

การปรับสัญญาณของประสาทอัตโนมัติของหัวใจมีอยู่จริงหรือไม่ในวัยรุ่นไทยที่เป็นโรคอ้วน

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Does Cardiac Autonomic Modulation Exist in Obese Adolescents?

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หลักการและเหตุผล: การศึกษาครั้งก่อนๆ เกี่ยวกับผลของโรคอ้วนต่อสมดุลระหว่างซิมพาเทติกและพาราซิมพาเทติกของหัวใจในวัยรุ่นยังคงไม่ชัดเจน

วัตถุประสงค์: ตรวจสอบการทำงานของระบบประสาทอัตโนมัติของหัวใจ (cardiac autonomic activity : CAA) ในวัยรุ่นที่เป็นโรคอ้วนโดยใช้ spectral heart rate variability (HRV)

วิธีการ: วัยรุ่นที่มีดัชนีมวลกาย (body mass index, BMI) มากกว่าเปอร์เซ็นต์ไทล์ที่ 95 และมากกว่าเปอร์เซ็นต์ไทล์ที่ 5 แต่น้อยกว่าเปอร์เซ็นต์ไทล์ที่ 85 ซึ่งอิงตามอายุและเพศถือว่าเป็นโรคอ้วนและน้ำหนักปกติตามลำดับ อาสาสมัครทุกคนไม่มีอาการทางคลินิกที่แสดงถึงโรคหัวใจและปอด ใช้ low frequency (LF) (0.04-0.15 Hz) และ high frequency (HF) (0.15-0.4 Hz) spectral powers, LF and HF in normalized units (n.u.) และอัตราส่วนของ LF ต่อ HF เป็นดัชนีของ HRV เพื่อวัด CAA ทำการวัดค่า HRV (mean±SD) (median) เป็นเวลานาน 5 นาทีในท่านอนภายหลังนอนพักในท่าเดียวกันเป็นเวลา 10 นาที อาสาสมัครวัยรุ่นที่เป็นโรคอ้วนมีจำนวน 23 คน (ชาย 9 คน) อายุระหว่าง 12 ถึง 17 ปี และน้ำหนักปกติ 24 คน (ชาย 6 คน)

ผลการศึกษา: ค่าเฉลี่ยของ BMI ของอาสาสมัครวัยรุ่นที่เป็นโรคอ้วนและวัยรุ่นน้ำหนักปกติคือ 33.9 ± 5.0 kg/m² (median 33.0) และ 20.5 ± 1.6 kg/m² (median 20.3) ($p < 0.001$) ตามลำดับ ค่า spectral power แสดงปริมาณเป็น total power (TP), very low-frequency power (VLF), low-frequency power (LF), high-frequency power (HF) และอัตราส่วนของ LF

Background: Previous studies regarding the effect of obesity on cardiac sympathetic-parasympathetic balance in adolescents remain unclear.

Objectives: To examine the cardiac autonomic activity (CAA) in adolescent obesity using spectral heart rate variability (HRV).

Methods: A body mass index (BMI) greater than 95th and more than 5th but less than 85th percentile according to age and sex were accepted as obesity and normal weight, respectively. None of the subjects had clinical evidence of cardiopulmonary disease. Low frequency (LF) (0.04-0.15 Hz) and high frequency (HF) (0.15-0.4 Hz) spectral powers, LF and HF in normalized units (n.u.), and the ratio of LF to HF were used as the conventional indices of HRV to measure CAA. HRV (all as mean±SD) (median) was measured for 5 minutes in the supine position after 10 minutes of rest in the same position. The subjects were 23 obese adolescents (9 male), aged 12 to 17 years, and 24 normal-weight peers (6 male).

Results: The averaged values of the BMI of obese and healthy subjects were 33.9 ± 5.0 kg/m² (median 33.0) and 20.5 ± 1.6 kg/m² (median 20.3) ($p < 0.001$), respectively. The spectral power was quantified in total power (TP), very low-frequency power (VLF), low-frequency power (LF), high-frequency power (HF) and LF to HF ratio. LF and HF expressed in normalized unit were also calculated. When compared with healthy adolescents, no significant

ต่อ HF สำหรับค่า LF และ HF ซึ่งแสดงเป็น normalized unit ถูกคำนวณเช่นกัน เมื่อเปรียบเทียบกับอาสาสมัครวัยรุ่นที่มีน้ำหนักปกติพบว่าไม่มีการลดลงอย่างมีนัยสำคัญทางสถิติใน R-R interval, TP, VLF, LF, HF และ LF/HF ในวัยรุ่นที่เป็นโรคอ้วน

สรุป: ไม่มีการปรับสัญญาณของประสาทอัตโนมัติของหัวใจ ซึ่งเป็นผลพวงของความอ้วนในวัยรุ่น จากผลการศึกษาครั้งนี้ไม่สนับสนุนข้อสรุปที่ว่าโรคอ้วนเพิ่มการกระตุ้นการทำงานของซิมพาเทติกและ/หรือลดการทำงานของพาราซิมพาเทติกในวัยรุ่นไทย

คำสำคัญ: heart rate variability, การปรับสัญญาณของประสาทอัตโนมัติของหัวใจ, โรคอ้วนในวัยรุ่น

reductions were observed in; R-R interval, TP, VLF, LF, HF and LF/HF in obese adolescents.

Conclusions: There was no cardiac autonomic modulation as a consequence of obesity in adolescents. Our findings do not support the conclusion that obesity increases sympathetic activation and/or reduces parasympathetic tone.

Key words: heart rate variability, cardiac autonomic modulation, adolescent obesity

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Introduction

Recently, data from a nation-wide survey of 47,389 grade 6 students from 268 primary schools in the urban settings in Thailand indicate that 16.7 % of them were overweight and obese¹. More importantly, obesity is a major public health burdens worldwide. The current remarkable rise of childhood and adolescent obesity is a threat of a future cardiovascular disease as these youth reach the adult years². Several health problems associated with obesity in adult including type 2 diabetes, cardiovascular disease, renal vascular disease, asthma, arthritis, certain neoplasm are probably consequences of childhood adiposity³⁻⁵. Moreover, obese children demonstrate higher systolic blood pressure compared to healthy peers^{6,8}. Clearly, there is an association between obesity and hypertension but underlying mechanisms has not been identified. In recent years, heart rate variability (HRV) has been used as one of the noninvasive methods to quantitatively assess cardiac autonomic function⁹. Most studies have shown that obese children have reduced parasympathetic activity compared to those normal-weight counterparts^{6,8, 10-13}. Studies indicating no differences^{8, 13} or an increase^{6, 12, 14-15} or a decrease¹⁰ in sympathetic activities

coupled with a reduction in parasympathetic activity between obese and normal-weight children have been reported. Nevertheless, there have been disagreements over these investigations in regard to whether obesity in children is characterized by increased or decreased sympathetic to parasympathetic balance. We, therefore, investigated whether there was cardiac autonomic modulation in obese adolescents, as compared with normal-weight control, by analyzing frequency domain of HRV.

Methods

Participant Population

Twenty three obese (9 male) between the ages of 12-17 years and 24 normal-weight adolescents (6 male) in the same age group recruiting from a municipal area of Khon Kaen Province were included in this study. All studies took place at the Khon Kaen University. A BMI>95th percentile and 5th percentile<BMI<85th percentile according to age and sex were accepted as obese and normal-weight, respectively. Participants with clinical evidence of cardiopulmonary disease were not allowed to participate in this study.

Experimental Protocol

A standard informed consent including purpose, risks, and benefits were fully explained to each child and his/her parent or guardian. Written informed consent from the parent/guardian and assent from the participants were obtained before testing. The methods of this study were reviewed and approved by the Khon Kaen University Ethics Committee for Human Research. Hip circumference, waist circumference, height and weight were taken and BMI (kg/m^2) was calculated as the body weight (kg) divided by height squared (m^2). All measurements were performed according to World Health Organization (WHO) guidelines¹⁶.

HRV Analyses

Participants were prepared for electrode placement for measurement of R-R interval via a 3-lead electrocardiograph (EKG). After 10 minutes of rest in the supine position, the EKG was recorded for at least 5 minutes in the same position. The EKG (lead II) was digitally recorded continuously using a desktop computer and acknowledge data collection software (Biopac Systems, USA). Each signal was sampled at 1000 Hz throughout all testing. This programme allowed for instantaneous analog to digital conversion of the EKG with recording stored for off-line analysis. HRV refers to the beat-to-beat alteration in heart rate. In this study, it was measured by the frequency domain method. We performed a power spectral analysis by Fast Fourier transformation after being filtered through a Hamming window. Files were imported to a STATA software programme version 9.0 for descriptive analyses of HRV variables based on current recommendations⁹. All resting HRV variables were calculated from the last 5 minutes of resting period.

Power spectral density was quantified in total power (the energy in the heart period power spectrum between 0-0.4 Hz); very low frequency (VLF) (the energy of the spectrum power below 0.04), which it's physiological significance is obscure; low frequency (LF) (the energy of the spectrum power between 0.04 to 0.15 Hz), which indicate

primarily sympathetic nervous activity (SNS) with minor influence from parasympathetic activity; high frequency (HF) (the energy of the spectrum power between 0.15 to 0.4 Hz), which reflects solely parasympathetic activity of cardiac function. The LF to HF ratio reflects relative sympathovagal balance⁹. VLF, LF and HF power components were measured in absolute values of power (ms^2), but LF and HF were also measured in normalized units [$\text{n.u.}=(\text{LF or HF})/(\text{total power}-\text{VLF})$]¹⁸⁻¹⁹. The representation of LF and HF in n.u. emphasizes the controlled and balanced behaviour of the sympathetic (SNS) and parasympathetic (PSN) branches of the autonomic nervous system (ANS). Moreover, normalization tends to minimize the effect on the values of LF and HF components of the changes in total power. Nevertheless, as it is recommended that n.u. should always be quoted with absolute values of LF and HF power in order to describe in total the distribution of power in spectral components⁹, we, therefore presented LF and HF in n.u. as well as in ms^2 .

Statistical Analysis

Values were expressed as means±standard deviation (SD) and medians. Fitness to the normal distribution was carried out with the Shapiro-Wilk W test for normal data. Two-sample Wilcoxon rank-sum (Mann-Whitney) test when data showed departure from normality was used to compare differences in characteristics and the parameters of the HRV between obese and healthy adolescents. An α level of 0.05 was considered as statistical significance.

Results

Characteristics variables are summarized in table 1. As can be seen, significant differences were observed among the 2 groups for weight, BMI, waist, hip, and waist to hip ratio (WHR). Male to female ratio in the two groups were not matched. However, age and height were not different between the normal-weight and obese groups.

Table 1 Characteristics of the study participants.

Variables	Normal (N=24)		Obese (N=23)		p
	Mean±SD	median	Mean±SD	median	
Age (year)	14.7±1.4	15	14.7±1.6	14	NS
Male: Female	6:18		9:14		
Weight (kg)	52.1±5.3	51.5	89.4±16.4	90	0.0001
Height (cm)	1.59±0.06	1.59	1.62±0.08	1.61	NS
BMI (kg/m ²)	20.5±1.6	20.3	33.9±5.0	33.0	0.0001
Waist (cm)	70.1±5.8	70	99.1±11.5	98	0.0001
Hip (cm)	90.6±3.6	90	113.7±6.5	113	0.0001
WHR	0.77±0.06	0.77	0.88±0.07	0.86	0.0001

Values are mean±SD and median tested by Two-sample Wilcoxon rank-sum (Mann-Whitney) test. BMI, body mass index; WHR, waist to hip ratio

The HRV variables among obese and healthy adolescents at rest are shown in table 2 and figure 1. The obese group had similar R-R intervals compared with the normal-weight group (0.804±0.101, median 0.808 vs. 0.838±0.104, median 0.824 s).

Two major components of the HRV parameters were detectable at low and high frequencies in both obese and

normal-weight. In obese, the total variance of the spectrum was 749±583 ms² (median 552), and its VLF, LF, and HF components were 341±430 ms² (median 194), 170±114 ms² (median 150), and 233±249 ms² (median 146), respectively. The LF and HF when expressed in n.u. were 44.33±14.98 (median 40.99) and 54.21±14.82 (median 54.47), respectively. The LF/HF ratio was 0.97±0.64 (median 0.69).

Table 2 Spectral HRV parameters of the study participants.

Variables	Normal (N=24)		Obese (N=23)		p
	Mean±SD	median	Mean±SD	median	
R-R interval (s)	0.838±0.104	0.824	0.804±0.101	0.808	NS
TP (ms ²)	592±371	437	749±583	552	NS
VLF (ms ²)	225±167	169	341±430	194	NS
LF (ms ²)	163±150	103	170±114	150	NS
HF (ms ²)	203±136	145	233±249	146	NS
LF (n.u.)	41.22±16.37	37.21	44.33±14.98	40.99	NS
HF (n.u.)	58.63±16.38	62.78	54.21±14.82	54.47	NS
LF/HF	0.94±0.99	0.59	0.97±0.64	0.69	NS

HRV, heart rate variability; R-R, inter-beat; VLF, very low frequency; LF, low frequency power; LF (n.u.), low frequency normalized unit; HF, high frequency power; HF (n.u.), high frequency normalized unit; LF/HF, low frequency to high frequency ratio. Values are mean±standard deviation (SD) and median tested by Two-sample Wilcoxon rank-sum (Mann-Whitney) test.

The statistical analyses revealed that all of these HRV parameters were not significantly different from those of normal-weight (table 2 & figure 1) indicating that either SNS or PSN activity did not change in obese adolescents

compared with the normal-weight peers. It was also found that there were no gender differences for any of the HRV values (Data not shown).

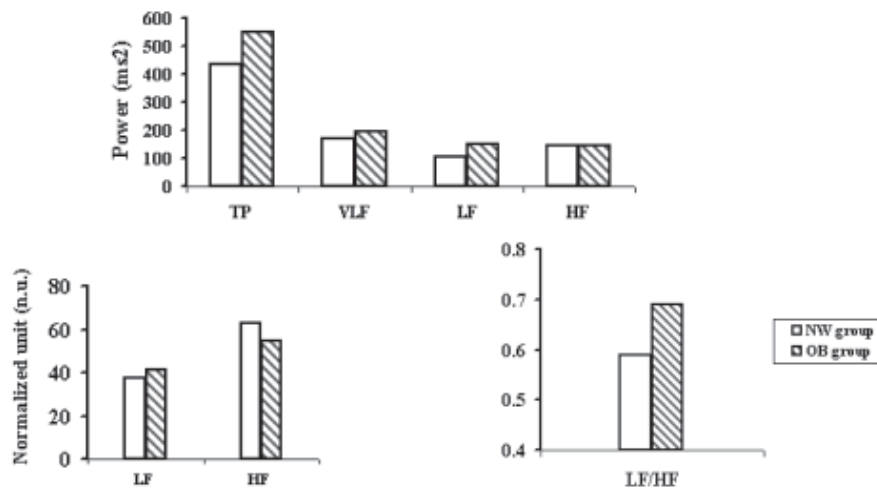


Figure 1 HRV indices, LF and HF in normalized unit, and LF to HF ratio in normal (NW) and obese (OB) groups at rest. Symbols are as in table 2. Values are medians.

Discussion

The aim of the present study was to examine whether the cardiac autonomic function of obese adolescents was altered when compared to healthy adolescents of similar ages. Our main findings have shown that adolescents with obesity had indices of HRV similar to those of normal-weight subjects. Thus, we did not find such an alteration in cardiac autonomic function in obese adolescents.

That no significant differences in HRV indices between the normal-weight and obese adolescents in the present study are in line with those reported recently¹¹. They showed that only children who were recently obese (< 4 years) had a significant increase in sympathetic activity, but for those who had been obese for > 4 years had no difference from healthy controls. We did not collect the exact duration of obesity but all participants have been obese since their childhood as interviewed by us. Thus the sympathovagal balance was still well preserved in Thai obese adolescents possibly being due to a long period of obesity. However, a number of studies published previously provide evidence that there are significantly lower PSN^{6, 7, 9-13}, and an increased

sympathovagal balance^{8, 12, 14, 17} in obese adolescents. Interestingly, no differences in sympathetic activity but reduced parasympathetic nervous system activity¹³ or reductions in both SNS and PSN, and hence LF/HF ratio in obese compared to normal-weight children have also been reported¹⁰. This suggests that the discrepancy observed in different studies might be due to the duration of obesity as suggested previously¹¹ and/or the level of physical activity, dietary and behavioural habits¹⁰ and male to female ratio studied as well. We found trends for higher LF (n.u.), lower HF (n.u.) and higher LF/HF ratio, although not significantly, among obese and normal-weight adolescents. Thus, it is crucial to promote cardiovascular health which is influenced by physical activity, fitness and fatness since youth irrespective of normal cardiac autonomic system functions.

Conclusion

The present study demonstrates data which indicate that obese adolescents are not characterized by cardiac autonomic modulation.

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