Diet and Exercise Training Restore Blood Pressure and Vasodilatory Responses During Physiological Maneuvers in Obese Children

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Background—The effects of diet and diet plus exercise training on muscle vasodilatation during physiologic maneuvers in obese children are unknown. We tested the hypothesis that (1) blood pressure (BP) and forearm vascular conductance (FVC) responses during handgrip exercise and mental stress would be altered in obese children and (2) diet plus exercise training would restore BP and FVC responses during exercise and mental stress in obese children.

Methods and Results—Thirty-nine obese children (aged 10 ± 0.2 years) were randomly divided into 2 groups: diet plus exercise training (n = 21; body mass index [BMI] = 28 ± 0.5 kg/m²) and diet (n = 18; BMI = 30 ± 0.4 kg/m²). Ten age-matched lean control children (BMI = 17 ± 0.5 kg/m²) were also studied. Forearm blood flow was measured by venous occlusion plethysmography. BP was monitored noninvasively. Handgrip exercise was performed at 30% maximal voluntary contraction for 3 minutes. Stroop color word test was performed for 4 minutes. Baseline BP was significantly higher and FVC was significantly lower in obese children. During exercise and mental stress, BP responses were significantly higher and FVC responses were significantly lower in obese children. Diet and diet plus exercise training significantly reduced body weight. Diet and diet plus exercise training significantly decreased BP levels during exercise and mental stress. Diet plus exercise training, in contrast to diet alone, significantly increased FVC responses during exercise (3.7 ± 0.3 versus 5.6 ± 0.4 U; P = 0.01) and mental stress (3.5 ± 0.5 versus 4.5 ± 0.4 U; P = 0.02). After diet plus exercise training, BP and FVC responses during exercise and mental stress were similar between obese children and the control group.


Key Words: obesity ■ children ■ blood pressure ■ muscles ■ vasodilatation

Obesity has been considered one of the most worrisome health problems in occidental countries. More dramatic is that this epidemic has reached young individuals. The rate of obesity in children and adolescents has doubled in the past 3 decades in the United States. These statistics have directed our attention to a new challenge in human obesity. In recent years, our understanding about the implications of adulthood obesity has improved considerably. We have learned that cardiovascular functioning and regulatory mechanisms are altered substantially in human obesity. Muscle sympathetic nerve activity is increased during exercise and mental stress in obese individuals. In contrast, the reflexively mediated increase in muscle blood flow during these physiological maneuvers is attenuated in obese individuals. During the cold pressor test, muscle sympathetic nerve activity and muscle vascular resistance are increased in obese women compared with lean women. These neurovascular alterations seem to be linked to the exacerbated blood pressure levels during sympahtoexcitation. However, hemodynamic regulation during physiological maneuvers in childhood obesity is poorly understood.

Hypocaloric diet and exercise training have been recommended as a nonpharmacological treatment to obese adult individuals. This regimen reduces body weight, preserves lean body mass, and improves insulin sensitivity. In addition, diet plus exercise training, in contrast to diet alone, improves muscle vasodilatation during exercise in obese adult individuals. However, the effects of diet and/or exercise training on muscle vasodilatory responses during exercise and mental challenge in children with obesity are unknown.

In the present study we tested the hypothesis that (1) blood pressure responses and muscle vasodilatory responses to...
handgrip exercise and mental stress would be altered in obese children compared with lean children and (2) hypocaloric diet and exercise training in obese children would have greater effects on blood pressure responses and muscle vasodilatory responses during exercise and mental stress than diet alone.

**Methods**

**Study Population**

After written informed consent was obtained, 39 consecutive outpatient children from the Obesity Ambulatory of the Endocrinology Department, University of São Paulo Medical School, meeting the following inclusion/exclusion criteria were offered participation in the study: (1) age between 8 and 12 years; (2) body mass index (BMI) >95%; (3) no medication; (4) no evidence of metabolic, hormonal, and cardiovascular disease at the time of the study; and (5) no engagement in an exercise program. These children were randomly divided into 2 groups: hypocaloric diet plus exercise training (n=21; BMI 23 to 35 kg/m², z score BMI 2.8 to 6.13) and hypocaloric diet (n=18; BMI 24 to 35 kg/m², z score BMI 2.8 to 6.37). Obesity was defined according to the age- and sex-specific BMI cutoff criteria recently described. Ten age-matched normal control lean children were also studied (BMI 16 to 19 kg/m²). The study protocol was approved by the Human Subject Protection Committees of the Heart Institute and Clinical Hospital, School of Medicine, University of São Paulo.

**Measurements and Procedures**

**Anthropometric Measurements**

Body weight was measured with an electronic body weight scale with children dressed in a light T-shirt and shorts. Height was measured by Harpenden stadiometer. The body weight status was recorded as BMI and z score of BMI with the use of the LMS method.

**Forearm Blood Flow**

Forearm blood flow was measured by venous occlusion plethysmography. The nondominant arm was elevated above heart level to ensure adequate venous drainage. A mercury-filled silastic tube attached to a low-pressure transducer was placed around the forearm and connected to a plethysmograph (Hokanson). Sphygmomanometer cuffs were placed around the wrist and upper arm. At 15-second intervals, the upper cuff was inflated above venous pressure for 7 to 8 seconds. Forearm blood flow (mL/min per 100 g) was determined on the basis of a minimum of 4 separate readings. Forearm vascular conductance was calculated by dividing forearm blood flow by mean arterial pressure. The reproducibility of forearm blood flow measured at different time intervals in the same individual expressed as mL/min per 100 mL tissue in our laboratory is r=0.93.

**Blood Pressure and Heart Rate**

During mental stress, mean blood pressure was monitored noninvasively by a finger photoplethysmograph device (Finapress 2300; Ohmeda) on a beat-to-beat basis (AT/CODAS) at a frequency of 500 Hz. During handgrip exercise, mean blood pressure was monitored noninvasively and intermittently from an automatic and oscillometric cuff (DX 2710, Dixtal) placed on the ankle with cuff width adjusted to ankle circumference. Mean blood pressure was chosen because this parameter is measured accurately by the automatic and oscillometric device. The cuff inflated every 30 seconds. Heart rate was monitored continuously through lead II of the ECG.

**Handgrip Exercise**

After the maximal voluntary contraction (mean of 3 trials) was obtained, static handgrip exercise was performed with the dominant arm with the use of a handgrip dynamometer. Children were instructed to breathe normally during exercise and to avoid inadvertent performance of a Valsalva maneuver.

**Mental Stress Testing**

Mental stress was elicited by the Stroop color word test. During the Stroop color word test, subjects were shown a series of names of colors written in a different color of ink from the color specified. The children were asked to identify the color of the ink, not read the word.

**Insulin Resistance**

Plasma insulin levels were determined by an immunofluorometric AutoDELFIA device (Wallac Oy). Insulin resistance was estimated by homeostasis model assessment (HOMA score) and calculated with the following formula: fasting serum insulin (µU/mL)×fasting plasma glucose (mmol/L)/22.5.

**Blood Chemistry**

Blood samples were collected to determine concentrations of cholesterol and substractions (LDL and HDL cholesterol), triglycerides, and fasting blood glucose. Enzymatic calorimetric assays were used to analyze cholesterol and substractions and glucose levels.

**Dietary Protocol**

The basal energy requirements were estimated during the Food and Agriculture Organization/World Health Organization/United Nations University equation multiplied by a factor of 1.3. During 16 weeks, energy intake was 1400 kcal/d. The hypocaloric diet consisted of 50% to 70% carbohydrates, 10% to 15% protein, and 15% to 30% fat. On alternate weeks, every child visited the clinical nutritionist for a regular checkup. On each visit, the children were weighed and encouraged to record their intake to ensure adherence to the dietary protocol. The expected weight loss was ~5% to 10% of the initial weight.

**Exercise Training**

Exercise training consisted of three 60-minute exercise sessions per week during 4 months. Each exercise session consisted of 30 minutes of walking and/or jogging and 30 minutes of recreational exercise. The exercise intensity was established by heart rate levels that corresponded to an anaerobic threshold up to 10% below the respiratory compensation point obtained in a progressive cardiopulmonary exercise test. The anaerobic threshold was determined to occur at the point where there was a loss of linearity between oxygen uptake and carbon dioxide production or at the point where the ventilatory equivalent for oxygen or end-tidal oxygen partial pressure curves reached their respective minimum values and began to rise during the progressive exercise test. The respiratory compensation point was determined as the point where the ventilatory equivalent for carbon dioxide was the lowest before a systematic increase or where end-tidal carbon dioxide partial pressure reached a maximum value and began to decrease. The peak oxygen uptake was considered at the end of the cardiopulmonary exercise test on treadmill (ramp protocol with increments every minute up to exhaustion).

**Experimental Protocol**

**Protocol 1: Handgrip Exercise**

The arm was positioned for venous plethysmography. Baseline forearm blood flow, mean blood pressure, and heart rate were recorded for 3 minutes. Handgrip isometric exercise was performed for 3 minutes at 30% of maximal voluntary contraction. Blood pressure, forearm blood flow, and heart rate were recorded continuously during handgrip exercise.

**Protocol 2: Mental Stress**

Baseline forearm blood flow, mean blood pressure, and heart rate were recorded for 3 minutes. Mental stress was performed for 4 minutes. Blood pressure, forearm blood flow, and heart rate were recorded continuously during mental stress. The task difficulty was determined on completion of the protocol with the use of a standard 5-point scale: 0, not stressful; 1, somewhat stressful; 2, stressful; 3, very stressful; and 4, very very stressful.
Forearm vascular conductance increased significantly during handgrip exercise in lean children but not in obese children (Table 2). In contrast, forearm blood flow increased significantly in lean children but not in obese children (Table 2). During mental stress, forearm vascular conductance increased significantly in lean children but not in obese children, in whom forearm blood flow was unchanged (Table 2). Similarly, forearm vascular conductance increased significantly during mental stress in lean children (Figure 2). In contrast, in obese children, forearm vascular conductance was unchanged during mental stress (Figure 2). The comparisons between groups showed that the magnitude of forearm blood flow and forearm vascular conductance responses during mental stress, analyzed by the interaction of phase effect and time effect, was significantly lower in obese children compared with lean children (P<0.01 and P=0.02, respectively; Table 2, Figure 2).

Statistical Analysis
The possible differences between obese children and lean children were tested by unpaired t test. Two-way ANOVA with repeated measures was performed to test (1) the differences between obese children and lean children during handgrip exercise and mental stress; (2) the resting differences between obese children subjected to a diet and obese children subjected to a diet plus exercise training; and (3) the differences between obese children subjected to a diet or diet plus exercise training and lean children. Three-way ANOVA with repeated measures was performed to test the differences between obese children subjected to a diet or diet plus exercise training during handgrip exercise and mental stress. When significance was found, the Scheffé post hoc comparison was performed. The data are presented as mean±SE. P<0.05 was considered statistically significant.

Results
Effects of Obesity
Baseline Measurements
Anthropometric and hemodynamic characteristics in obese and lean children are shown in Table 1. Age and height were similar in obese and lean children. Body weight and BMI were significantly higher in obese children. Peak VO₂ was significantly lower in obese children. In regard to hemodynamic measurements, mean blood pressure was significantly increased in obese children compared with lean children. Forearm blood flow and forearm vascular conductance were significantly lower in obese children.

Handgrip Exercise
Mean blood pressure increased progressively and significantly during handgrip exercise in obese children but not in lean children in whom mean blood pressure was unchanged (Figure 1). The comparisons between groups showed that the magnitude of mean blood pressure responses during exercise, analyzed by the interaction of phase effect and time effect, was significantly higher in obese children (Table 2). Similarly, forearm vascular conductance increased significantly during handgrip exercise in lean children (Table 2). In contrast, forearm blood flow was unchanged during exercise in obese children (Table 2). Forearm vascular conductance increased significantly during handgrip exercise in lean children but not in obese children (Table 2). During mental stress, forearm vascular conductance increased significantly in lean children but not in obese children, in whom forearm blood flow was unchanged (Table 2). Similarly, forearm vascular conductance increased significantly during mental stress in lean children (Figure 2). In contrast, in obese children, forearm vascular conductance was unchanged during mental stress (Figure 2). The comparisons between groups showed that the magnitude of forearm blood flow and forearm vascular conductance responses during mental stress, analyzed by the interaction of phase effect and time effect, was significantly lower in obese children than in lean children (P=0.01 and P=0.02, respectively; Table 2, Figure 2).

FIGURE 1. Mean blood pressure during static handgrip exercise and mental stress in obese and lean children. Note that mean blood pressure responses during both static handgrip exercise and mental stress are significantly increased in obese children. *P<0.05 vs rest; †P<0.05 vs lean. (Figure 2). The comparisons between groups showed that the magnitude of forearm blood flow and forearm vascular conductance responses during exercise, analyzed by the interaction of phase effect and time effect, was significantly lower in obese children compared with lean children (P=0.01, P=0.02, respectively; Table 2, Figure 2).
Effects of Diet and Exercise Training

Baseline Measurements

Anthropometric and metabolic characteristics before and after diet plus exercise training and diet alone are shown in Table 3. Before interventions, age, body weight, height, BMI, \( z \) score of BMI, total cholesterol, HDL cholesterol, LDL cholesterol, and glucose levels were similar between obese children randomized to diet plus exercise training or diet alone. Triglycerides and insulin levels were higher in the diet group compared with the diet plus exercise training group. The HOMA score was not different in the diet group and the diet plus exercise training group.

Diet plus exercise training significantly decreased body weight, BMI, \( z \) score of BMI, total cholesterol, triglycerides, glucose and insulin levels, and HOMA score. Diet decreased body weight, BMI, \( z \) score of BMI, total cholesterol, triglycerides, glucose and insulin levels, and HOMA score. Diet plus exercise training or diet alone significantly reduced body weight, BMI, \( z \) score of BMI, total cholesterol, triglycerides, glucose and insulin levels, and HOMA score. Diet caused no changes in HDL cholesterol, LDL cholesterol, and peak \( \dot{V}O_2 \). The comparisons between groups showed that body weight, BMI, \( z \) score of BMI, total cholesterol, glucose levels, and HOMA score were similar in children subjected to diet plus exercise training and diet alone. However, HDL cholesterol levels and peak \( \dot{V}O_2 \) were significantly higher in the diet plus exercise training group compared with the diet alone group. In addition, insulin and triglyceride levels were lower in the diet plus exercise training group.

The hemodynamic measurements before and after interventions are shown in Tables 4 and 5. Before interventions, there were no differences between groups.

Diet plus exercise training or diet alone significantly reduced mean blood pressure. Diet plus exercise training significantly decreased body weight, BMI, \( z \) score of BMI, total cholesterol, triglycerides, glucose and insulin levels, and HOMA score. Diet caused no changes in HDL cholesterol, LDL cholesterol, and peak \( \dot{V}O_2 \). The comparisons between groups showed that body weight, BMI, \( z \) score of BMI, total cholesterol, glucose levels, and HOMA score were similar in children subjected to diet plus exercise training and diet alone. However, HDL cholesterol levels and peak \( \dot{V}O_2 \) were significantly higher in the diet plus exercise training group compared with the diet alone group. In addition, insulin and triglyceride levels were lower in the diet plus exercise training group.

The hemodynamic measurements during handgrip exercise and mental stress are shown in Figures 2 and 3. Before interventions, there were no differences between groups.

Diet plus exercise training or diet alone significantly reduced mean blood pressure levels during handgrip exercise and mental stress. Diastolic blood pressure was significantly lowered in the diet plus exercise training group compared with the diet group during mental stress. Further analysis showed that resting mean blood pressure in obese children subjected to diet plus exercise training or diet alone was similar to that found in lean children (Figure 3). In addition, the difference in resting forearm vascular conductance between obese children subjected to diet plus exercise training and diet alone was no longer observed (Figure 4). In contrast, resting forearm vascular conductance remained significantly lower in obese children subjected to diet alone compared with lean children (Figure 4).

### Table 2. Hemodynamic Responses in Obese Children and Lean Children During Handgrip Exercise and Mental Stress

<table>
<thead>
<tr>
<th></th>
<th>Handgrip Exercise</th>
<th>Mental Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest 1 min 2 min 3 min</td>
<td>Rest 1 min 2 min 3 min</td>
</tr>
<tr>
<td>HR, bpm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lean</td>
<td>81±3 84±3* 88±3* 92±3*</td>
<td>83±3 86±2* 87±3* 86±3*</td>
</tr>
<tr>
<td>Obese</td>
<td>81±2 85±2* 89±2* 90±2*</td>
<td>78±1 82±3* 83±1* 84±2*</td>
</tr>
<tr>
<td>FBF, mL·min⁻¹·100 g⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lean</td>
<td>3.7±0.4 4.5±0.6* 5.2±0.4* 5.1±0.5*</td>
<td>3.4±0.4 3.6±0.6 3.9±0.4* 4.2±0.4*</td>
</tr>
<tr>
<td>Obese</td>
<td>2.5±0.1† 2.7±0.2† 2.8±0.2† 3.1±0.1†</td>
<td>2.3±0.1† 2.4±0.2† 2.5±0.2† 2.6±0.2†</td>
</tr>
</tbody>
</table>

HR indicates heart rate; FBF, forearm blood flow.

*P<0.05 vs rest; †P<0.05 vs lean.
Diet plus exercise training significantly decreased heart rate levels during handgrip exercise and mental stress. Diet alone did not change heart rate levels during handgrip exercise and mental stress. Diet plus exercise training provoked a significant increase in the magnitude of forearm blood flow and forearm vascular conductance responses during handgrip exercise and mental stress. In contrast, diet alone caused no change in the magnitude of forearm blood flow and forearm vascular conductance responses during handgrip exercise and mental stress. The comparisons between groups showed that the magnitude of mean blood pressure responses during handgrip exercise and mental stress was similar in diet plus exercise training and diet groups. Heart rate during handgrip exercise and mental stress was not different in diet plus exercise training and diet groups. The magnitude of forearm blood flow responses during exercise and mental stress, analyzed by the interaction of phase effect, time effect, and group effect, was significantly higher in the diet plus exercise training group compared with the diet group (exercise: $P<0.001$; mental stress: $P=0.008$). Similarly, the magnitude of forearm vascular conductance responses during exercise and mental stress was significantly higher in the diet plus exercise training group than in the diet group (exercise: $P=0.001$; mental stress: $P=0.001$).

Further analysis showed that the difference in mean blood pressure during handgrip exercise and mental stress in obese children subjected to diet plus exercise training or diet and lean children was no longer observed (exercise: $P=0.07$; mental stress: $P=0.08$; Figure 3). In the diet plus exercise training group, the magnitude of forearm vascular conductance responses during exercise and mental stress increased significantly toward the level found in the lean group (Figure 4). Thus, the differences in forearm vascular conductance during exercise and mental stress between obese children subjected to diet plus exercise training and lean children were no longer found (exercise: $P=0.10$; mental stress: $P=0.10$; Figure 4). In contrast, the magnitude of forearm vascular conductance responses during exercise and mental stress remained significantly lower in obese children subjected to a diet compared with lean children (Figure 4).

**Discussion**

The main and new findings of the present study are as follows: (1) blood pressure responses during static handgrip exercise and mental stress are exacerbated in obese children; (2) muscle vasodilatory responses during static handgrip exercise and mental stress are blunted in obese children; (3) diet plus exercise training or diet reduces blood pressure responses during static handgrip exercise and mental stress toward normal levels; and (4) diet plus exercise training, in contrast to diet alone, improves muscle vasodilatory responses during static handgrip exercise and mental stress in obese children.

**Impact of Obesity on Hemodynamic Responses**

The link between obesity and high blood pressure, hypertriglyceridemia, and increased fasting insulin levels has been reported consistently in children. The study confirms the increased blood pressure levels in obese children compared with lean children. Moreover, our study shows that obese children have augmented blood pressure responses during exercise and mental stress. This increased pressor response in obese children may be due to abnormal neurovascular control during physiological maneuvers. In obese adult individuals, muscle sympathetic nerve activity is increased during exercise and mental stress. This sympathetic activation seems to increase muscle peripheral vascular resistance and, in consequence, blood pressure. Despite the fact that muscle sympathetic nerve activity has not been measured in our study, we can suspect that sympathetic nerve activity was increased in obese children. On the other hand, the possibility of increased cardiac output has been suggested to explain high blood pressure in obese children. Our results do not support this
Four months of diet plus exercise training provoked a significant reduction in body weight and BMI and a significant increase in functional capacity in obese children. In addition, this regimen had favorable effects on the metabolic profile. However, the most remarkable finding of our study is the fact that diet plus exercise training significantly increased muscle vasodilatation during exercise and mental stress in obese children. This increase was so dramatic that the muscle vasodilatation during these physiological maneuvers reached normal levels. After diet plus exercise training, the differences in vasodilatory responses between obese children and lean children were no longer observed. Although diet alone reduces body weight and BMI, it does not change muscle vasodilatation during physiological maneuvers.

**Effects of Diet and Exercise Training on Hemodynamic Responses**

Four months of diet plus exercise training provoked a significant reduction in body weight and BMI and a significant increase in functional capacity in obese children. In addition, this regimen had favorable effects on the metabolic profile. However, the most remarkable finding of our study is the fact that diet plus exercise training significantly increased muscle vasodilatation during exercise and mental stress in obese children. This increase was so dramatic that the muscle vasodilatation during these physiological maneuvers reached normal levels. After diet plus exercise training, the differences in vasodilatory responses between obese children and lean children were no longer observed. Although diet alone reduces body weight and BMI, it does not change muscle vasodilatation during exercise and mental stress. Taken together, these results are consistent with the inherent effects of exercise training on blood vessel functioning in obese children. Moreover, they show that diet alone is insufficient to restore resting muscle blood flow and muscle vasodilatory responses in obese children. The improvement in blood vessel functioning after diet plus exercise training in obese children has been also reported during reactive hyperemia. These investigators observed that diet and exercise improved calf...
vasodilatation during hyperemia. Moreover, these effects were lost after discontinuation of exercise training.

The mechanisms involved in the vasodilatory responses during exercise and mental stress after diet plus exercise training in obese children are outside the scope of the present study. However, we can speculate that diet plus exercise training improves endothelial function. First, the increase in muscle blood flow during exercise and mental stress in humans is, in great part, endothelially mediated. Second, exercise training substantially improves endothelial function in skeletal muscle and cardiac muscle in humans.20,21 Alternatively, diet and exercise training may reduce muscle sympathetic nerve activity in obese children. The attenuation in sympathetic nerve activity would improve forearm vascular responsiveness during mental stress and exercise by decreasing the muscle vasoconstrictor force. It is also possible that the attenuation in sympathetic activation may have reversed the structural changes in resistance vessels that, in turn, favor the increase in forearm vascular conductance during physiological maneuvers. In a recent study we found that diet plus exercise training significantly reduced muscle sympathetic nerve activity in obese adult individuals.5 Moreover, muscle vasodilatation in response to handgrip exercise was significantly increased after diet plus exercise training.5

Another important finding in our study is related to blood pressure. In agreement with previous studies,22 body weight loss significantly reduced blood pressure in obese children. The novelty of our study is that body weight loss by diet plus exercise training or diet alone significantly reduced blood pressure levels during handgrip exercise and mental stress toward normal levels in obese children. It is unlikely that the reduction in blood pressure was due to heart rate because it was similar in diet plus exercise training and diet alone groups. We did not measure stroke volume or blood volume in the present study. Therefore, we do not know whether the reduction in blood pressure was due to any change in cardiac output. Thus, we can suggest that blood pressure reduction was associated with neurovascular sympathetic attenuation.

The 2 interventions, diet and diet plus exercise training, provoked a significant reduction in plasma insulin levels and

| TABLE 5. Hemodynamic Responses in Obese Children Subjected to a Diet or Diet Plus Exercise Training During Mental Stress |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| MBP, mm Hg                                      | Rest            | 1 min           | 2 min           | 3 min           | 4 min           |
| Diet                                            |                 |                 |                 |                 |                 |
| Before                                          | 83 ± 3          | 87 ± 4*         | 91 ± 4*         | 93 ± 3*         | 95 ± 4*         |
| After                                           | 76 ± 2†         | 86 ± 2*†        | 86 ± 2*†        | 86 ± 2*†        | 89 ± 2†         |
| Diet + ET                                       |                 |                 |                 |                 |                 |
| Before                                          | 79 ± 3          | 83 ± 3*         | 86 ± 3*         | 87 ± 1*         | 86 ± 2*         |
| After                                           | 73 ± 1†         | 78 ± 2*†        | 82 ± 1*†        | 81 ± 1†         | 83 ± 2†         |
| HR, bpm                                         |                 |                 |                 |                 |                 |
| Diet                                            |                 |                 |                 |                 |                 |
| Before                                          | 81 ± 3          | 87 ± 3*         | 88 ± 3*         | 89 ± 3*         | 92 ± 3*         |
| After                                           | 74 ± 3          | 79 ± 3*         | 82 ± 3*         | 83 ± 3*         | 82 ± 3*         |
| Diet + ET                                       |                 |                 |                 |                 |                 |
| Before                                          | 82 ± 3          | 86 ± 3*         | 85 ± 3*         | 87 ± 3*         | 86 ± 3*         |
| After                                           | 73 ± 3†         | 76 ± 3†         | 78 ± 3†         | 79 ± 3†         | 77 ± 3†         |
| FBF, mL·min⁻¹·100 g⁻¹                           |                 |                 |                 |                 |                 |
| Diet                                            |                 |                 |                 |                 |                 |
| Before                                          | 2.1 ± 0.2       | 2.3 ± 0.2       | 2.3 ± 0.2       | 2.5 ± 0.2       | 2.5 ± 0.2       |
| After                                           | 2.2 ± 0.1       | 2.3 ± 0.1       | 2.4 ± 0.1       | 2.5 ± 0.1       | 2.4 ± 0.1       |
| Diet + ET                                       |                 |                 |                 |                 |                 |
| Before                                          | 2.6 ± 0.1       | 2.6 ± 0.1       | 2.8 ± 0.2       | 2.7 ± 0.1       | 2.8 ± 0.1       |
| After                                           | 3.3 ± 0.2†‡     | 4.2 ± 0.2†‡     | 4.4 ± 0.2†‡     | 4.6 ± 0.3†‡     | 4.1 ± 0.2†‡     |
| FVC, U                                           |                 |                 |                 |                 |                 |
| Diet                                            |                 |                 |                 |                 |                 |
| Before                                          | 2.6 ± 0.2       | 2.7 ± 0.2       | 2.7 ± 0.2       | 2.9 ± 0.1       | 2.8 ± 0.1       |
| After                                           | 2.9 ± 0.1       | 2.7 ± 0.1       | 2.8 ± 0.1       | 3.0 ± 0.1       | 2.8 ± 0.1       |
| Diet + ET                                       |                 |                 |                 |                 |                 |
| Before                                          | 3.3 ± 0.1       | 3.2 ± 0.1       | 3.3 ± 0.2       | 3.1 ± 0.1       | 3.2 ± 0.1       |
| After                                           | 4.6 ± 0.1†‡     | 5.4 ± 0.2†‡     | 5.4 ± 0.1†‡     | 5.6 ± 0.1†‡     | 5.0 ± 0.1†‡     |

MBP indicates mean blood pressure; HR, heart rate; FBF, forearm blood flow; and ET, exercise training.

*P < 0.05 vs rest; †P < 0.05 vs before; ‡P < 0.05 vs after diet.
Despite the fact that these findings are associated with improvement in insulin sensitivity in children and adolescents,\textsuperscript{17,23} they may simply be a consequence of reduction in body fat.

Limitations
We recognize several limitations in our study. We have not included an obese trained group in our study. However, we can suggest that exercise training alone would have improved muscle vasodilatory responses during static handgrip exercise and mental stress in obese children. A recent study showed that flow-mediated dilation of the brachial artery was improved after exercise training in obese children despite the fact that body weight and BMI were unchanged.\textsuperscript{24} The normal control lean children were not subjected to exercise training. Thus, we do not know the effects of exercise training in our lean control group. The augmented forearm blood flow responses in children subjected to diet plus exercise training could be attributed to the workload during exercise or the level of perceived stress during the color word test. This seems unlikely because both the workload during exercise and the perception of stress during the color word test were similar in the diet plus exercise training and diet groups.

Perspectives
The reduction in blood pressure and the restoration in muscle blood flow after diet plus exercise training have clinical implications. First, hypocaloric diet plus exercise training should be the strategy of choice for treatment in children with obesity. Second, it is conceivable that the restoration in blood pressure levels and muscle vasodilatation responses during physiological maneuvers, achieved by this nonpharmacological treatment, prevents future cardiovascular disease in adulthood.

In conclusion, body weight loss by diet plus exercise training or diet alone prevents exaggerated blood pressure responses during sustained static handgrip exercise and mental stress in obese children. In addition, diet plus exercise training, in contrast to diet alone, restores forearm vasodilation responses during these physiological maneuvers in obese children.

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References


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