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Training, muscle volume, and energy expenditure in nonobese American girls

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Eliakim, Alon, Tim Scheett, Nicki Allmendinger, Jo Anne Brasel, and Dan M. Cooper. Training, muscle volume, and energy expenditure in nonobese American girls. *J Appl Physiol* 90: 35–44, 2001.—Little is known about the relationship among training, energy expenditure, muscle volume, and fitness in prepubertal girls. Because physical activity is high in prepubertal children, we hypothesized that there would be no effect of training. Forty pre- and early pubertal (mean age 9.1 ± 0.1 yr) nonobese girls enrolled in a 5 day/wk summer school program for 5 wk and were randomized to control ($n = 20$) or training groups ($n = 20$; 1.5 h/day, endurance-type exercise). Total energy expenditure (TEE) was measured using doubly labeled water, thigh muscle volume using magnetic resonance imaging, and peak $\dot{V}O_2$ uptake ($\dot{V}O_{2\text{ peak}}$) using cycle ergometry. TEE was significantly greater (17%, $P < 0.02$) in the training girls. Training increased thigh muscle volume ($+4.3 \pm 0.9\%$, $P < 0.005$) and $\dot{V}O_{2\text{ peak}}$ ($+9.5 \pm 6\%$, $P < 0.05$), effects surprisingly similar to those observed in adolescent girls using the same protocol (Eliakim A, Barstow TJ, Brasel JA, Ajie H, Lee W-NP, Renslo R, Berman N, and Cooper DM, *J Pediatr* 129: 537–543, 1996). We further compared these two sample populations: thigh muscle volume per weight was much lower in adolescent compared with prepubertal girls (17.0 ± 0.3 vs. 27.8 ± 0.6 ml/kg body mass; $P < 0.001$), and allometric analysis revealed remarkably low scaling factors relating muscle volume (0.34 ± 0.05 , $P < 0.0001$), TEE (0.24 ± 0.06 , $P < 0.0004$), and $\dot{V}O_{2\text{ peak}}$ (0.28 ± 0.07 , $P < 0.0001$) to body mass in all subjects. Muscle and cardiorespiratory functions were quite responsive to brief training in prepubertal girls. Moreover, a retrospective, cross-sectional analysis suggests that increases in muscle mass and $\dot{V}O_{2\text{ peak}}$ may be depressed in nonobese American girls as they mature.

exercise; doubly labeled water; magnetic resonance imaging; oxygen uptake

CHILDREN TEND TO BE AMONG the most spontaneously physically active human beings (4), yet there appears to have been a decline in levels of physical activity in American children, particularly in girls, over the past 15–20 years (17, 20). Despite the increasing awareness that adult diseases such as osteoporosis and obesity

are very likely associated with insufficient physical activity during childhood (33, 45), little is known about precisely what constitutes optimal levels of exercise in prepubertal girls or boys.

In the context of the growing child, the assessment of cardiopulmonary fitness is virtually impossible without accurate measurements of muscle and fat volume, because, unlike in adults, these important determinants of exercise performance are themselves in a state of flux (11, 19, 42). Accordingly, understanding the interrelationships among “dose” of exercise training, muscle volume, fat depots, and cardiorespiratory function would be essential in designing exercise interventions that can effectively influence health in children. Although there has been recent increased interest in the relationship between physical activity and obesity in children (23, 24), there exists very few prospective studies of exercise training in nonobese, prepubertal girls. Furthermore, the results of these studies have been inconsistent (29, 37, 44).

In this study, we examined the effect of a 5-wk school-based program of endurance-type exercise training in healthy, nonobese, prepubertal girls. We used magnetic resonance imaging (MRI) of the thigh to measure muscle volume, MRI of the abdomen and thigh to determine adiposity, breath-by-breath measurements of gas exchange in response to progressive exercise to assess cardiorespiratory function and fitness, and doubly labeled water (DLW) to measure energy expenditure.

The study was designed to permit both a cross-sectional and prospective analysis of muscle and fat volume, energy expenditure, and cardiorespiratory function in prepubertal girls. The data for the cross-sectional study were obtained during the initial enrollment phase. Subsequently, participants were randomized to either control or exercise training groups. The present study parallels recent similar prospective interventions that our laboratory has performed in adolescent (postpubertal) female high school students (17),

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and this enabled us to compare the responsiveness to exercise training and the interaction of muscle volume, body fat, and energy expenditure in pre- and late pubertal girls.

Because naturally occurring physical activity in prepubertal children tends to be high, and because the hormonal milieu of the prepubertal child is so different from that of the adolescent (36) (in whom our laboratory's previous studies demonstrated a significant response to brief training), we hypothesized that there would be no effect of the exercise training intervention on structural or functional variables in the girls that we studied. Although we did find that the prepubertal girls in our study were relatively fit, a number of recent investigations indicate that levels of physical activity may be falling in certain populations of children (39). We further hypothesized that the data would support the observation that there exists decline in cardiorespiratory fitness as girls mature through the pubertal years.

An additional objective of the study was to analyze the cross-sectional data using allometric (or power function) approaches. The latter has gained widespread use in gauging the effect of size on metabolic function during growth (28). Moreover, allometric analysis has been suggested as a means to understand better size-function relationships obtained from ratio analysis alone (10, 11, 42).

METHODS

Sample Population and Protocol

Forty girls volunteered to participate in the study. The subjects were all students in the Greater Hartford elementary school district (Hartford, CT) and were enrolled in a 5-wk summer school program in the town of West Hartford during the summer of 1997 (July-August), with class hours from 8–11 AM (5 days/wk). The ethnic configuration of the group was 77% Caucasian, 10% African American, 10% Hispanic, and 3% Asian. No attempt was made to recruit subjects who participated in competitive extramural athletic programs. The study was designed to examine pre- and early pubertal subjects with an age range of 8–10 yr (mean, 9.1 ± 0.1 yr). Measurements of height and weight were made using standard techniques. Assessment of pubertal status was performed by examination of each subject. Thirty-three (82%) of the subjects were found to be at Tanner level I and seven (18%) at Tanner level II.

The participants were randomized to a control ($n = 20$) or training group ($n = 20$). All subjects participated in a daily 45-min science program in physiology. During the remaining time, the training group members participated in two sessions of endurance-type training (45 min each) consisting of running, jumping, aerobic dance, and age-appropriate competitive sports (e.g., basketball, soccer, etc.). These two exercise sessions were separated by an elective in-class traditional course (45 min), which was selected by the study participants from the summer school curriculum. The intervention was designed to mimic the type and intensity of exercise that elementary school girls normally perform. These activities were varied in duration and intensity throughout the week and were designed primarily as games to encourage enthusiasm and participation of the subjects. "Aerobic" or endurance-type activities accounted for about all

of the time spent in training (~50% team sports and 50% running games). Training was directed by a member of the West Hartford Elementary School faculty.

During the same time, the control group subjects participated in three elective in-class courses from the summer school curriculum. No attempt was made to influence extracurricular levels of physical activity in either the control or trained groups, but participants were asked not to change their activity patterns from those before the study. The study was approved by the Institutional Human Subject Review Board. Informed assent was obtained from the subjects, and an informed consent was obtained from their parents or guardians.

Measurements of Fitness

Fitness was assessed by traditional approaches using both gas-exchange and functional indexes of exercise performance. The gas-exchange variables were derived from measurements of peak oxygen consumption ($\dot{V}O_{2\text{ peak}}$) before and after the training intervention. Each subject performed a ramp-type progressive exercise test on a cycle ergometer in which she exercised to the limit of her tolerance. Subjects were vigorously encouraged during the high-intensity phases of the exercise protocol. Gas exchange was measured breath by breath (6), and the $\dot{V}O_{2\text{ peak}}$ was determined as previously described for children and adolescents (12). Mean heart rate (HR) peak was 188 ± 3 beats/min, and mean respiratory exchange ratio peak was 1.14 ± 0.01 , suggesting that close to maximal values were likely achieved. $\dot{V}O_{2\text{ peak}}$ values were normalized to body weight, a commonly used method to normalize exercise responses in subjects of different body size and weight (10). Additionally, we analyzed $\dot{V}O_{2\text{ peak}}$ by normalizing to the MRI determination of right thigh muscle volume.

We measured functional indexes of exercise performance using the time required for each subject to complete an 800-m run. Testing in both groups was performed on the same track at the same time of day before and after the intervention. In an attempt to minimize possible confounding effects of group (i.e., being a member of the control or training group), we capitalized on the children's natural competitive spirit and actively encouraged both the training and control groups during the run.

MRI of Thigh Musculature and Fat

Studies were done before and immediately after the 5-wk protocol in all subjects. We chose to examine the musculature of the right thigh because these muscles would be largely involved in the endurance-type training program, as described above. MRI has been used previously to assess muscle and fat (1, 18, 31, 35).

MRI was performed on a General Electric 1.5-T whole body MRI system. A body coil was used both for signal detection and for radio-frequency transmission for imaging. The subject was positioned with the lower extremities moved into the isocenter of the magnet bore. Pilot image coronal sections were obtained to select an image including the distal femur. Seven axial sections, beginning at the knee to a level of 2–3 cm below the femoral neck, were obtained. These axial sections were 2 cm thick with no gap and were obtained with a T1-weighted sequence with a time to echo of 12 ms and repetition time of 400 ms. The matrix was 192×256 with two acquisitions at each phase-encode step.

The muscle and fat were easily identified in the serial MRI sections and were measured using computerized planimetry to determine the cross-sectional area (CSA) of muscle and fat. In the thigh, intraobserver variability of fat and muscle was

~2%. The percentage of each thigh section consisting of fat and muscle was then calculated. The total thigh muscle and fat volumes (in ml) were estimated by summing the respective volumes in each serial section, i.e., fat CSA (in cm²) × 2 cm (the thickness of each section).

Abdominal MRI

Abdominal MRI was performed at the level of the umbilicus. Subcutaneous abdominal adipose tissue (SAAT) was clearly demarcated in the magnetic resonance images and, therefore, easily measured by trained observers. Intraobserver variability was ~2%. Intra-abdominal adipose tissue (IAAT) was not as well outlined in this population, and this was reflected in an intraobserver variability of ~15%. The percentages of SAAT and IAAT were calculated as the fat CSA divided by the whole abdomen CSA at the level of the umbilicus (i.e., %SAAT and %IAAT). The values are expressed as percentages because we are comparing the relative proportion of two different fat depots within the abdomen. Studies were done before and after the training intervention.

Total Energy Expenditure

The DLW technique was used to measure total energy expenditure (TEE) for a 10-day period beginning on *week 3* of the protocol. Ideally, pre- and postintervention measurements of TEE using DLW would have been performed; however, this was prohibited by the extremely high cost of H₂¹⁸O. As an alternative, we studied all subjects in both the control and training groups and compared the results.

After a baseline urine sample was obtained, each subject was given a standard oral dose of DLW. To minimize calculation error, a standard dose of 25 ml of a 1:1 mixture of ²H₂O and H₂¹⁸O (99% enriched; Isotec, Williamsburg, OH) was given. The dose is calculated to provide an average of 0.22 g/kg of ²H₂O or H₂¹⁸O with a range of 0.15–0.29 g/kg. A urine sample was obtained 2 h later and daily for the next 10 days. Oxygen and hydrogen isotopic ratios were measured at the Core Laboratory of the General Clinical Research Center at the University of Vermont.

For measurement of ¹⁸O, aliquots of urine were placed in vacutainers and equilibrated over CO₂ overnight before the ¹⁸O isotopic enrichment of the water was measured by isotope ratio mass spectrometry. For measurement of ²H enrichment, duplicate 5-ml aliquots of urine were placed in reaction vessels containing zinc catalyst to reduce the water to hydrogen gas by heating. The ²H enrichments of the hydrogen samples were measured by isotope ratio mass spectrometry on the same day that they were prepared. Aliquots of the ²H₂¹⁸O dose were also measured for ²H and ¹⁸O enrichment after being quantitatively diluted with unlabeled water. The urine sample ²H and ¹⁸O enrichments were calculated using

the diluted dose ²H and ¹⁸O enrichments as calibrants for each analysis. The isotope ratio data were analyzed using linear regression analysis after log transformation. Converting CO₂ production rate to TEE was done according to methods recommended by the International Dietary Energy Consultancy Group in 1990 (15, 16).

Allometric Analysis

Allometric equations have the general form

$$q \propto a \cdot M^b$$

where q indicates a metabolic rate (e.g., TEE or $\dot{V}_{O_2 \text{ peak}}$), M is a parameter related to body dimension (e.g., mass), a is the mass coefficient, and b is the scaling factor (22). In mammals, most aerobic functions such as $\dot{V}_{O_2 \text{ peak}}$ or TEE have scaling factors to body mass in the range of 0.67–1.0 (30, 41).

To determine the scaling factor, we used iterative curve-fitting techniques (SigmaPlot for Windows, version 5.0, SPSS). The accuracy and biological relevance of scaling factors are enhanced when they are estimated over as large a range of body mass as possible. Consequently, we combined data from the present study in prepubertal girls with observations of muscle volume, $\dot{V}_{O_2 \text{ peak}}$, and TEE that our laboratory made previously in adolescent girls using virtually the same techniques (17). Finally, we took advantage of TEE data published by Bandini et al. (5) who used the DLW in 12 girls whose age range was between the 8- to 10- and 16- to 17-yr-olds of our two studies (present study and Ref. 17).

Statistical Analysis

Unpaired t -tests were used to compare data of subjects randomized to either the control or training group before the training intervention. ANOVA for repeated measures was used to determine the effect of the training intervention on cardiorespiratory and fitness data, thigh muscle and fat volume, %SAAT, and %IAAT with time serving as the within-group factor and training as the between-group factor. When ANOVA was found to be significant, intergroup comparisons were made using modified t -tests by the method of Duncan. Standard techniques of regression and correlation were used for the cross-sectional studies relating fitness and adiposity. Data are presented as means ± SE. Statistical significance was taken at $P < 0.05$.

RESULTS

Effect of Training

Height, weight, and body mass index. There were no significant differences in height, weight, and body mass index (BMI) between the groups before the exercise intervention (Table 1). Height increased signifi-

Table 1. Anthropometric data of the sample population pre- and postintervention

	Age, yr	Weight, kg		Height, cm		BMI, kg/m ²	
		Pre	Post	Pre	Post	Pre	Post
Control	9.25 ± 0.17	32.2 ± 2.2	32.9 ± 2.3*	133.9 ± 2.1	134.6 ± 2.1†	17.6 ± 0.7	17.8 ± 0.7
Training	9.09 ± 0.12	35.5 ± 2.3	35.7 ± 2.4	135.6 ± 1.5	136.6 ± 1.4†	19.2 ± 1.1	19.0 ± 1.1
Total	9.17 ± 0.10	33.8 ± 1.6	34.3 ± 1.6	134.7 ± 1.3	135.6 ± 1.2†	18.4 ± 0.7	18.4 ± 0.7

Values are means ± SE; $n = 20$ girls/group. BMI, body mass index. There were no significant differences between the control and training groups at the beginning of the study. Height significantly increased in both groups over the course of the 5-wk intervention, but no differences between the groups were noted. Weight significantly increased in the control group only. Significant difference, Pre vs. Post: * $P < 0.05$, † $P < 0.001$.

cantly in both groups, but there was no difference in the increase between control and trained subjects. Interestingly, weight increased significantly in the control subjects by $2.2 \pm 0.8\%$ ($P < 0.04$), but no significant change was observed in the training group.

TEE. In week 4 of the intervention, TEE was 17% greater in the training compared with the control group ($2,117 \pm 73$ vs. $1,812 \pm 103$ kcal/day; $P < 0.02$) (Fig. 1).

Thigh muscle volume. There were no significant differences in thigh muscle volumes between the groups before the program (880 ± 49 vs. 935 ± 43 ml in control and training groups). There were no significant changes in thigh muscle volume in the control group after the course (884 ± 50 ml). In contrast, there was a small but significant increase in thigh muscle volume in the training group subjects (15 of 17 participants, 973 ± 41 cm³; $P < 0.02$, Fig. 1). The increase in thigh muscle volume occurred mainly in the central and distal parts of the muscle and not in the proximal region of the thigh muscle (Fig. 2).

Thigh and abdominal fat. There were no significant differences in thigh fat, %SAAT, and %IAAT between control and training groups before the study. There were no significant training effects on thigh fat, %SAAT, and %IAAT.

Indexes of cardiopulmonary and functional fitness. Before randomization, the group was heterogeneous in fitness with $\dot{V}O_{2\text{ peak}}$ per kilogram body weight ranging from fit (66 ml $O_2 \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$) to sedentary (23 ml $O_2 \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$). There were no significant differences in $\dot{V}O_{2\text{ peak}}$ between control and training group subjects before the intervention. There was no significant increase in $\dot{V}O_{2\text{ peak}}$ in the control subjects after the course, whereas $\dot{V}O_{2\text{ peak}}$ increased significantly in the training group subjects. There was a significant in-

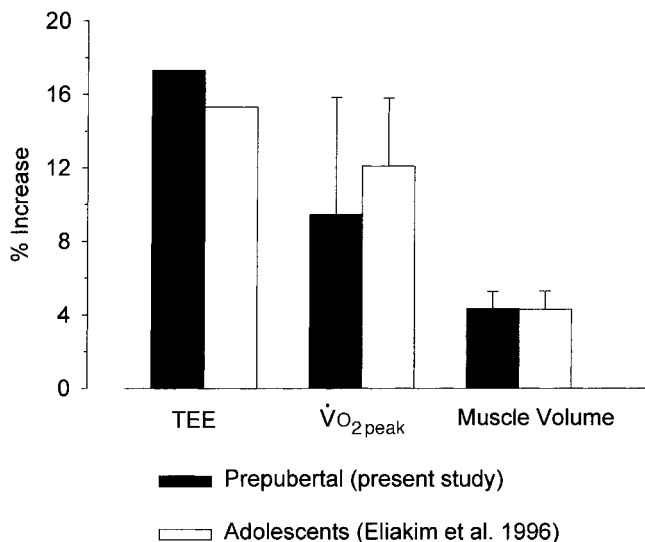


Fig. 1. Effect of 5-wk endurance type exercise training. In prepubertal girls, training led to significantly greater total energy expenditure (TEE), peak oxygen consumption ($\dot{V}O_{2\text{ peak}}$), and thigh muscle volume (see text). The increases were remarkably similar to those observed in late adolescent girls in a previous study by this research group (17).

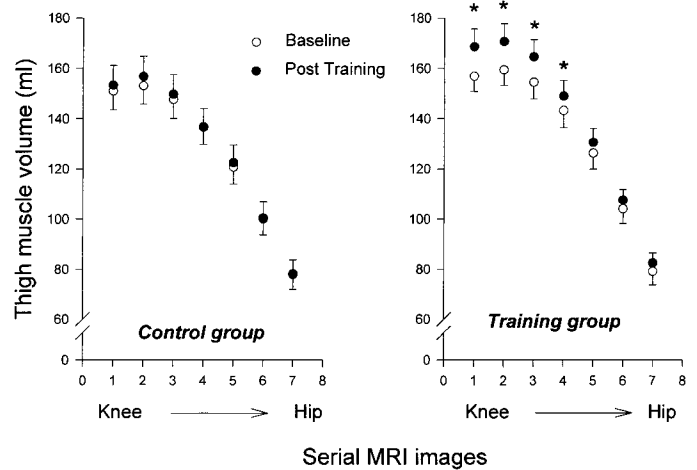


Fig. 2. Effect of training on thigh muscle in prepubertal girls. The multiple magnetic resonance images (MRI) of the thigh muscular revealed that the effect of the endurance-type training program occurred primarily in the distal muscle. Significant difference, post-training vs. baseline, * $P < 0.05$ by ANOVA and modified t -tests.

verse correlation between the initial level of fitness (calculated as percent predicted $\dot{V}O_{2\text{ peak}}$) and the percent improvement in $\dot{V}O_{2\text{ peak}}$ resulting from the intervention ($r = -0.81$, $P < 0.01$) (i.e., the least fit subjects had the greatest improvement). Finally, times for the 800-m run were unchanged in the control subjects ($-2.50 \pm 3\%$) but were significantly decreased in the training subjects ($-14 \pm 2\%$, $P < 0.001$). Similar to the results for $\dot{V}O_{2\text{ peak}}$, the greatest improvement was seen in those training group subjects whose initial fitness (i.e., 800-m run time) was lowest (Fig. 3).

Cross-sectional analysis: Relationships among $\dot{V}O_{2\text{ peak}}$, body weight, and thigh muscle volume. Comparisons among muscle volume, body weight, and $\dot{V}O_{2\text{ peak}}$ are shown in Figs. 4 and 5. As noted, these values were obtained at baseline before randomization to control or training group. Although thigh muscle volume was significantly greater in the adolescent girls, the increase was not nearly as great as the increase in

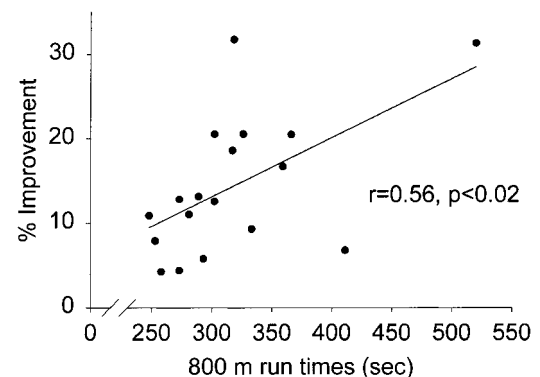


Fig. 3. Effect of initial fitness level (estimated as 800-m run time) on response to training in the training group members. Similar to the $\dot{V}O_{2\text{ peak}}$ data (not shown), the most marked improvements in the 800-m run times occurred in the least fit members of the training group. There was no significant change in the run times seen in the control group.

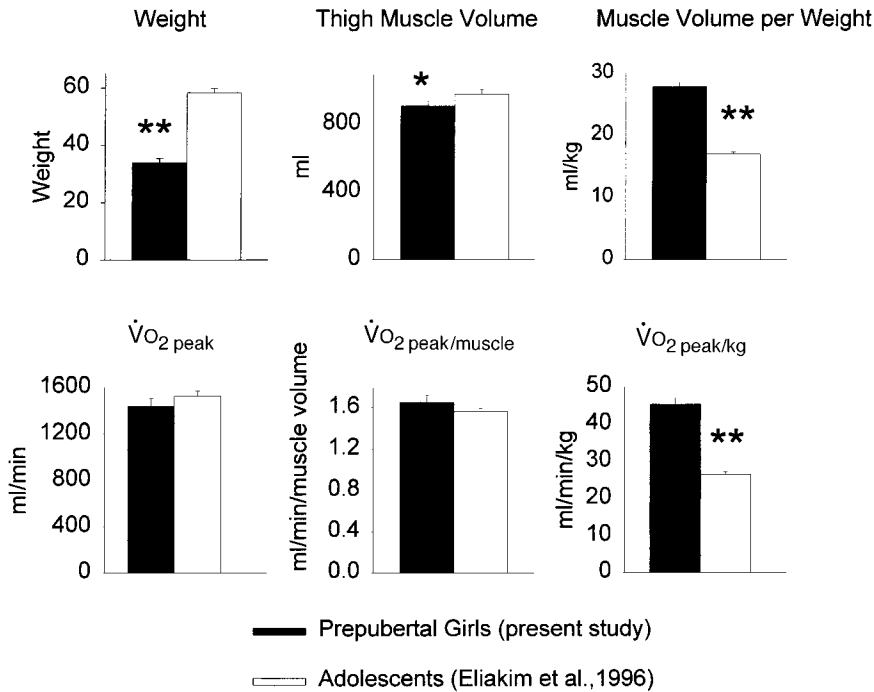


Fig. 4. Comparison of weight, thigh muscle volume, and $\dot{V}O_{2\text{ peak}}$ in prepubertal (present study) and late-adolescent girls (17). Although thigh muscle volume was significantly greater in the adolescent girls, the increase was not nearly as great as the increase in weight. Consequently, thigh muscle volume per weight was much lower in the adolescent girls. Neither $\dot{V}O_{2\text{ peak}}$ nor $\dot{V}O_{2\text{ peak}}$ normalized to muscle was significantly different between the 2 groups. Consequently, $\dot{V}O_{2\text{ peak}}$ per kilogram body mass was significantly smaller in the adolescent girls. Significant difference, prepubertal vs. adolescent girls, * $P < 0.0001$, ** $P < 0.05$.

weight (17). Consequently, thigh muscle volume per weight was much lower in the adolescent girls (17). Neither $\dot{V}O_{2\text{ peak}}$ nor $\dot{V}O_{2\text{ peak}}$ normalized to muscle were significantly different between the two groups. Consequently, $\dot{V}O_{2\text{ peak}}$ per kilogram body mass was significantly smaller in the adolescent girls (17).

There was a significant positive correlation between $\dot{V}O_{2\text{ peak}}$ and thigh muscle volume ($r = 0.51$, $P < 0.005$). In the prepubertal girls, the regression slope was $1.14 \pm 0.34 \text{ ml O}_2 \cdot \text{min}^{-1} \cdot \text{ml muscle volume}^{-1}$, which did not differ significantly from the slope found previously in our laboratory's study of teenagers ($1.42 \pm 0.20 \text{ ml O}_2 \cdot \text{min}^{-1} \cdot \text{ml}^{-1}$; Ref. 17). For the group as a whole, the regression slope was 1.26. In addition, $\dot{V}O_{2\text{ peak}}$ per kilogram body mass (a commonly used index of relative fitness) was highly correlated with muscle volume per kilogram body mass in the present study and in the previously studied adolescent girls (17) (Fig. 5).

The data comparing body fat distribution between the prepubertal and adolescent girls (17) are shown in Fig. 6. There was a significantly greater percentage of SAAT in the adolescent compared with the younger subjects, but no significant differences were observed in IAAT or thigh fat between the two groups.

Allometric analyses were performed to determine the scaling factors relating TEE and $\dot{V}O_{2\text{ peak}}$ to body mass and $\dot{V}O_{2\text{ peak}}$ to muscle volume. As seen in Fig. 7, the scaling factor for TEE to body mass (0.24 ± 0.06 , $P < 0.0004$) was substantially less than the anticipated 0.67 or 0.75. As a consequence, TEE per body weight progressively decreased with age [8- to 10-yr olds in the present study, $60.8 \pm 1.8 \text{ kcal} \cdot \text{day}^{-1} \cdot \text{kg}^{-1}$; 14 yr olds in Bandini study (5), $43.9 \pm 2.2 \text{ kcal} \cdot \text{day}^{-1} \cdot \text{kg}^{-1}$; our 1996 study of late adolescent females (17), 32.6 ± 2.2

$\text{kcal} \cdot \text{day}^{-1} \cdot \text{kg}^{-1}$; $P < 0.001$ for ANOVA and adjusted intergroup t -tests]. Using results from the present study and our previous study of adolescent girls (17), strikingly similar results were found for the scaling factor for $\dot{V}O_{2\text{ peak}}$ to body mass (0.28 ± 0.07 , $P < 0.0001$; Fig. 7). Finally, the scaling factor for thigh muscle volume to body mass (again, using data from the present study and our previous study in adolescent girls) was 0.34 ± 0.05 , $P < 0.0001$.

In contrast to the above results, we found that $\dot{V}O_{2\text{ peak}}$ scaled very differently to muscle volume than it did to body mass. The scaling factor was substantially greater: 0.79 ± 0.11 , $P < 0.0001$, for all girls; 0.91 ± 0.13 , $P < 0.0001$, for adolescents; and 0.69 ± 0.21 , $P < 0.0023$, for prepubertal girls.

DISCUSSION

Effect of Exercise Training in Prepubertal Girls

In contrast to our hypothesis, 5 wk of endurance-type training led to significant increases in both anatomic and functional indexes of cardiopulmonary fitness in prepubertal girls (Fig. 1). Moreover, the school-based program led to an $\sim 17\%$ difference in TEE between the control and training groups. Whereas both groups had small but significant increases in body height, a significant weight gain was noted only in the control subjects (Table 1). These changes occurred despite the fact that, even before the intervention, $\dot{V}O_{2\text{ peak}}$, TEE, and the ratio of thigh muscle volume to body weight were relatively high in the prepubertal girls (e.g., see Fig. 4). The "dose response" of an exercise training input is remarkably similar between prepubertal and adolescent subjects, suggesting that the plasticity of the car-

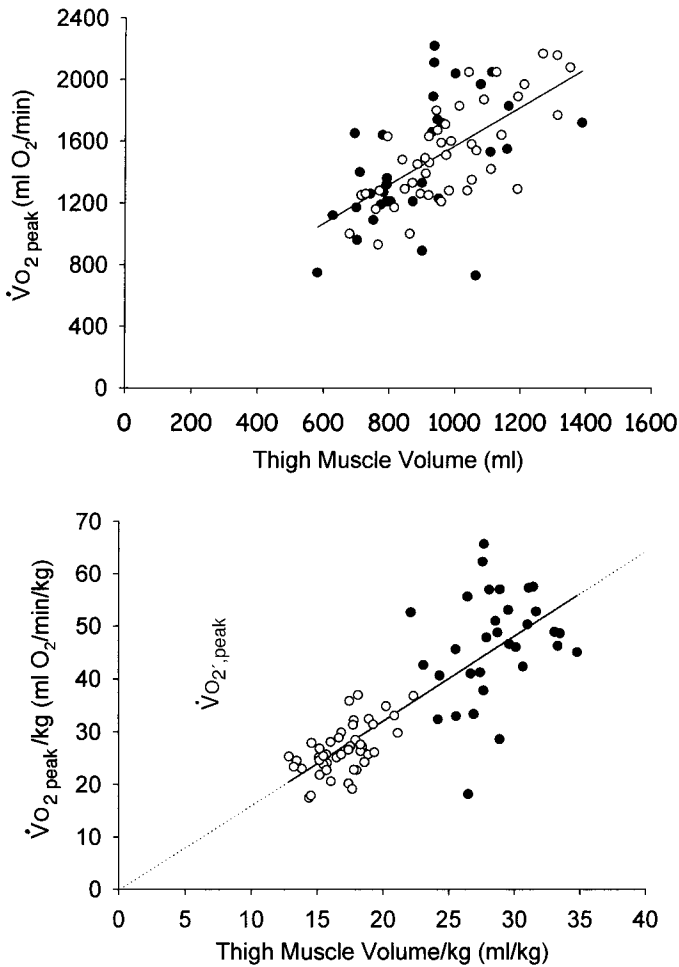


Fig. 5. *Top*: regression of $\dot{V}O_{2peak}$ and thigh muscle volume in prepubertal (●) and adolescent (○) girls. There was no statistically significant difference in the regression between the 2 groups (see text). *Bottom*: regression of $\dot{V}O_{2peak}$ per kilogram and thigh muscle volume per kilogram body mass in the 2 groups. The regression equation was $\dot{V}O_{2peak}/kg = 1.61 \times \text{muscle volume}/kg - 0.20$, $r = 0.82$.

diorepiratory and muscle systems is fairly constant between early and late puberty in girls (Fig. 1).

There is a lack of prospective, controlled studies examining exercise training, energy expenditure, and cardiorespiratory and anatomic responses to exercise in healthy, prepubertal children. Such studies in “free-living” children impose a variety of substantial methodological barriers, including standardization of the training input, willingness of children and parents to adhere to sometimes difficult exercise regimens, and compliance of the subjects in completing a battery of pre- and postintervention testing. The use of DLW may have lessened previous methodological difficulties in measuring energy expenditure, but availability of the ^{18}O isotope is sporadic, and the cost of the isotope and its subsequent analysis is prohibitive. As a consequence, although the DLW has been used in adults and children to find correlations between energy expenditure and obesity (7, 21, 40), there are few, if any, prospective controlled studies in nonobese prepubertal girls in which the effect of a training intervention on TEE has been quantified with DLW. Even in the present study, we did not have the luxury of studying control and training group subjects before and during the training, as was done by Van Etten et al. (43) in a study of resistive-type exercise training in sedentary adult men.

There remains controversy regarding the response of prepubertal children, particularly girls, to exercise training [see, for example, the review by Pate and Ward (32)]. Nonetheless, the present data combined with the work of previous investigators do permit some reasonable speculation into the dose-response relationship of exercise training in prepubertal girls. We used two recent prospective exercise training studies in this population [one authored by Welsman et al. (44) and the other by Rowland et al. (38)] with roughly comparable age ranges and an endurance-type (rather than

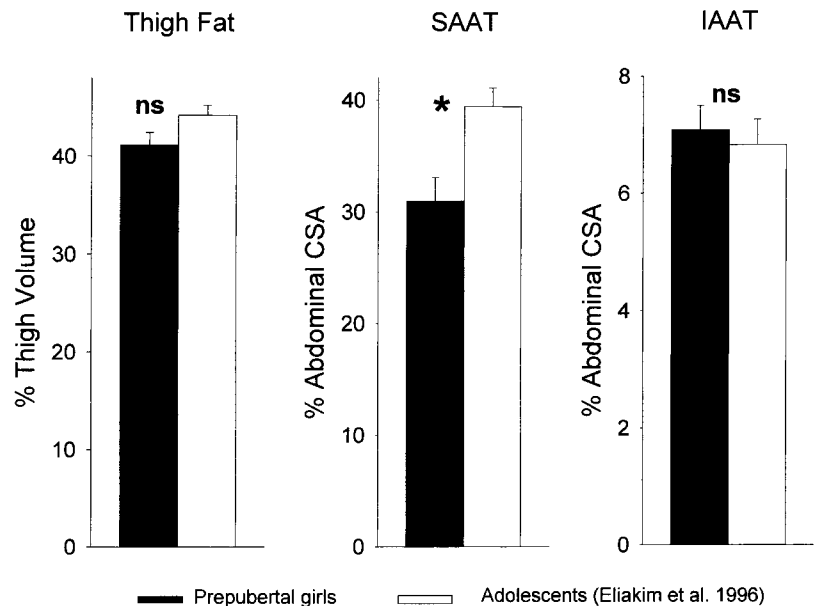


Fig. 6. Comparison of thigh, abdominal, and intra-abdominal fat in prepubertal and adolescent girls. A significant increase in percentage of subcutaneous abdominal adipose tissue (SAAT) was observed in the adolescent girls, $*P < 0.05$. IAAT, intra-abdominal adipose tissue; CSA, cross-sectional area; ns, not significant.

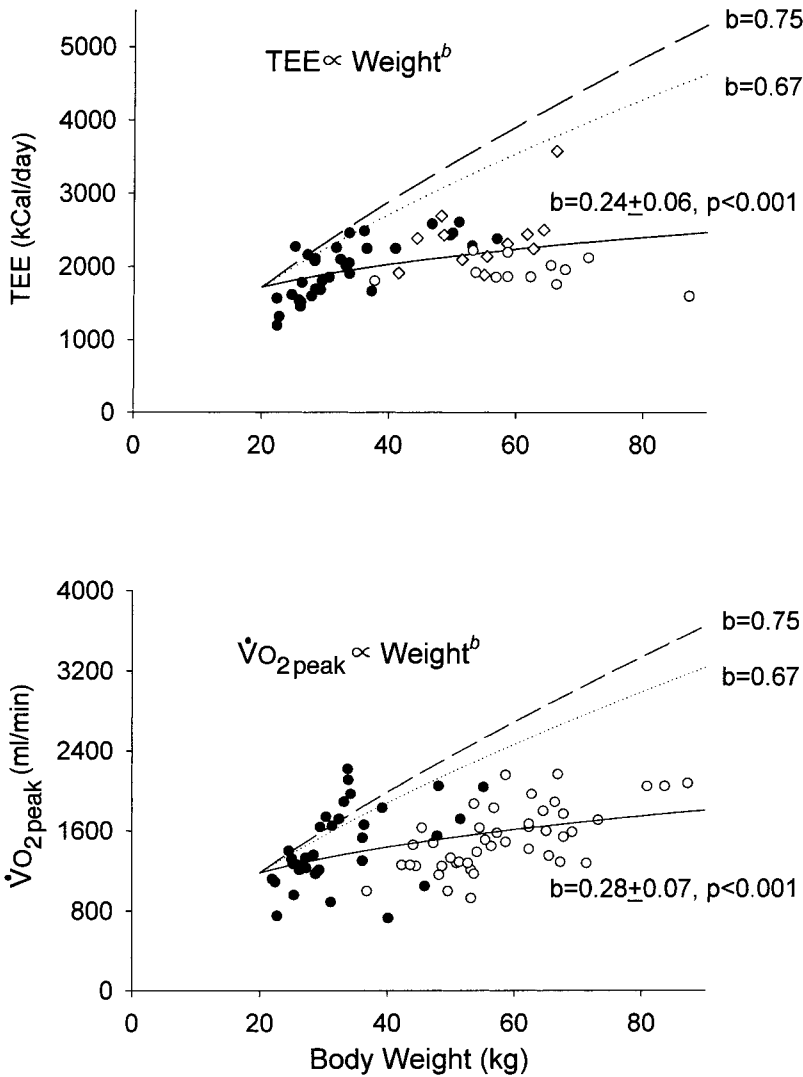


Fig. 7. Relationship between TEE and body mass (top) and $\dot{V}O_{2peak}$ and body mass (bottom). TEE data include results from the present study (\circ), our laboratory's previous study in adolescent girls (17) (\bullet), and data from Bandini et al. (5) in 14-yr-old nonobese girls (\diamond). $\dot{V}O_{2peak}$ data include results from the present study (\circ) and our laboratory's previous study in adolescent girls (17) (\bullet). For both TEE and $\dot{V}O_{2peak}$, the observed scaling factor (b) was much lower than expected.

resistive) exercise training protocol. Although neither of these studies used DLW to measure the effect of training on TEE, we were able to estimate this effect using the time and duration of the training sessions and the reported increase in HR [note, we used the relationship between oxygen consumption and HR during exercise (14) and the values for TEE found in the present study to estimate the impact of the training on overall energy expenditure]. The results of these estimates are shown in Fig. 8. This analysis suggests two important features of the exercise dose response in healthy children. First, there seems to be a minimum of about a 2–4% increase in TEE before any change in cardiorespiratory function occurs. Second, the training response appears to reach some maximal level above this threshold relatively rapidly.

Similar to our laboratory's previous study of adolescents (17), we found that the level of fitness before the intervention was inversely related to the response (i.e., less fit children had a greater increase in $\dot{V}O_{2peak}$ and 800-m running time; Fig. 3). This may explain why the overall response was somewhat greater in the adoles-

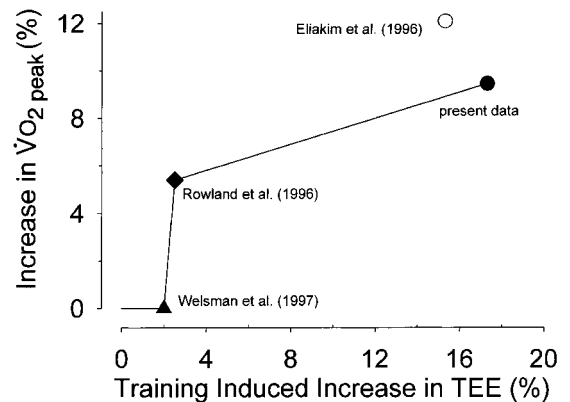


Fig. 8. Relationship between training-associated increase in TEE and increase in $\dot{V}O_{2peak}$. Data were estimated from published results of Welsman et al. (44), Rowland et al. (38), our laboratory's previous study of adolescent girls (17), and the present study of prepubertal girls. We speculate that there is a threshold effect, in which endurance-type training activities must lead to at least a 2–3% increase in TEE before any increase in $\dot{V}O_{2peak}$ can be measured. In addition, once exceeded, it appears that the increase in $\dot{V}O_{2peak}$ reaches a limit fairly rapidly. Adolescent girls seemed to have been more responsive to exercise training, perhaps because they were generally less fit than younger girls.

cents compared with the prepubertal subjects, because the initial level of fitness in the younger children, at least, as judged by the $\dot{V}O_{2\text{ peak}}$ per kilogram, was significantly lower in the older subjects (Fig. 4). We also noted that the training-associated increases in thigh muscle volume occurred predominantly in the central and distal regions of the muscle, an observation similar to the one made in our laboratory's study of adolescent girls (17) and by Roman and coworkers (35), who focused on biceps training in elderly men. Thus, whereas the midmuscle seems to be the most sensitive, measurements from this site alone may overestimate training-induced changes in total muscle volume. The mechanisms responsible for this particular anatomic distribution of muscle in response to training are not fully known but are likely related to distribution of load within the exercising muscle.

Our data show that the effect of training on fitness could not be explained solely by the increase in thigh muscle volume. The proportional training-induced increase in $\dot{V}O_{2\text{ peak}}$ was ~ 2.5 times the increase in muscle volume (Fig. 1). Thus factors other than muscle size alone likely contributed to the increased $\dot{V}O_{2\text{ peak}}$ after training. It is well recognized that, in addition to muscle hypertrophy, the "training effect" is composed of a variety of size-independent factors, including increases in mitochondrial oxidative activity, muscle capillary density, and improved cardiorespiratory function (34). The specific effect of endurance-type training on these factors has not yet been elucidated in prepubertal girls.

Cross-sectional Data: Inferences Concerning the Relationship Among Body Volume, Energy Expenditure, and Cardiorespiratory Response to Exercise in Girls

Cross-sectional observations are often the only feasible way to analyze growth, development, and fitness in children over a span of 6–8 yr, but inherent confounding variables must be recognized. Fitness levels may vary over time and geography: for example, Swedish adolescent girls studied by Åstrand in the 1950s (3) or Danish subjects in the 1980s (2) have substantially greater $\dot{V}O_{2\text{ peak}}$ per kilogram body mass than did the adolescents in our laboratory's 1996 study (17). Ethnic differences may also play a role: the prepubertal girls in the present study were predominately Caucasian, whereas the adolescents in our laboratory's previous study were largely of Asian origin. It is noteworthy, however, that, in a recent California statewide assessment of fitness and body composition in 5th, 7th, and 9th grade children, there were no differences between Asian and Caucasian girls (8).

Notwithstanding these potential confounding effects, the data collected in this and in our laboratory's previous study of adolescent girls (17) provide a unique opportunity to begin to examine a potentially troubling observation about the relationship between growth and development of cardiorespiratory responses to exercise in pre- and late pubertal girls. The present analysis revealed scaling factors of energy expenditure

and $\dot{V}O_{2\text{ peak}}$ to body mass that were much lower than those found in previous studies of both humans and other mammals (10, 30, 41). Energy expenditure, muscle volume, and $\dot{V}O_{2\text{ peak}}$ appear to increase at a much lower rate than did body mass or height in this sample.

Because we measured thigh muscle with MRI, the combined data provided a unique opportunity to examine the relationship between muscle volume and $\dot{V}O_{2\text{ peak}}$ in a cross section of pre- and late pubertal girls. Muscle is the tissue that drives oxygen consumption during exercise; thus, in contrast to the relationship between body volume and $\dot{V}O_{2\text{ peak}}$, the relationship between muscle and $\dot{V}O_{2\text{ peak}}$ is not confounded by factors such as fat and bone volume. As seen in Fig. 5, the regression slope of the relationship between thigh muscle volume and $\dot{V}O_{2\text{ peak}}$ did not differ between the two groups (Fig. 5, top).

The scaling factors of $\dot{V}O_{2\text{ peak}}$ to muscle volume, 0.91 for adolescents and 0.69 for the prepubertal girls, were well within the range expected from previous studies in both humans and other mammals (12, 30, 41). A variety of theoretical constructs have been used to explain these numbers. McMahon (27) suggested that the 0.75 scaling factor, identified as the scaling factor in the "mouse-to-elephant" curve of Kleiber (25), could be predicted from mechanical and structural considerations of loading factors associated with locomotion and joint elasticity. Classical biologists tend to support the 0.67 scaling factor (22). In this construct, mammals regulate body temperature by balancing heat production (determined by the volume of metabolically active tissue) with heat loss (determined by the ratio of surface area to body mass). We speculate that the mechanisms for the variations in scaling factors observed in the present study between pre- and late pubertal girls and among a variety of studies may depend on pubertal changes in muscle structure and function (e.g., mitochondrial density, vascularity, fiber type) that are not dependent per se on muscle size.

Although the relationship between muscle volume and $\dot{V}O_{2\text{ peak}}$ seemed appropriate, the data show clear abnormalities in the increase in muscle volume and, consequently, cardiorespiratory function relative to body weight. As shown in Fig. 4, although muscle volume was significantly greater in the older girls, the difference between the groups was small (8% greater in the adolescents) and substantially less than the differences in either height (19% greater in the adolescents) or weight (71% greater in the adolescents). It is important to reiterate that the sample population in these two studies did not meet current criteria for obesity: mean BMI of 18.4 in the prepubertal subjects and 22.5 in the adolescents do not exceed current "cutoff points" for obesity in girls (9).

It is, of course, recognized that puberty in girls is characterized by increases in both absolute and relative body fat (26), and it is not unexpected, therefore, to find lower ratios of muscle volume to body weight and, consequently, $\dot{V}O_{2\text{ peak}}$, in adolescent girls (Fig. 4). But the allometric examination suggests that, at least in the retrospective, cross-sectional data used in the

present analysis, the increase in muscle mass and $\dot{V}O_{2\text{ peak}}$ relative to body weight was substantially lower than expected.

The mechanism for this lower-than-expected increase in fitness and muscle mass is not clear, and we can only speculate from our data what the causes may be. An increase in the relative proportion of body fat was observed and certainly contributed. Interestingly, as seen in Fig. 6, this occurred primarily in the subcutaneous abdominal area with no significant changes in either intra-abdominal or thigh fat percentages, and, as noted, the children did not either appear "obese" or meet current criteria based on BMI. Of equal, perhaps even greater, importance appears to be a lack of appropriate increase in muscle volume. Our data clearly show that aerobic capacity per unit muscle volume was the same in prepubertal and adolescent girls (Figs. 4 and 5), i.e., it is unlikely that muscle oxidative capacity was profoundly different in the two populations. But the consequences of the relatively low muscle mass increase with growth are demonstrated in Fig. 7, showing an abnormal relationship between $\dot{V}O_{2\text{ peak}}$ and body mass. As can be seen, the observed scaling factor, 0.28, was substantially lower than the predicted values of 0.67 or 0.75 (see above in DISCUSSION) and lower than the scaling factor of 0.83 that our laboratory observed in 1984 (12).

The data suggest that reduced levels of energy expenditure may be playing a role in the inappropriately low increases in muscle volume that we observed. As can be seen in Fig. 7, TEE scaled to almost precisely the same factor, 0.24, as did $\dot{V}O_{2\text{ peak}}$. It is noteworthy that, in this analysis, we included data from 14-yr-old girls published in 1990 (5). Like $\dot{V}O_{2\text{ peak}}$, the scaling factor for TEE was much less than what has been observed for many studies of energy expenditure and body weight across many mammalian species (30). Although we did not measure basal metabolic rate or estimate activity energy expenditure in the present study, recent work by Goran et al. (20) strongly supports the idea of a rather profound decline in physical activity in American girls, and this may well explain the abnormal relationships between both TEE and $\dot{V}O_{2\text{ peak}}$ and body mass observed in the present study.

In summary, we found that prepubertal children, despite their relatively greater energy expenditure and fitness, respond to a brief, endurance-type exercise intervention program with increased thigh muscle volume and $\dot{V}O_{2\text{ peak}}$. The response in the prepubertal children was similar to that observed previously in adolescent girls, but, despite this remarkable fitness plasticity, a cross-sectional analysis of energy expenditure, thigh muscle volume, and $\dot{V}O_{2\text{ peak}}$ from a number of studies pointed toward an abnormally low increase in muscle volume and cardiorespiratory fitness with increasing body weight in nonobese, healthy girls from pre- to late pubertal developmental stages. Low levels of physical activity are contributing to the alarming increase in obesity presently observed in American children. It appears that low levels of energy expenditure are also contributing to reduced muscle volume

and fitness in nonobese girls as well. The long-term consequences of this reduction on subsequent muscle growth and on health in general are not known.

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