9 y	219 (32.10)	97 (29.60)	122 (34.50)	
10 - 12 y	201 (29.50)	103 (31.40)	98 (27.70)	
≥ 13 y	262 (38.40)	128 (39.00)	134 (37.90)	
BMI, n (%)				
CDC				0.597
Underweight and normal weight	614 (72.70)	302 (72.60)	312 (72.70)	
Overweight	128 (15.10)	67 (16.10)	61 (14.20)	
Obese	103 (12.20)	47 (11.30)	56 (13.10)	
WHO				0.057
Underweight and normal weight	553 (65.40)	265 (63.70)	288 (67.10)	
Overweight	172 (20.40)	98 (23.60)	74 (17.20)	
Obese	120 (14.20)	53 (12.70)	67 (15.60)	
IOTF				0.532
Underweight and normal weight	614 (72.70)	295 (70.90)	319 (74.40)	
Overweight	168 (19.90)	88 (21.20)	80 (18.60)	
Obese	63 (7.50)	33 (7.90)	30 (7.00)	
Percentage of body fat				0.111
Under fat and normal fat	564 (67.70)	289 (70.80)	275 (64.70)	
Overfat	134 (16.10)	63 (15.40)	71 (16.70)	
Obese	135 (16.20)	56 (13.70)	79 (18.60)	
Asthma, n (%)	80 (9.30)	49 (11.60)	31 (7.10)	**0.034**
Physical activity, n (%)	494 (64.20)	227 (60.20)	267 (67.90)	0.029
Sleep duration, hours [mean (SD)]	9.34 (0.85)	9.35 (0.85)	9.33 (0.86)	0.652
Total energy intake, Kcal [mean (SD)]	2182.46 (604.58)	2087.69 (564.78)	2273.73 (627.97)	**< 0.001**
Pupillometry parameters				
Initial pupil diameter, (mm)	5.30 (4.70 - 5.90)	5.30 (4.60 - 5.90)	5.40 (4.80 - 5.90)	0.229
Final pupil diameter, (mm)	3.40 (3.00 - 3.80)	3.40 (2.90 - 3.80)	3.40 (3.00 - 3.80)	0.888
Constriction amplitude, (%)	35.00 (32.00 - 38.00)	35.00 (32.00 - 38.00)	36.00 (33.00 - 39.00)	**0.011**
ACV, (mm/s)	4.02 (3.57 - 4.42)	3.99 (3.52 - 4.40)	4.05 (3.62 - 4.45)	0.065
MCV, (mm/s)	5.31 (4.72 - 5.89)	5.24 (4.64 - 5.83)	5.38 (4.83 - 5.96)	**0.011**
ADV, (mm/s)	1.15 (0.99 - 1.33)	1.15 (0.99 - 1.34)	1.17 (0.99 - 1.33)	0.917
T75, (s)	1.67 (1.20 - 2.13)	1.67 (1.14 - 2.09)	1.67 (1.23 - 2.16)	0.275

BMI: body mass index; CDC: US Centers for Disease Control and Prevention; WHO: World Health Organization; IOTF: International Obesity Task Force; ACV: average constriction velocity; MCV: maximum constriction velocity; ADV: average dilation velocity; T75: the total time taken by the pupil to recover to 75% of the initial resting pupil size after it reached the constriction peak.
Data reported as median (25^{th}, 75^{th} percentile) unless otherwise stated.
Significant differences are in bold.

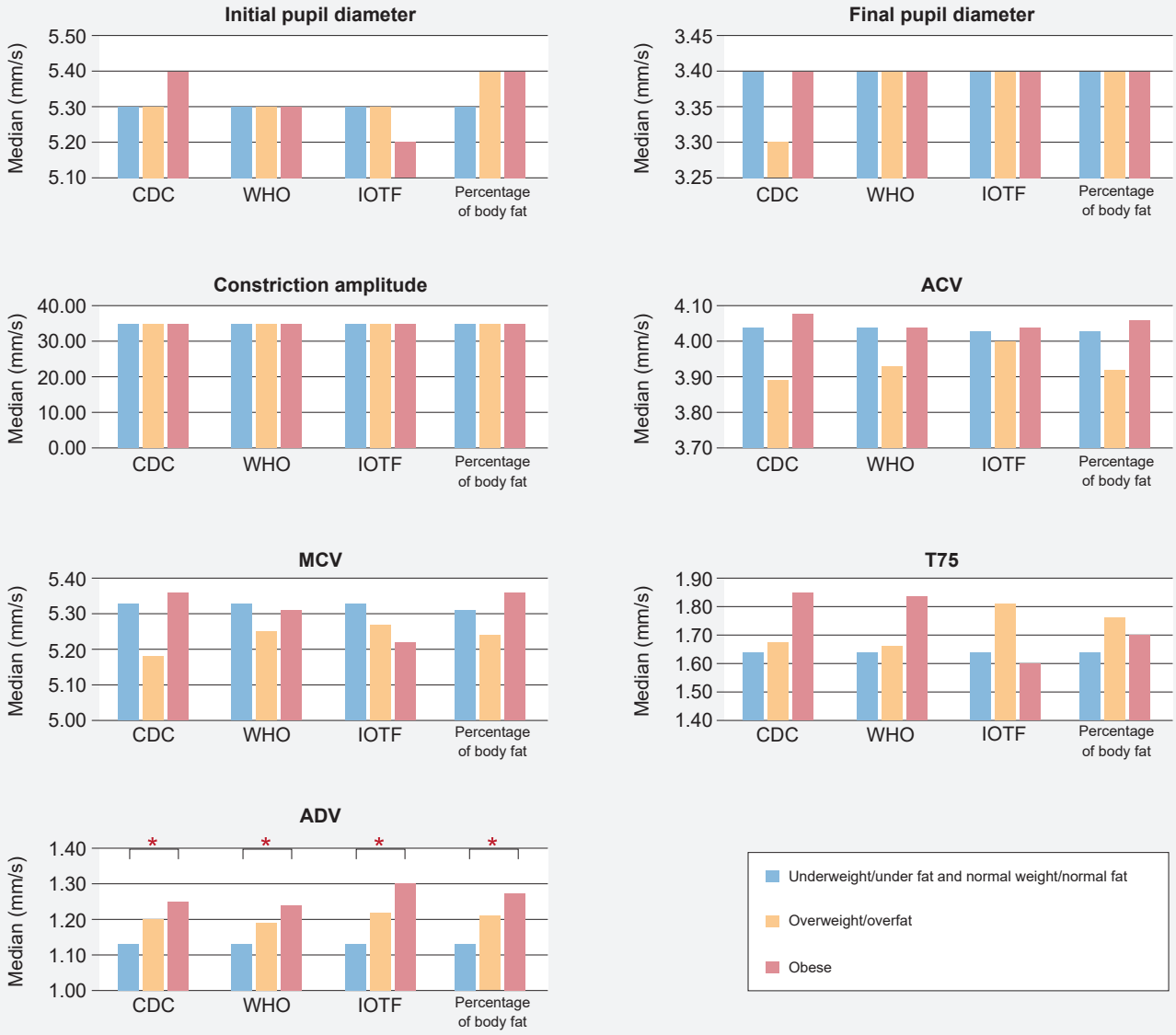

Figure 1 – Median of pupillometry parameters according to the different body mass criteria
CDC: US Centers for Disease Control and Prevention; WHO: World Health Organization; IOTF: International Obesity Task Force; ACV: average constriction velocity; MCV: maximum constriction velocity; ADV: average dilation velocity; T75: the total time taken by the pupil to recover to 75% of the initial resting pupil size after it reached the constriction peak.
*: $p < 0.05$

Children have a considerable variation in the amount of fat mass, total body water, total body protein and osseous mineral until they reach adulthood, which challenges the assessment of body composition.[28,29] Talma *et al.* concluded that BIA was not satisfactory as a valid method to estimate of the percentage of body fat in children and adolescents, although it was a practical method for that estimation.[30] Nevertheless, an almost perfect reproducibility was found in the percentage of body fat estimation through BIA in children and adolescents,[31] and this parameter has been adopted in several recent studies.[32,33] BIA is extensively used for population-based investigations, being a non-invasive, safe, quick and relatively low cost way of assessing body composition.[28]

- The use of total energy intake does not provide information about the quality of diet. Nonetheless, evidence suggests energy intake is related with portion sizes, and is associated with an increased risk of excessive body weight.[34] In addition, 24-hour recall was found to be an acceptable assessment of total energy intake at a group level,[35] being easy to apply,

cost-effective, and having a good compliance.[19]

- Physical activity assessment was based on a single question using self-reported data, which may not reflect how active the children really were and lead to some misclassification bias. Nevertheless, indirect methods of evaluation of physical activity in childhood are moderately correlated with direct methods,[36] and are a feasible approach to collect information about physical activity.[36]
- Birth weight was not included in the analysis, which might influence the results, since low birth weight children have been previously associated with having higher sympathetic activity.[37]
- The duration of obesity was not evaluated, limiting the assessment of the function and global activity of the ANS in children with obesity over time.[38]

Our study also has important strengths. This is, to the best of our knowledge, the first study assessing the association between body mass and the ANS in a large number of schoolchildren, using pupillometry. Pupillometry allows an accurate assessment of the ANS, in an easy, fast, non-invasive way.[39] In addition, the clinical assessments were performed in each primary school, considered as the normal environment for children, which may decrease the level of stress associated with clinical and physical assessments. Height and weight were measured, avoiding the bias associated with self-perceptions of weight by parents, who tend to underestimate their children's overweight/obese condition.[40] A recent systematic review and meta-analysis assessing the validity of BMI to identify obesity in children concluded that BMI had a high specificity to detect children with obesity.[25] The existence of entities using different BMI criteria makes it harder to unify results and draw conclusions out of studies.[25] However, in this study, we used different BMI criteria as well as the percentage of body fat to characterize schoolchildren. Our results suggested that, regardless of the BMI criteria, a significant association was observed between obesity and the ADV, but the strength of the association depends on the adopted definition.

Our findings showed that obesity was associated with higher values of ADV, suggesting a change in the activity of SNS among school-aged children with obesity. Similar

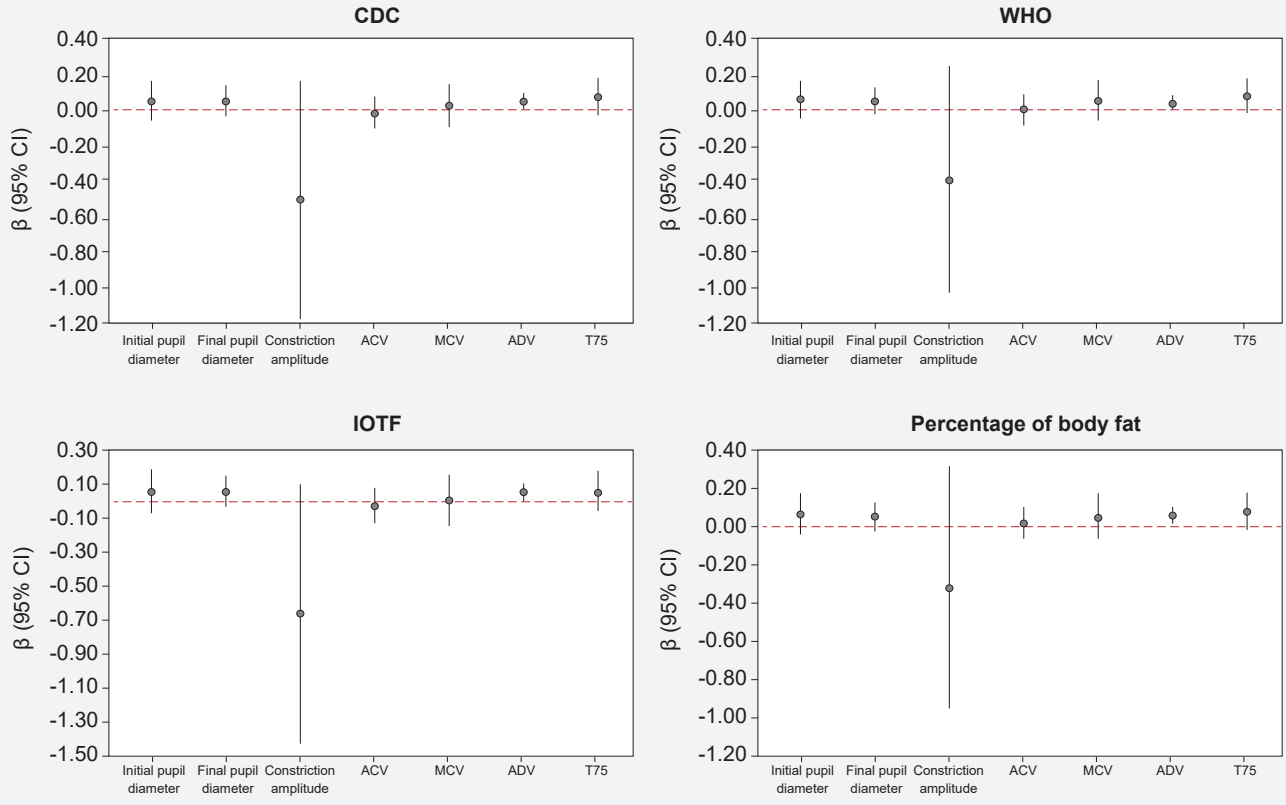

Figure 2 – Association between BMI and the percentage of body fat criteria and pupillometry parameters
CDC: US Centers for Disease Control and Prevention; WHO: World Health Organization; IOTF: International Obesity Task Force; ACV: average constriction velocity; MCV: maximum constriction velocity; ADV: average dilation velocity; T75: the total time taken by the pupil to recover to 75% of the initial resting pupil size after it reached the constriction peak.

studies reported a sympathetic dominance and a parasympathetic withdrawal among children and adolescents with obesity, using HRV to assess the ANS.[41,42] A study conducted in Germany including 149 children also demonstrated a change in ANS activity in overweight and obese children.[43] However, Baum *et al*[43] found a negative association between BMI and both pupil diameter and dilation velocity. Overweight and obese children had a lower dilation velocity and pupil diameter compared with normal weight children.[43] A Japanese study including 84 children assessed the ANS function through HRV and also found a decreased activity of the SNS and PNS in children with obesity. Interestingly, this study reported a negative correlation between HRV measures and the duration of obesity.[38] The differences between previous studies and our results may be explained by the continuous effect of obesity on ANS activity. As proposed by Nagai *et al*[38] a correlation may be observed between the activity of ANS and duration of obesity. Furthermore, a study performed in children with obesity showed an increase in sympathetic activity in participants with recent obesity (less than four years), while in participants with intermediate (four to seven years) or long (more than seven years) obesity, no changes were observed in the SNS activity, compared with participants with normal weight.[44] This decreasing trend of SNS activity suggests a biphasic behaviour of the cardiac SNS, in obesity.[44] However, our study did not evaluate the duration of obesity, not allowing the assessment of this effect on ANS activity. In addition, the categories of BMI used by the different studies may also be associated with the effect of obesity and ANS. Baum *et al*[43] classified overweight and obese participants into one category, whereas in our study these groups were classified separately, and we observed an association between children with obesity and ADV. Nevertheless, all studies suggested that obesity was associated with changes in the ANS.

The mechanisms related with sympathetic activation in obesity are still not fully understood. Landsberg[12] formulated a hypothesis advocating that the chronic overeating of people with obesity may promote a sympathetic activation intended to increase energy expenditure and normalize body weight. This activation of the SNS may occur as a homeostatic mechanism to prevent fat accumulation by stimulating lipolysis in the adipose tissue.[10,13] As a result of lipolysis, the free fatty acids (FFAs) pool will increase, contributing to insulin resistance[13] and lipotoxicity in the peripheral tissues that lead to metabolic dyshomeostasis, thus increasing the production of very low density lipoproteins in the liver, and promoting dyslipidaemia.[45] Further evidence supports the hypothesis of a sympathetic defence against obesity with an increased sympathetic activity in order to stimulate β-adrenergic thermogenesis, and to promote energy expenditure.[46] However, Guarino *et al*[9] reported that this feedback of the SNS may not favour the intended energy expenditure and, consequently, may not be associated with weight loss. The hyperactivity of the SNS may also be driven by the overexpression of several pro-inflammatory adipokines, including leptin, interleukin-6, tumour necrosis factor-α and angiotensinogen.[6,13] There are studies showing that weight loss reverses the sympathetic supremacy in people with obesity, being even associated with parasympathetic activation.[6,9] A study in children which assessed the HRV during a weight reduction program also showed a parasympathetic dominance.[47] The positive weight loss effects seem to be potentiated by the association of an hypocaloric diet with exercise.[6,48] In addition, Silva *et al* showed that a Mediterranean diet meal may also improve ANS function compared with an energetically similar fast food-like meal. The authors suggested that fast food meals may cause dysfunction of adipokines, increasing insulin secretion and, consequently, the activity of the SNS.[49]

Importantly, there is evidence showing that a dysfunction in the ANS may be implicated in the pathogenesis of obesity.[9] Guarino *et al*[9] reported a connection between the ANS and the GI system that keeps a balanced energy homeostasis. ANS is involved in the regulation of food intake and gastric emptying, by the action of gut hormones on vagal afferent neurons.[9] The exposure to a high fat diet impairs the capacity of the vagal afferents to react to GI peptides. The disruption of the GI vagal afferents causes amplified orexigenic (appetite inducer) and reduced anorexigenic signalling ability, which may be the cause for weight gain and obesity.[50] A chronic elevation of the SNS activity has been reported as being detrimental for the human body as it decreases the stimulation of the metabolism, and impairs β-adrenergic signalling, leading to changes in target tissues, which contributes to a vicious cycle of weight gain, worsening the state of obesity and associated comorbidities.[10,13] A sympathetic hyperactivity may also activate the adipose triglyceride lipase, increase the triglyceride hydrolysis, and thus promote the continuity of obesity.[9,45]

CONCLUSION

Our results suggested that childhood obesity may be associated with a change in the ANS activity, particularly a dysautonomia in the sympathetic activity. Moreover, our results highlight the need to create strategies to reduce the prevalence of obesity and, consequently, restore the balance of ANS.

AUTHOR CONTRIBUTIONS

BGT: Data analysis; conception and critical review of the manuscript.

IP, JCR: Data collection analysis and interpretation; critical review of the manuscript.

FM: Data collection and interpretation; clinical and physical evaluation; critical review of the manuscript.

MF: Data interpretation; critical review of the manuscript.

PP: Data analysis and interpretation; critical review of the manuscript.

PM: Data interpretation; critical review of the manuscript.

AM: Study design and first draft; conception of the manuscript; data interpretation; critical review of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

PM has patents planned, issued or pending for iMC Salt Control device.

All other authors have declared that no competing interests exist.

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