Does menarche mark a period of elevated resting metabolic rate?

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1General Clinical Research Center, Massachusetts Institute of Technology, Cambridge 02139; 2Department of Health Sciences, Boston University, Boston, 02215; 3Gerald J. and Dorothy R. Friedman School of Nutrition Science and Policy, 4Jean Mayer United States Department of Agriculture Human Nutrition Research Center on Aging, and 5Department of Family Medicine and Community Health, Tufts University School of Medicine, Boston, Massachusetts 02111; and 6Division of Nutrition and Physical Activity, Center for Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia 30341

Submitted 10 September 2003; accepted in final form 12 November 2003

Spadano, Jennifer L., Linda G. Bandini, Aviva Must, Gerard E. Dallal, and William H. Dietz. Does menarche mark a period of elevated resting metabolic rate? Am J Physiol Endocrinol Metab 286: E456–E462, 2004. First published November 18, 2003; 10.1152/ajpendo.00410.2003.—Resting metabolic rate (RMR) and body composition were measured in 44 initially nonoverweight girls at three time points relative to menarche: premenarche (Tanner stage 1 or 2), menarche (±6 mo), and 4 yr after menarche. Mean absolute RMR was 1,167, 1,418, and 1,347 kcal/day, respectively. Absolute RMR was statistically significantly higher at menarche than at 4 yr after menarche despite statistically significantly less fat-free mass (FFM) and fat mass (FM), suggesting an elevation in RMR around the time of menarche. The pattern of change in RMR, adjusted for FFM, log transformed FM, age, race, parental overweight, and two interactions (visit by parental overweight, parental overweight by FFM), was also considered. Adjusted RMR did not differ statistically between the visits for girls with two normal-weight parents. For girls with at least one overweight parent, adjusted RMR was statistically significantly lower 4 yr after menarche than at premenarche or menarche. Thus parental overweight may influence changes that occur in RMR during adolescence in girls.

ADOLESCENCE, THE PERIOD OF GROWTH from puberty to adulthood, has been proposed as a critical period in the development of obesity (13). Females in particular appear to be at greater risk for the onset of obesity during this time and are more likely than males to develop obesity that persists into adulthood (9). Because obesity results from positive energy balance, understanding the pattern of change in energy intake and energy expenditure that occurs during adolescence may provide insight into the etiology of incident obesity during this time period.

Approximately 60–80% of daily energy expenditure is accounted for by resting metabolic rate (RMR) (39). The single best predictor of metabolic rate is fat-free mass (FFM) (39), whose metabolically active components are organ mass and muscle mass. On average, organ mass has a metabolic rate 15–25 times greater than that of muscle mass (24). After the first year of life, muscle mass increases more rapidly than organ mass and therefore makes up an increasingly greater proportion of FFM (52). As the ratio of muscle mass to organ mass increases, RMR per kilogram of FFM decreases (26). The metabolic contribution of 1 kg of FFM to RMR has been shown cross-sectionally to decrease from infancy to adolescence to adulthood (52). Observations of an inverse relationship between age (30, 46) or pubertal maturation (32, 44) and RMR adjusted for FFM in children and adolescents have been attributed to a decline in the metabolic activity of FFM. Longitudinal data are needed to evaluate this proposed decline.

Fat mass (FM) (4, 18, 30, 46), sex (7, 18, 30, 46), and race/ethnicity (4, 12, 32, 44, 46, 48) also independently predict metabolic rate in children. In addition, an influence of parental weight status on metabolic rate has been explored, but the findings lack accord (4, 17, 20, 48, 58). Finally, because of known pubertal changes in growth velocity and hormone concentrations (28), an effect of puberty on metabolic rate has been hypothesized. Among the studies (4, 5, 7, 8, 10, 30, 32, 44, 46, 47) that have examined a relationship with pubertal maturation, the findings are inconsistent. Most of these studies have been cross-sectional and used Tanner staging (45) to gauge pubertal maturation, and many have presented combined results for boys and girls. The aim of the present study was to examine longitudinally the pattern of change in RMR relative to menarche, a well-defined event in the course of pubertal maturation for females. We measured RMR and body composition in 44 girls before menarche [Tanner stage 1 or 2 (45)], at menarche (±6 mo), and 4 yr after menarche.

PARTICIPANTS AND METHODS

Participants. Between September 1990 and June 1993, 196 girls aged 8–12 yr were enrolled in the Massachusetts Institute of Technology (MIT) Growth and Development study, a prospective cohort study. Criteria for enrollment were premenarchal status and a triceps skinfold thickness less than the 85th percentile for age and sex (33). Girls were recruited from the Cambridge and Somerville (Massachusetts) public school systems and the MIT summer day camp; other recruits were friends and siblings of enrollees. All participants were initially healthy, free of disease, and not taking any medications known to affect body composition or metabolic rate. The study was approved by both the Committee on the Use of Humans as Experimental Subjects at MIT (Cambridge, MA) and the Tufts-New England Medical Center Institutional Review Board (Boston, MA). As part of the cohort study design, RMR and body composition were measured at study entry and at the study exit visit, which was scheduled for the 4-yr anniversary of menarche (±1 mo). Some of the girls had additional measure(s) of RMR and body composition during the course of the study as part of their participation in one of the two...
nested subcohorts (energy expenditure subcohort and menarcheal subcohort). Inclusion criteria for the present analyses were a valid measure of RMR and body composition (by total body water) at three specific time points: at study entry (hereafter referred to as the premenarcheal visit), within ±6 mo of menarche, and at the exit visit 4 yr after menarche. The analyses were further restricted to those girls who were classified as Tanner stage 1 or 2 (45) at their premenarcheal visit. Forty-four girls met the inclusion criteria.

Body composition. At all three time points, participants were admitted to the General Clinical Research Center at MIT for an overnight stay. A study physician obtained a medical history and performed a brief examination to assess the participant’s health. Body composition was estimated from total body water (TBW) measured by 18O dilution space. A baseline urine sample was collected, and an overnight fast was initiated approximately an hour before the administration of H218O. Between 7:00 and 8:00 PM, a dose of either 0.25 or 0.07 g of H218O/kg estimated TBW was administered to the study participant. The larger dose was provided when 18O was used to estimate total energy expenditure as well as TBW. Urine was then collected until 6:00 AM the next morning to determine urinary losses and the second urine void of the morning was used to measure 18O enrichment above the baseline value. The 18O enrichment of the urine samples was measured on a Hydra Gas Isotope Ratio Mass Spectrometer (Spex Accumass 8 Plus; Spex Industries, Edison, NJ) at the mass spectrometry laboratory of the Jean Mayer US Department of Agriculture Human Nutrition Research Center on Aging at Tufts University (Boston, MA). The 18O dilution space was calculated according to the method of Halliday and Miller (22) and assumed to be 1% higher than TBW. FFM was estimated from TBW assuming a hydration constant of 0.73. FM was calculated as the difference between body weight and FFM, and percent body fat was calculated by dividing FM by body weight (×100%).

RMR. RMR was measured in the morning, as described previously (3), by use of an open-circuit indirect calorimeter that was fitted with a ventilated hood. Each participant fasted overnight for ≥12 h and engaged in minimal activity before the determination of her metabolic rate. After body temperature was measured to confirm the absence of a fever, the participant lay down to rest for 30 min. A 5-min equilibration period preceded the 30-min measurement period. RMR was calculated from measures of oxygen consumption and carbon dioxide production according to the modified Weir’s equation (53). On the morning of each measurement, the linearity of the gas analyzers was confirmed by calibrating them against two standard gases and checking the concentration of a third standard gas. In addition, the calibration of the entire system was checked before each scheduled visit by pushing known amounts of a standard gas through the hood at a constant rate with a 3-L calibrated syringe (Warren E. Collins, Braintree, MA). At the premenarcheal visit, RMR was measured in two separate occasions, after 2 wk apart, with the average of the two values used in all analyses. The intraclass correlation of these two measures for the overall cohort was 0.96 (4). Because there was no evidence of a training effect and the reproducibility of the two measures was so high, only a single measure of RMR was made at subsequent visits.

Pubertal status. Tanner staging (45) of breast development was assessed by either the study physician or a female coinvestigator. The girls were instructed to call the study when they had their first period. For some participants, the date of menarche was based on self-report during one of their annual follow-up visits. At these abbreviated visits, girls were asked whether they had started their period during the preceding year; if the answer was yes, the girl was asked to recall the date.

Other variables. At each visit, weight was measured in the morning with participants in a fasted state, by means of a digital scale (Seca, Hamburg, Germany) accurate to 0.1 kg. Height (without shoes) was also measured at this time with a wall-mounted stadiometer (gauge, 200 cm). Percentiles of body mass index (BMI, kg/m2) for age, using the 2000 Centers for Disease Control growth charts (11), were calculated for each girl on the basis of her measured height and weight at each visit. Race/ethnicity (white, black, Hispanic, Asian, and “other”) was based on self-report on a questionnaire completed at study entry.

Early in the study, data on the height and weight of each participant’s biological parents were collected from either direct measurements at MIT (in normal clothing, without shoes) or from self-report. Parental overweight was defined as a BMI ≥25 (54). Girls were classified as having two normal-weight biological parents (NWP group) or at least one overweight biological parent (OWP group). Four sister pairs were among the 44 participants; for analyses considering parental overweight, we randomly selected one sister from each pair. In addition, we were missing data on parental overweight status; consequently, only 36 of the 44 participants are included in the analyses involving parental overweight. Parental weight status for 33 of the 36 girls was based on measured values.

Statistical analysis. All statistical analyses were performed using SAS version 8.01 (SAS Institute, Cary, NC). Mean (±SD) age, height, weight, BMI percentile, FFM, FM, and percent body fat were calculated for each visit and for each parental weight group at each visit. A log transformation was applied to FM (lnFM) before formal analyses, because its distribution was skewed to the right. The relationship between RMR and FM at each visit was assessed cross-sectionally using simple linear regression. A mixed-model repeated-measures analysis (using Proc Mixed in SAS) was then performed to test whether there was any univariate relationship between RMR and FM changed with pubertal maturation by evaluating the interaction term “FFM by visit.” A three-way interaction term (FFM by visit by parental overweight) was tested to determine whether parental overweight (assessed around the time of the premenarcheal visit) influenced any changes that occurred in the relationship between RMR and FFM across the three visits. Mixed-model repeated-measures analyses (Proc Mixed in SAS) were used to examine the pattern of change in RMR from premenarche (Tanner stage 1 or 2) to menarche (≥6 mo) to 4 yr after menarche. The changes in both absolute RMR and RMR adjusted for age, racial identity, parental overweight status, and puberty, and FFM, and lnFM were evaluated after first determining the most appropriate covariance structure for the data by use of the log likelihood ratio test and Aikaike Information Criterion. The unrestricted covariance structure proved best for the absolute RMR analyses, whereas the compound symmetry covariance structure was the most appropriate for the adjusted RMR analyses. Time was modeled as a categorical variable with the assumption that the premenarcheal measures, after adjustment for body composition and age, could be treated similarly among the Tanner 1 and Tanner 2 girls. This assumption was supported by the results of cross-sectional analyses using baseline data from the full MIT Growth and Development cohort (4), which revealed no difference in RMR adjusted for age, FFM, and FM between the 121 Tanner 1 girls and the 69 Tanner 2–3 girls (1,216 and 1,217 kcal/day, respectively). Because RMR adjusted for body composition has been observed to be lower in black than in white girls (4, 32, 48), we evaluated a race by visit interaction term to assess whether there were any racial differences in the change that occurred in adjusted RMR over the course of pubertal maturation. In addition, we tested a parental overweight by visit interaction term to assess whether the effect of parental overweight observed in the baseline cross-sectional analyses of our larger cohort (4) persists throughout maturation. The parental overweight by visit interaction term was statistically significant, while the race by visit interaction term was not. We also found a statistically significant interaction between parental overweight and FFM after testing a global interaction term of parental overweight with the other covariates in our model. Consequently, our final adjusted RMR model was as follows:

\[
RMR_i = \beta_0 + \beta_1 \text{age} + \beta_2 \text{FFM}_i + \beta_3 \ln \text{FM}_i + \beta_4 \text{race},
\]

\[
+ \beta_5 \text{parental overweight} + \beta_6 \text{visit}_i + (\beta_7 \text{parental overweight}) \times \text{visit}_i + (\beta_8 \text{parental overweight}) \times \text{FFM}_i + \epsilon_i
\]
RESULTS

At the premenarchal visit, 37 of the 44 girls were classified as Tanner stage 1 and seven as Tanner stage 2. Thirty-two reported their race/ethnicity as white, 6 as black, 4 as Hispanic, 1 as Asian, and 1 as “other.” Mean age (±SD) of actual menarche was 13.1 ± 1.0 yr, and the mean duration between menarche and the menarcheal visit was 1.8 ± 1.2 mo. Statistically significant increases in both FFM and FM were observed across the three visits; FFM increased from 23.4 to 37.3 kg, and FM increased from 7.3 to 11.8 to 16.5 kg (P < 0.001 for each comparison between visits). (See Supplemental Material, available at the journal web site.)

Among the 36 girls included in the analyses considering parental overweight, 10 had two normal-weight parents (NWP girls), whereas the remaining 26 had at least one overweight parent (OWP girls). Thirty of these 36 girls were Tanner stage 1 and six were Tanner stage 2. Twenty-eight described themselves as white; three as black; three as Hispanic; one as Asian; and one as “other.” Mean characteristics of the parental weight groups at each visit are presented in Table 1. The OWP girls, on average, weighed more and had a greater percentage of body fat at each visit than the NWP girls. In addition, menarche was experienced at a younger age in the OWP girls (13.0 ± 0.8 yr) than in the NWP girls (13.9 ± 1.1 yr).

Individual line plots of absolute RMR across the three visits are provided in Fig. 1; mean values differed significantly between the visits. RMR measured around the time of menarche (1,418 kcal/day) was statistically significantly elevated above RMR measured at premenarche (1,167 kcal/day, P < 0.001) or 4 yr after menarche (1,347 kcal/day, P = 0.001). The pattern of change across the three visits did not differ statistically between the NWP girls and the OWP girls. Mean absolute RMR was 1,087, 1,339, and 1,308 kcal/day, respectively, in the NWP group, and 1,203, 1,443, and 1,365 kcal/day, respectively, in the OWP group.

FFM was a statistically significant predictor of RMR cross-sectionally at premenarche, menarche, and 4 yr after menarche, explaining 58, 59, and 63% of the variance in RMR, respectively. The slope of the regression of RMR on FFM decreased from 30.3 to 25.3 to 23.6 kcal·kg⁻¹·day⁻¹. This apparent decline in the metabolic contribution of 1 kg of FFM to RMR when tested longitudinally was not statistically significant however (P = 0.62). On the other hand, the three-way interaction between FFM, visit, and parental overweight was found to be significant (P < 0.0001), indicating that the relationship between FFM and RMR across the three visits differed between the NWP and OWP girls. For the NWP girls, the slope of the regression of RMR on FFM was 38.7, 14.9, and 15.5 kcal·kg⁻¹·day⁻¹ (Fig. 2A), with FFM explaining 71, 25, and 74% of the variance in RMR at premenarche, menarche, and 4

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Table 1. Characteristics of the 36 girls by parental weight status at 3 visits relative to menarche: premenarche (Tanner stage 1 or 2), menarche (±6 mo), and 4 yr after menarche

<table>
<thead>
<tr>
<th></th>
<th>Premenarche</th>
<th>Menarche (±6 mo)</th>
<th>4 yr After menarche</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Normal-Weight Parents (n = 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>9.9±1.0*</td>
<td>14.1±1.1†</td>
<td>18.0±1.1‡</td>
</tr>
<tr>
<td>Height, cm</td>
<td>137.9±5.6*</td>
<td>161.4±7.2†</td>
<td>169.6±6.8‡</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>28.2±4.3*</td>
<td>46.9±5.8†</td>
<td>55.2±6.9†</td>
</tr>
<tr>
<td>BMI-for-age percentile</td>
<td>18.9±20.7*</td>
<td>22.2±22.6*</td>
<td>24.3±25.8*</td>
</tr>
<tr>
<td>%Body fat</td>
<td>20.5±5.0*</td>
<td>22.3±4.8*‡</td>
<td>25.4±4.3*‡</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>5.9±2.3*</td>
<td>10.5±3.0†</td>
<td>14.1±3.4‡</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>22.3±2.5*</td>
<td>36.5±4.9†</td>
<td>41.1±5.1‡</td>
</tr>
<tr>
<td>Absolute RMR, kcal/day</td>
<td>1,087±114*</td>
<td>1,339±147†</td>
<td>1,308±92‡</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Premenarche</th>
<th>Menarche (±6 mo)</th>
<th>4 yr After menarche</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 Overweight Parent (n = 26)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>9.7±0.8*</td>
<td>13.2±0.8†</td>
<td>17.1±0.9‡</td>
</tr>
<tr>
<td>Height, cm</td>
<td>139.3±6.8*</td>
<td>161.9±6.1†</td>
<td>167.9±6.3‡</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>32.0±4.4*</td>
<td>50.2±7.0†</td>
<td>61.4±8.9‡</td>
</tr>
<tr>
<td>BMI-for-age percentile</td>
<td>42.8±27.6*</td>
<td>48.7±23.3*†</td>
<td>53.3±25.2‡</td>
</tr>
<tr>
<td>%Body fat</td>
<td>24.9±4.7*</td>
<td>24.7±4.7*‡</td>
<td>28.7±4.7†</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>8.1±2.3*</td>
<td>12.6±3.7†</td>
<td>17.9±5.2‡</td>
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<tr>
<td>Fat-free mass, kg</td>
<td>24.0±3.0*</td>
<td>37.6±4.7†</td>
<td>43.5±4.9‡</td>
</tr>
<tr>
<td>Absolute RMR, kcal/day</td>
<td>1,203±114*</td>
<td>1,443±160†</td>
<td>1,365±160‡</td>
</tr>
</tbody>
</table>

Values are means ± SD. BMI, body mass index; RMR, resting metabolic rate. Means with the same symbol within a row of a parental weight group do not differ statistically, P > 0.05.

1 The Supplemental Material for this article (a table) is available online at http://ajpendo.org/cgi/content/full/00410.2003/DC1

![Fig. 1. Individual line plots of absolute resting metabolic rate (RMR) measured in 44 girls at 3 visits relative to menarche: premenarche (Tanner stage 1 or 2), menarche (±6 mo), and 4 yr after menarche.](http://ajpendo.org)
yr after menarche, respectively. By comparison, the slopes for the OWP girls were 28.7, 30.8, and 27.8 kcal/kg/day (Fig. 2). The regression equations for the OWP girls at the 3 visits, respectively, are RMR = 516 + 28.7FFM, RMR = 286 + 30.8FFM, and RMR = 155 + 27.8, respectively. By use of a repeated-measures mixed model, the slopes between the 3 visits were not statistically different in either the NWP girls (P = 0.26) or the OWP girls (P = 0.68).

DISCUSSION

Our study is among the first to publish longitudinal data on concomitant measures of RMR and body composition over the course of adolescence. Based on the comparison of absolute RMR, FFM, and FM between menarche and 4 yr after menarche, our data suggest an elevation in RMR around the time of menarche. In addition, our adjusted RMR analyses suggest that parental overweight may influence the changes that occur in RMR during pubertal maturation and adolescence in girls.

The physiological and morphological changes that characterize puberty are extensive. Sex differences in pubertal changes become manifest not only with respect to secondary sexual characteristics and sex steroid concentrations but also with respect to factors that may affect metabolic rate, such as...
changes in body composition (21), timing of the pubertal growth spurt [both chronologically and with respect to pubertal development (49)], and changes in growth hormone (GH) concentrations [in both magnitude and timing (1, 42)]. Most studies that have explored a possible effect of puberty on RMR have used Tanner staging to classify pubertal maturation and have presented combined results for boys and girls adjusted for sex. Such an approach may mask changes in metabolic rate associated with menarche or that occur around the time of menarche, because some girls become menarchal at Tanner stage 3 and others at stage 4 or 5 (28). Furthermore, statistical adjustment for gender will not reveal the true relationship between pubertal maturation and RMR for either sex if sexual dimorphism in the relationship exists.

Our observation that mean absolute RMR was statistically significantly greater at menarche than 4 yr after menarche is surprising in light of the fact that FFM, the major determinant of RMR (39), and FM, an independent contributor to RMR (4, 18, 30, 46), increased significantly over this period. Our findings are consistent, however, with a 1932 longitudinal study that measured basal metabolic rate (BMR) at intervals of 6 mo to 1 yr for 1–4 yr in 28 girls and 10 boys aged 10 to 16 yr (47). In girls, an increase in absolute BMR above what was predicted was observed 1–8 mo before menarche and was maintained until 1–6 mo after menarche, with individual differences noted in the degree, duration, and timing of the increase in BMR. These results, coupled with our own, suggest that metabolic rate is elevated in girls around menarche. Whether the elevation is specific to menarche or begins earlier in the pubertal process and is maintained through menarche cannot be addressed with these data.

Changes in GH during puberty in girls provide one plausible mechanism for the observed elevation in metabolic rate. GH administration appears to elevate metabolic rate by ~7–8% in both normal adults (29, 56, 57) and GH-deficient children (19), independent of changes in lean body mass. In addition, in normal, healthy girls, BMR adjusted for FFM is associated with the area under the GH-time curve for endogenous overnight GH release \( P = 0.054 (41) \). During Tanner stages 3 and 4 in girls, the secretion rate and nighttime concentration of GH are elevated (1, 42), with baseline GH concentrations elevated by Tanner stage 4. The secretion rate, nighttime level, and baseline concentration of GH all return to approximately prepubertal levels at Tanner stage 5. With most girls experiencing menarche while at Tanner stage 3 (≈25%) or 4 (~65% (28)), the transient increases in GH during puberty may explain the observed elevation in metabolic rate around the time of menarche. Any elevation in metabolic rate attributed to GH may be reduced or absent in obese children, because obese children (27), as well as obese adults (55), have a blunted GH response to GH-releasing hormone. The absence or blunting of a rise in metabolic rate around the time of menarche in obese girls may lead to either a continuation or a new period of positive energy balance that perpetuates their obesity into adolescence and adulthood.

Elevations in GH during puberty may also be responsible for pubertal insulin resistance (2, 31), which in turn may contribute to the elevation in metabolic rate around the time of menarche. Insulin sensitivity is significantly decreased during puberty (2), reaching its lowest level at Tanner stage 3 and returning by Tanner stage 5 to levels that are slightly yet statistically lower than prepubertal levels (31). In obese adults with insulin resistance (those with type 2 diabetes or impaired glucose tolerance), RMR per kilogram of FFM is significantly greater than in obese and normal-weight adults with normal glucose tolerance (34). A high rate of gluconeogenesis (34, 40) and/or a high rate of protein turnover may be responsible for the elevated energy expenditure.

As much as two-thirds of metabolic activity (24) is accounted for by the heart, brain, liver, and kidney. The metabolic rate of an organ is believed to be constant from infancy to maturity, with an organ’s metabolic activity proportional to its size (24, 25). Differences in organ size account for as much as 5% of the variance in metabolic rate between individuals (16, 26). Around the time of peak height velocity, a growth spurt of the transverse diameter of the heart (28, 49), the length and breadth of the head, and the abdominal viscera, including the liver and kidneys, has been demonstrated or hypothesized (28). Because peak height velocity almost always precedes menarche and usually occurs in girls around Tanner stage 3 (28), an increase in the growth velocity of the more metabolically active organs may contribute to an elevation in RMR around the time of menarche.

Many studies have examined a possible influence of parental weight status on RMR in children. Since the initial study by Griffiths and Payne (20), suggesting a lower adjusted resting energy expenditure in children with at least one overweight parent, most studies have observed either no association between parental weight status and metabolic rate in children (17, 48) or a higher adjusted metabolic rate in children with at least one overweight parent (4, 58). The conflicting findings may be due, in part, to differences in the classification of parental weight status, the weight status of the children themselves (normal-weight or overweight), sample size, or measurement techniques. In the present study, parental overweight among the 36 girls was not a statistically significant predictor of RMR cross-sectionally at any time point in a model adjusting for FFM, lnFM, age, and race. However, a statistically significant interaction between parental overweight and visit was observed in the longitudinal analyses, suggesting that the pattern of change in RMR from premenarche to late adolescence may differ between girls with two normal-weight parents and girls with at least one overweight parent.

In the OWP girls, adjusted RMR 4 yr after menarche was statistically significantly lower than at premenarche or menarche, whereas in the NWP girls no statistically significant differences were noted in adjusted RMR between any of the visits. The values for the NWP girls should be interpreted with caution, because the estimates were extremely sensitive to the covariance structure, most likely because of the small sample size of this subgroup. A study with a larger sample is needed to confirm these findings. We did, however, rerun the analyses after reclassifying parental overweight by using the older BMI cutoffs (35) of 27.3 for women and 27.8 for men, which resulted in a larger sample size for the NWP group \( n = 19 \) and greater balance between the parental weight groups. The observed pattern of change in adjusted RMR for both groups (unpublished observations) was similar to our original findings. An influence of parental weight status was not considered in the few cross-sectional studies (30, 32) that have compared RMR between premenarcheal and postmenarcheal girls and the one longitudinal study (44) that assessed changes in adjusted
RMR across pubertal maturation (as defined by Tanner staging). The inverse relationship between Tanner stage and adjusted RMR observed in the longitudinal study by Sun et al. (44) and the lower adjusted RMR in the postmenarcheal girls in the cross-sectional study by Morrison et al. (32) were both attributed to the changing composition of FFM during growth.

Supporting the notion that the metabolic contribution of 1 kg of FFM declines during growth, Weinsier et al. (52), using pooled data from various cross-sectional studies, found that the slope of RMR on FFM declined significantly from 79 kcal·kg⁻¹·day⁻¹ in infants and preschool age children (n = 58) to 28.3 kcal·kg⁻¹·day⁻¹ in adolescents (n = 70) to 21.0 kcal·kg⁻¹·day⁻¹ in adults (n = 534). Our data allowed us to examine in a similar fashion changes over time in the metabolic contribution of 1 kg of FFM to RMR, this time focusing on the period of pubertal maturation in girls and using repeated-measures data on the same 44 persons. We observed a decrease in the slope of the regression of RMR on FFM from 30.3 to 25.3 to 23.6 kcal to 28.3 kcal/H18528/kg/H11002 day/H11002 in the period of pubertal maturation in girls and using repeat-time measures data on the same 44 persons. We observed a decrease in the slope of the regression from 30.3 to 25.3 to 23.6 kcal·kg⁻¹·day⁻¹ from premenarche to menarche to 4 yr after menarche, respectively. Although suggestive and potentially biologically important, this apparent decline in slopes was not statistically significant, perhaps because of the small sample size of our study. The three-way interaction between FFM, visit, and parental overweight, however, was statistically significant, suggesting that changes in the relationship between FFM and RMR across the three visits depended on parental overweight status.

Several potential limitations of our study are noteworthy. First, our sample was predominantly white. We assumed that the pattern of change in RMR from premenarche to menarche to 4 yr after menarche does not differ between black and white girls despite the lower metabolic rate we and others (4, 32, 48) have observed in black girls than in white girls. Although a race-by-visit interaction term was not significant (P = 0.19) in our models, our small sample limited power. When we excluded the three black girls from the analyses considering parental overweight, the pattern of change in adjusted RMR for both parental weight groups remained consistent. In further support of our assumption, Sun et al. (44) found no ethnic differences in the pattern of change in RMR across Tanner stage in their longitudinal study of 156 children. Second, because the cyclical variation in metabolic rate over the full course of the menstrual cycle is not fully characterized (6, 23, 42), we elected not to correct the RMR data from 4 yr after menarche for timing of the menstrual cycle. RMR at that visit was measured during the luteal phase of the menstrual cycle for roughly one-quarter of the 44 girls, with an approximately equal distribution between the NWP girls and the OWP girls. An effect of the menstrual phase would not be a potential factor for the menarcheal RMR, because ovulation does not occur until there have been several menstrual periods (28), and 50–80% of menstrual cycles are anovulatory during the first 2 yr of menses (36). A final potential limitation is the lack of control for use of oral contraceptives (OC). Because of the conflicting results in the few published studies comparing metabolic rate in OC users and nonusers (14, 15, 38), the limited data on the effect of OC use on RMR within the individual (37), and the large number of hormonal formulations of OCs commercially available, we decided not to adjust for OC use in the nine girls who were taking OCs 4 yr after menarche.

In conclusion, we observed that absolute RMR was higher at menarche than 4 yr after menarche, which is surprising given that mean FFM and FM were statistically significantly higher 4 yr after menarche than at menarche. We observed no statistically significant differences between adjusted RMR at premenarche and at menarche in both parental weight groups, and we found a statistically significant decline in adjusted RMR at 4 yr after menarche only in the OWP girls. When RMR is adjusted for FFM and the comparison is made between adjusted RMR at premenarche and menarche, the proposed elevation in RMR around the time of menarche may be masked or mitigated by the counteracting effect of the changing composition of FFM. The changing composition of FFM would be expected to play a role during the perimenarche period in particular because of the substantial gains in FFM that occur during this time. Additional longitudinal studies with larger samples are needed to test the hypotheses generated from our analyses and to confirm these findings.

ACKNOWLEDGMENTS

We gratefully acknowledge the girls who participated in this study as well as the staff at the General Clinical Research Center at MIT for their assistance. In addition, we thank Gail Rogers for statistical input.

GRANTS

This research was supported by National Institutes of Health Grants DK-HD-50537, MO1 RR-00088, and 5 PD30 DK-46200.

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