Altered hemodynamic regulation and reflex control during exercise and recovery in obese boys

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Dipla K, Zafeiridis A, Koidou I, Geladas N, Vrabas IS. Altered hemodynamic regulation and reflex control during exercise and recovery in obese boys. Am J Physiol Heart Circ Physiol 299: H2090–H2096; 2010. First published October 15, 2010; doi:10.1152/ajpheart.00087.2010. — The aims of the present study were to assess in obese and lean boys 1) the hemodynamic responses and baroreflex sensitivity (BRS) to isometric handgrip exercise (HG) and recovery and 2) the muscle metaboreflex-induced blood pressure response and the variables that determine this response. Twenty-seven boys (14 obese and 13 lean boys, body mass index: 29.2 ± 0.9 vs. 18.9 ± 0.3 kg/m², respectively) participated. The testing protocol involved 3 min of baseline, 3 min of HG (30% maximum voluntary contraction), 3 min of circulatory occlusion, and 3 min of recovery. The same protocol was repeated without occlusion. At baseline, no differences were detected between groups in beat-to-beat arterial pressure (AP), heart rate (HR), and BRS; however, obese boys had higher stroke volume and lower total peripheral resistance than lean boys (P < 0.05). During HG, lean boys exhibited higher HR and lower BRS compared with their obese counterparts. In lean boys, BRS decreased during HG compared with baseline, whereas in obese boys, it was not significantly modified. In lean boys, TPR was elevated during HG and declined after exercise, whereas in obese boys, TPR did not significantly decrease after exercise cessation. In the postexercise period, BRS in lean boys returned to baseline, whereas an overshoot was observed in obese boys. Postexercise BRS was correlated with body mass index (whereas an overshoot was observed in obese boys). Postexercise BRS did not significantly decrease after exercise cessation. In addition, based on previous reports in obese children, the increased prevalence of hypertension (34) has been linked to alterations in cardiovascular functioning and reflex-mediated regulatory mechanisms. More specifically, obesity is characterized by sympathetic nervous system (SNS) overactivity in many organs, such as the kidneys and muscles, in the basal state, and reduced SNS responsiveness to physiological stimuli, such as hyperinsulinemia (46). In normotensive obese adults, muscle sympathetic nerve activity at rest (27) is increased, whereas it is blunted after metaboreflex activation (27). This diminution is partially reversible after weight loss (42). In contrast, SNS activity to the heart is reduced in normotensive obese patients, whereas it is normal or increased in hypertensive obese patients (45). These dysfunctions have been partly related to the baroreflex downregulation and reduced insulin sensitivity (8, 10) that accompany obesity.

In children, increased levels of adiposity have also been partially linked to autonomic nervous system dysfunction and an increased prevalence of hypertension in adulthood (17). Yet, the mechanisms by which the excess weight is translated into hypertension remain unresolved. Increased resting blood pressure (BP) (36), reduced baroreceptor sensitivity (BRS) (24) and HR variability (HRV) (20) as well as decreased resting forearm blood flow have been reported from an early stage in obese children (37). However, the regulation of hemodynamic variables during sympathetic system activation, the role of muscle metaboreflex, and its interaction with arterial baroreflexes in the regulation of BP in childhood obesity have not been examined. Isometric exercise has been used as a mean for evaluating autonomic nervous system function and ability for prompt adjustments in hemodynamic regulation (32) that might not be apparent at resting measurements. Therefore, the first purpose of this study was to test the hypothesis that obese compared with lean prepubertal boys exhibit differences in hemodynamic regulation and baroreflex control during isometric handgrip (HG) exercise and recovery. The second purpose was to assess the MAP response during metaboreflex activation and to examine the hemodynamic variables that determine this response. We anticipated that obese normotensive boys would exhibit similar MAP with lower BRS and peripheral resistance adaptations during exercise and recovery. In addition, based on previous reports in obese normotensive adults, we hypothesized that obese boys would demonstrate a blunted MAP response during the isolated metaboreflex compared with their lean counterparts.

MATERIALS AND METHODS

Participants. A total of 27 children (11–12 yr old) with stable body weight over the past 3 mo were recruited for the study. The sample comprised 13 lean boys [body mass index (BMI): 18.9 ± 0.3 kg/m², 11.8 ± 0.22 yr old, Tanner stage 1–2] and 14 obese boys (BMI: 29.2 ± 0.3 kg/m², 10.9 ± 0.4 yr old, Tanner stage 1–2). The inclusion criteria were: 1) age 11–12 yr, 2) BMI ≥ 85% above the 95th percentile for age and sex, 3) Tanner stage 1–2 and 4) no history of cardiac disease and hypertension. The study protocol was approved by the Institutional Review Board of Serres University of Athens and the parents gave their written informed consent.

CARDIOVASCULAR AND HEMODYNAMIC ADAPTATIONS TO EXERCISE ARE REGULATED BY THREE NEURAL MECHANISMS: 1) “CENTRAL COMMAND,” WHICH ORIGINATES IN THE HIGHER BRAIN (9); 2) THE “EXERCISE PRESSOR REFLEX,” A PERIPHERAL “FEEDBACK” MECHANISM THAT TRANSMITS NERVE IMPULSES RELATED TO MECHANICAL, CHEMICAL, OR THERMAL STIMULI. 3) THE “METABOREFLEX,” THE INTERACTION BETWEEN THE MUSCLE BAROREFLEX AND SYSTEMIC BAROREFLEX. THE METABOREFLEX IS >5 TIMES MORE POWERFUL THAN THE BAROREFLEX, DUE TO THE AMPLIFICATION OF THE BAROREFLEX BY THE MUSCLE, AND IS MODULATED BY NEUROTRANSMITTERS SUCH AS NOREPINEPHRINE, ADRENALINE, AND PROSTAGLANDINS. THE METABOREFLEX, TOGETHER WITH THE BAROREFLEX, REGULATES THE HEMODYNAMIC RESPONSES TO EXERCISE.

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All participants were “healthy,” that is, they had no evidence of any major cardiovascular, respiratory, metabolic, or renal disease and were not using any medication. More specifically, participants had fasting glucose levels of <100 mg/dl, a normal thyroid-stimulating hormone, free thyroxine, and lipedemic profile, and BP levels within the normal range. This study was in accordance with the Declaration of Helsinki of 1975, as revised in 1983, and was approved by the institutional Review Board Committee. All risks and benefits were explained to the children and their parents. Each child’s parent signed the written informed consent form and completed a medical questionnaire. The participant was asked to follow his normal diet, to abstain from intense exercise activity for 48 h before the study, and to have sufficient rest the night before the study.

Testing procedures and instrumentation. After the participants’ arrival at the laboratory, they were oriented and familiarized with the experimental procedures, and their physical characteristics were assessed. Height and body mass were measured using a stadiometer and a weighting scale (SECA, Hamburg, Germany). BMI (in kg/m²) was calculated, and the pubertal development (Tanner score) was assessed. Consequently, maximal voluntary contraction (MVC) was evaluated using a Jamar hydraulic dynamometer (5030J, Sammons Preston, Chicago, IL). The participant performed three maximal isometric HG trials with the dominant hand (elbow flexed at 90°, with a 60-s interval in between trials), and the highest reading produced was considered as the MVC. The participant then remained idle for ~12–15 min while the preparation of the ECG electrodes took place. An inflatable cuff for arterial occlusion was placed on the upper arm of the dominant hand. Beat-to-beat BP was obtained from the middle finger of the nondominant hand, which was supported at the heart’s level, using finger photoplethysmography (Finometer, Finapres Medical Systems, Amsterdam, The Netherlands). Before the initiation of the protocol, an automated sphygmomanometer (Omron, Matsuakura, Japan) was used to measure brachial artery BP in the dominant arm to verify Finapres measurements of absolute BP. The Finapres system was calibrated according to the manufacturer’s instructions. The Finometer has been shown to track acute changes in BP at rest and during laboratory testing including exercise, providing accurate estimates of intraarterial pressure (30).

The experimental procedures consisted of two protocols: 1) a postexercise circulatory occlusion protocol (PECO) and 2) a control protocol, without PECO (non-PECO). The PECO protocol began with a 3-min rest period (baseline). Next, the participant performed 3 min of isometric HG exercise at 30% MVC. During HG exercise, the participant had visual feedback to maintain force output to the predetermined percentage of his MVC. The participant was also requested not to tense any other muscles apart from those of the forearm and to continue squeezing the dynamometer at the predetermined intensity for the whole duration of the exercise period to minimize metabolite release into the systemic circulation. Ten seconds before the cessation of exercise, the cuff on the exercising arm was rapidly inflated to suprasystolic levels (50 mmHg above peak exercise arm systolic BP), causing circulatory occlusion, as this protocol has been shown to trap the muscle metabolites and stimulate the metaboreceptors (5). The circulatory occlusion period (+occlusion) was maintained for 3 min after the cessation of exercise. After the cuff was deflated, a 3-min recovery period followed. After a subsequent 60-min recovery period, the participant repeated the same protocol without circulatory occlusion (non-PECO): 3 min of rest (baseline), 3 min of exercise (HG exercise), 3 min without occlusion (−occlusion), and 3 min of recovery. The order of the PECO and non-PECO protocols was random. Children were instructed to breathe normally during exercise. In addition, an experienced researcher closely monitored the participant’s respiration during testing to avoid the Valsalva maneuver.

During the protocols, arterial (systolic and diastolic) BP and HR were continuously recorded. SV was computed by arterial pressure wave analysis, the Modelflow method, as described by Jansen et al. (18). Briefly, this method derives an aortic flow waveform from arterial pressure by simulation of a nonlinear three-element aortic input impedance model and integrates SV from the flow waveform. The flow pulsation is integrated over a period between the beginning of the upstroke and notch to yield SV. The method is fully automatic, has a fast response, and is very accurate in tracking changes in SV (SD 7%) (47). In addition, this noninvasive method has been shown to be a reliable alternative to invasive thermodilution techniques (18). Mean values in BP (MAP), SV, and total peripheral resistance (TPR) were calculated using BeatScope software (version 1.1). The effect of metaboreflex on MAP was assessed as the difference in MAP values between the +occlusion and −occlusion periods. BRS (in ms/mmHg) was assessed by the sequence method (14) using BeatScope software (BeatScope 1a, Finometer, Finapres Medical Systems). Briefly, this method consists of the identification of episodes of consecutive beats in which BP ramps (upward or downward) are followed by similar R-R interval alterations. The slope of these sequences has been considered as an index of BRS (14). HRV was assessed according to the recommendations of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (40a). Briefly, a continuous ECG was obtained from a chest lead (MP150, Biopac, Santa Barbara, CA). R-R interval series were checked for ectopic beats or artifacts using a detecting algorithm followed by visual inspection. The HRV analysis was performed using HRV Analysis software 1.1 (kindly provided by The Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Kuopio, Finland; http://venda.uku.fi/research/biosignal). The root mean square of successive differences (RMSSD) was computed in the time domain as an index of parasympathetic activity (40a). A Poincaré plot analysis was also used, as this quantitative method is based on the notion of different temporal effects of changes in vagal and sympathetic modulation of HR on the subsequent R-R intervals without a requirement for stationarity of data, as previously described (43). The Poincaré plot is a two-dimensional graphic representation of the correlation between consecutive R-R intervals in which each interval is plotted against the following interval (43). An ellipse is fitted to the shape formed by the plot, and the SD1 and SD2 indexes are formed. The SD1 index reflects beat-to-beat variability and represents parasympathetic activity (43). The SD2 index reflects the overall variability, and the ratio of SD2 to SD1 reflects the long-term to short-term balance.

Statistical analysis. Data are reported as means ± SE. Differences in physical characteristics and MVCs between the two groups were assessed by Student’s t-tests for independent samples. For statistical analysis, the Finapres-derived physiological variables were averaged over the 3-min periods. Three-way ANOVAs (group × PECO × time) with repeated measures on “PECO” and “time” were used, followed by Newman-Keuls post hoc tests. Linear regression was used to determine the relationship of BRS with BMI. Statistical significance was set at α = 0.05. All analyses were conducted using Statistica (version 7, StatSoft, Tulsa, OK).

RESULTS

Subject characteristics. By study design, the obese group had significantly higher (P < 0.001) body mass (43.6 ± 2.0 vs. 74.1 ± 3.2 kg in lean vs. obese boys, respectively) and BMI (18.9 ± 0.3 vs. 29.2 ± 0.9 kg/m² in lean vs. obese boys, respectively) than the lean group. No differences were detected between the two groups in age (11.83 ± 0.22 and 11.74 ± 0.23 yr old in lean and obese boys, respectively), height (1.51 ± 0.3 vs. 1.59 ± 0.01 m in lean vs. obese boys, respectively, P = 0.051), and MVC (25.4 ± 1.9 vs. 28.4 ± 2.18 kg in lean vs. obese boys, respectively).
Hemodynamic responses and metaboreflex evaluation. Absolute values for MAP and heart rate (HR) during the PECO and non-PECO protocols are shown in Table 1. During baseline, no differences were detected between lean and obese boys in MAP and HR (in the PECO and non-PECO protocols). During HG exercise, a significant increase \( (P < 0.05) \) compared with baseline levels was detected in MAP and HR in both groups. Although during exercise MAP was not significantly different between the groups, HR was higher \( (P < 0.05) \) in lean boys than in obese boys in both protocols. During the \(+/-\) occlusion period, MAP remained elevated \( (P < 0.05) \) similar to HG exercise, whereas HR significantly declined compared with HG exercise, in lean and obese boys in the PECO protocol; MAP and HR significantly declined compared with HG exercise in lean and obese boys in the non-PECO protocol. During the recovery period, no differences were detected between the groups in MAP and HR in both protocols. Obese boys had higher \( (P < 0.05) \) absolute SV and lower TPR than lean boys at rest and throughout the protocols.

In separate analyses, MAP and its determinants, HR, SV, and TPR were calculated as differences from resting values (changes from baseline). \( \Delta \)MAP responses during the protocols are shown in Fig. 1A. During HG exercise, \( \Delta \)MAP was not significantly different between lean and obese boys (PECO protocol: 24.4 ± 2.0 vs. 21.4 ± 1.9 mmHg in lean vs. obese boys and non-PECO protocol: 22.7 ± 2.6 vs. 19.6 ± 1.5 mmHg in lean vs. obese boys). During the \(+/-\) occlusion period, \( \Delta \)MAP remained elevated similarly to HG exercise in lean and obese boys in the PECO protocol (i.e., during the occlusion), whereas \( \Delta \)MAP declined \( (P < 0.05) \) from HG exercise in both groups in BRS (lean boys: 13.27 ± 0.91 ms/mmHg in the lean group within the same time period; \*\); HR responses during the protocols are shown in Fig. 1B. During HG exercise, \( \Delta \)HR was higher in lean boys than in obese boys in both protocols (PECO protocol: 16.73 ± 2.3 vs. 10.4 ± 1.7 beats/min in lean vs. obese boys and non-PECO protocol: 14.5 ± 1.6 vs. 8.2 ± 1.3 beats/min in lean vs. obese boys, \( P < 0.05) \). During the \(+/-\) occlusion period, \( \Delta \)HR significantly declined \( (P < 0.05) \) from HG exercise in both protocols. \( \Delta \)HR responses during this period were not significantly different in lean and obese boys in the PECO protocol than their respective values in the non-PECO protocol. During the recovery period, no differences were observed between the groups in \( \Delta \)HR in both protocols.

\( \Delta \)SV and \( \Delta \)TPR responses during the protocols are shown in Fig. 1, C and D, respectively. During HG exercise, \( \Delta \)SV and \( \Delta \)TPR were not significantly different \( (P = 0.07–0.13 \) and \( P = 0.58–0.69, \) respectively) between lean and obese boys within the same protocol. During the \(+/-\) occlusion period, \( \Delta \)SV was not different in lean boys in the PECO versus non-PECO protocol, whereas \( \Delta \)TPR was higher in the PECO protocol, and \( \Delta \)SV \( (P < 0.05) \) was higher in the PECO versus non-PECO protocol in obese boys \( (8.7 ± 2.3 vs. 4.6 ± 0.9 \) mmHg, respectively), whereas \( \Delta \)TPR was not significantly different between the two conditions. In addition, in the lean group during the non-PECO protocol, \( \Delta \)TPR decreased \( (P < 0.05) \) compared with HG exercise, whereas in obese boys during the same (non-PECO) protocol, \( \Delta \)TPR was not significantly modified compared with HG exercise levels.

BRS. Absolute BRS data during the PECO and non-PECO protocols in both groups are shown in Fig. 2A. None of the participants exhibited BRS values that were indicative of hypertension (i.e., resting BRS of 97 ms/mmHg) \( (11) \).

During baseline, no differences were observed between the two groups in BRS (lean boys: 13.27 ± 1.68 and 14.63 ± 1.87 mg/mmHg in the PECO vs. non-PECO protocol and obese boys: 14.53 ± 1.12 and 12.88 ± 0.91 mmHg in the PECO vs. non-PECO protocol). However, the obese and lean groups followed a different response \( (P < 0.05) \) in BRS during the time course of the protocols. During HG exercise, BRS in lean boys significantly declined from baseline \( (7.16 ± 0.89 \) and 8.03 ± 0.90 mmHg in the PECO and non-PECO protocols, respectively). During the \(+/-\) occlusion period, BRS significantly declined \( (P < 0.05) \) in lean boys \( (8.22 ± 1.81 \) and 6.34 ± 1.72 mmHg, respectively) and increased \( (P < 0.05) \) in obese boys \( (3.22 ± 1.21 \) and 3.90 ± 1.54 mmHg, respectively) in the PECO protocol. During the recovery period, no differences were observed between the groups in BRS in both protocols.

### Table 1. Absolute BP and HR measurements in lean and obese boys

<table>
<thead>
<tr>
<th>Mean BP, mmHg</th>
<th>HG Exercise</th>
<th>+/- Occlusion</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PECO protocol</td>
<td>88.3 ± 2.5</td>
<td>112.7 ± 3.2*</td>
<td>107.7 ± 3.3*</td>
</tr>
<tr>
<td>non-PECO protocol</td>
<td>89.4 ± 3.2</td>
<td>112.1 ± 3.3*</td>
<td>91.7 ± 3.1*$</td>
</tr>
<tr>
<td>Obese group</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PECO protocol</td>
<td>88.9 ± 1.9</td>
<td>110.3 ± 2.4*</td>
<td>106.7 ± 3.4*</td>
</tr>
<tr>
<td>non-PECO protocol</td>
<td>92.2 ± 2.7</td>
<td>111.8 ± 3.1*</td>
<td>91.4 ± 1.4*$</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lean group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PECO protocol</td>
<td>82.5 ± 2.2</td>
<td>99.2 ± 1.7*</td>
<td>80.1 ± 2.5*</td>
</tr>
<tr>
<td>non-PECO protocol</td>
<td>83.2 ± 2.4</td>
<td>97.7 ± 2.0*</td>
<td>79.7 ± 2.6*</td>
</tr>
<tr>
<td>Obese group</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>PECO protocol</td>
<td>81.2 ± 2.4</td>
<td>91.6 ± 2.4**</td>
<td>77.4 ± 3.3*$</td>
</tr>
<tr>
<td>non-PECO protocol</td>
<td>83.1 ± 2.3</td>
<td>91.3 ± 2.1**</td>
<td>78.2 ± 2.3*$</td>
</tr>
</tbody>
</table>

Values are means ± SE; \( n = 13 \) boys in the lean group and \( 14 \) boys in the obese group. BP, blood pressure; HR, heart rate; HG, isometric handgrip; \(+/-\) occlusion, postexercise with circulatory occlusion; –occlusion, postexercise without circulatory occlusion; PECO, postexercise circulatory occlusion. \*\( P < 0.05 \) vs. baseline within the same protocol; \#\( P < 0.05 \) vs. the PECO protocol in the same group within the same time period; \$\( P < 0.05 \) vs. respective values in the lean group within the same time period; \%\( P < 0.05 \) vs. HG exercise in the same group within the same protocol.

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A: average mean arterial pressure values with respect to baseline during the postexercise circulatory occlusion (PECO) and non-PECO protocols. *Significant vs. handgrip (HG) exercise the same protocol ($P < 0.05$); †significant vs. the PECO protocol in the same group within the +/-occlusion period ($P < 0.05$); ‡significant vs. within the +/-occlusion period within the same protocol ($P < 0.05$); ††significant vs. HG exercise within the same protocol ($P < 0.05$). B: average heart rate values (in beats/min) with respect to baseline during the PECO and non-PECO protocols. §significant vs. lean boys in the PECO protocol within the HG exercise period ($P < 0.05$); #significant vs. lean boys in the non-PECO protocol within the HG exercise period ($P < 0.05$); ††significant vs. the PECO protocol within the +/-occlusion period ($P < 0.05$). C: average stroke volume values with respect to baseline during the PECO and non-PECO protocols. *Significant vs. HG exercise within the same protocol and group ($P < 0.05$); †significant vs. the PECO protocol within the +/-occlusion period ($P < 0.05$); ††significant vs. the PECO protocol in the same group within the recovery period. D: average total peripheral resistance values with respect to baseline during the PECO and non-PECO protocols. *Significant vs. HG exercise within the same protocol and group ($P < 0.05$); †significant vs. lean boys in the PECO protocol within the +/-occlusion period ($P < 0.05$); #significant vs. lean boys in the non-PECO protocol within the +/-occlusion period ($P < 0.05$); ‡significant vs. the +/-occlusion period within the same group ($P < 0.05$).

cols), whereas BRS in obese boys was not significantly modified compared with baseline (11.74 ± 1.35 and 9.72 ± 0.73 ms/mmHg in PECO and non-PECO protocols). During this period, significant differences in BRS were observed between the two groups. During the +/-occlusion period, BRS in the lean group returned to baseline levels, whereas BRS in the obese group exceeded baseline levels ($P < 0.05$). During the same time period, BRS in lean children was significantly lower than BRS in obese children (lean boys: 10.01 ± 0.78 and 13.47 ± 2.16 ms/mmHg in PECO and non-PECO protocols vs. obese boys: 19.62 ± 1.8 and 19.29 ± 1.9 ms/mmHg in PECO and non-PECO protocols). When BRS values during PECO versus non-PECO protocol were compared, no significant differences within each group were detected. Thus, within each group, no significant effects of occlusion (metaboreflex) on BRS were observed. During the recovery period, BRS returned to baseline levels (lean boys: 13.07 ± 2.33 and 13.70 ± 2.54 in PECO and non-PECO protocols and obese boys: 16.94 ± 1.44 and 15.11 ± 1.41 in PECO and non-PECO protocols) in both groups. No differences were detected between groups during this period.

A significant linear correlation ($P < 0.05, R = 0.56$) between BRS during the PECO period and BMI was observed. As shown in Fig. 2B, lean boys exhibited more clustering in BRS response during the PECO period, whereas more dispersion in the BRS response was observed in obese boys.

**HRV.** To explore the mechanism of the lower rise in HR during exercise that was observed in obese compared with lean children, we proceeded with the HRV analysis (non-PECO protocol). No differences were detected during baseline between lean and obese boys in RMSSD (57.7 ± 5.59 vs. 56.66 ± 4.7 ms, respectively), SD1 (41.35 ± 4.4 vs. 38.42 ± 3.4 ms, respectively), SD2 (90.1 ± 6.3 vs. 91.8 ± 7.4 ms, respectively), and the SD2-to-SD1 ratio (2.3 ± 0.1 vs. 2.4 ± 0.2, respectively). Changes from resting values to HG exercise in the above indexes were calculated. During HG exercise,
DISCUSSION

The present study revealed signs of disturbed hemodynamic control and impaired BRS during exercise and recovery in obese boys. The BRS response during the postexercise period was positively correlated with BMI. Although the muscle metaboreflex control of BP was not found to be altered at this stage of childhood obesity, it was achieved via different mechanisms. Our findings may be indicative of the onset of damage of the autonomic nervous system and/or differences in muscle metabolism that are evident before alterations observed at rest and might be tracked subsequently into adulthood.

Hemodynamic regulation. BP increased during HG in both groups, which is consistent with findings in nonobese children (44), and this increase was comparable between groups. These findings are not in line with results by Ribeiro et al. (36), which reported unchanged MAP during HG exercise in lean 10-yr-old children and greater MAP at rest and during HG exercise in obese aged-matched children. The conflicting results between our study and the latter study could be partly explained by differences in the participants’ age (12 vs. 10 yr old, respectively) (25). Lenard et al. (25) demonstrated that cardiovascual autonomic function undergoes a gradual maturation from 7 to 14 yr and that carotid pulse pressure is higher in 11- to 14-yr-old children than in 7- to 10-yr-old children. Genetic factors (3) could also have influenced resting and exercise BPs, since it has been demonstrated that the offspring of parents with a family history of hypertension exhibit higher basal BP levels and greater MAP during mental stress and HG exercise than children of normotensive parents (3). Our obese participants were normotensive without a family history of hypertension. Differences in body fat distribution (31) could have also played a role.

The higher resting SV observed in the obese boys is partly the consequence of the expanded body mass (39), and their lower resting TPR is in accordance with findings in obese adults (8). Proposed underlying mechanisms for the chronic low resistance resting state in obese adults include hormonal and hemodynamic factors (8).

Differential control of HR, SV, and TPR in response to exercise and recovery was observed between groups. In lean boys, the increase in BP during exercise was mainly the result of the rise in HR and vasoconstriction, whereas in obese boys, it was less dependent on HR and relied more on SV. As previously shown in a paced heart model (28), the role of SV during HG exercise varies with the ability to elevate HR: in case of chronotropic insufficiency and preserved myocardial function, SV (through longer filling time and involvement of the Frank-Starling mechanism) instead of HR produces the increase in cardiac output and BP during HG exercise, when there is sufficient cardiac reserve. The participants’ postural position (i.e., seated) and the moderate intensity exercise used allowed the use of the SV reserve by the obese participants, which was sufficient to compensate for their reduced HR during exercise. The lower rise in HR during exercise that was observed in obese compared with lean children was, at least partially, the result of a lower vagal withdrawal, as reflected by their lower removal in RMSSD (22% decrease from baseline in obese children vs. 37% in lean children) and SD1 (21% decrease from baseline in obese children vs. 35% in lean children) indexes of HRV. A reduced capacity for TPR adaptations from exercise to recovery was evident in obese boys compared with lean boys, suggesting an early vascular dysfunction, possibly by the accumulation of adipose tissue surrounding the blood vessels. In support to our results, previous studies have reported forearm resistance vessel abnormalities in obese adolescents (37) and arterial endothelial dysfunction with intima media thickening at rest (6) and a blunted muscle perfusion response to lower limb dynamic exercise (19) in overweight children. Additional mechanisms that have been proposed in obese adults for the pathology of these dysfunc-
tions include augmentations in plasma leptin and rennin-angiotensin, increased adipokines, dyslipidemia (22), and mitochondrial dysfunction (41). The exact mechanism for the pathology of postexercise responses in obese children requires further investigation.

**BRS.** Resting BRS values were similar (7) or slightly lower (1) compared with previously reported values, which is possibly related to the different posture used, since BRS recordings during supine rest are higher than those recorded upright (7). Although in obese adults blunted resting BRS has been reported (40), we did not observe differences between obese and lean children at rest, which is in accordance with findings in adolescents (23) reporting no significant correlation between resting BRS and BMI.

In lean boys, the spontaneous baroreflex slope was attenuated during exercise compared with baseline, which is in line with reports in adults (16, 29). The functional role of the baroreflex during exercise has been a question of considerable debate. A number of studies have suggested that the baroreflex is actively involved in BP regulation during exercise by resetting to a higher pressure (33). In contrast, other studies have suggested that during exercise arterial baroreceptors are selectively attenuated. These contradictory results can be explained in part by differences in baroreflex measurement techniques. In several studies where a neck chamber device was used for BRS assessment, the resetting of the carotid baroreflex during exercise took place without a change in the maximal gain (33). However, in studies using dynamic analyses, such as the sequence technique (15) used in our study, a reduced baroreflex slope during exercise was reported. The sequence technique is a noninvasive technique that provides an index of the sensitivity of the baroreflex slope around the operating point of the reflex (13) and is different from the maximal gain obtained from logistic modeling of the stimulus-response curve (29, 35). Although Iellamo et al. (13) demonstrated that during HG exercise the reflex is largely operating near the linear region of the arterial pressure-pulse interval relationship, the possibility that the decrease in BRS during exercise reflects the movement of the operating point away from the centering point and closer to a locus of lower gain or a shift to a nonlinear region of the baroreflex-stimulus curve cannot be disregarded (29).

In obese boys, the BRS slope was not significantly modified by exercise, and it did not follow the same time pattern as in lean boys. During the postexercise period, BRS in lean boys returned to baseline, whereas an augmentation in BRS was observed in obese boys (in both PECO and non-PECO protocols). In fact, the postexercise augmentation in BRS was positively correlated with BMI levels. The different exercise-induced responses between the lean and obese children involved differences in vagal tone, as reflected by the sequence technique, which represents mainly vagally mediated responses (29), and HRV indexes (RMSSD and SD1). Future studies should also explore the role of different activation patterns of central command and skeletal afferents (26) between lean and obese children. The atypical BRS alterations after increased hemodynamic stress (i.e., exercise) precede alterations observed at rest and may identify an early stage of the disease.

**Metaboreflex control of BP.** To the best of our knowledge, this is the first study that examined the metaboreflex control of BP in obese normotensive children. The muscle metaboreflex is a powerful activator of the SNS, as reflected by the elevated TPR values during the occlusion period. During the isolated metaboreflex, we observed the phenomenon of “accentuated antagonism,” which is a progressive fall in HR, below resting levels, although BP remains high (16, 32). In lean boys, the maintenance of BP during the isolated metaboreflex relied mainly on peripheral vasoconstriction, as previously observed in adults (12). In contrast, in obese boys, SV significantly contributed to BP maintenance during the metaboreflex. In obese adult females during metaboreflex activation, muscle sympathetic nerve activity responses were blunted, supporting the idea that the increased fat content or the reduced glycolysis as a result of insulin resistance as well as an attenuation in muscle acidosis during exercise possibly contributed to this reduction (27). In our study, we did not observe blunted metaboreflex control of BP. Whether the observed differences between lean and obese boys in the hemodynamic control of the metaboreflex are also influenced by differences in muscle metabolite concentration, mitochondrial dysfunction, and insulin resistance remain to be elucidated.

In the postexercise period, when occlusion to nonocclusion was compared within each group, we did not observe any significant differences in spontaneous BRS, which is in accordance to the results by Iellamo et al. (16) in adults. Sala-Mercado et al. (38), who applied dynamic exercise in canines, reported an upward and rightward resetting of baroreflex control of HR with a decrease in BRS during metaboreflex activation. The different exercise mode, the metaboreflex evaluation method (postexercise occlusion vs. occlusion during dynamic exercise), as well as species differences possibly differently affected the metaboreflex control of BRS (12).

**Conclusions.** Obese children demonstrated differences in cardiovascular hemodynamic control during exercise and recovery compared with lean children that precede alterations detected at rest. The muscle metaboreflex-induced increase in BP was similar in obese and lean children; however, it occurred via different mechanisms: in lean boys, TPR was the major contributor to BP maintenance during the metaboreflex, whereas in obese boys, maintenance of BP during the metaboreflex relied mainly on SV. In childhood obesity, altered reflex control during exercise and recovery is evident even when metabolic syndrome is not fully developed.

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**DISCLOSURES**

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**REFERENCES**


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