The effect of puberty on fat oxidation rates during exercise in overweight and normal-weight girls

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1Physiology and Experimental Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada; 2School of Kinesiology and Health Sciences, Faculty of Health, York University, Toronto, Ontario, Canada; 3University of Toronto, Toronto, Ontario, Canada; 4Labatt Family Heart Centre, The Hospital for Sick Children, Toronto, Ontario, Canada; and 5Division of Endocrinology, The Hospital for Sick Children, Toronto, Ontario, Canada

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Chu L, Riddell MC, Schneiderman JE, McCrindle BW, Hamilton JK. The effect of puberty on fat oxidation rates during exercise in overweight and normal-weight girls. J Appl Physiol 116: 76–82, 2014. First published November 14, 2013; doi:10.1152/japplphysiol.00888.2013.—Excess weight is often associated with insulin resistance (IR) and may disrupt fat oxidation during exercise. This effect is further modified by puberty. While studies have shown that maximal fat oxidation rates (FOR) during exercise decrease with puberty in normal-weight (NW) and overweight (OW) boys, the effect of puberty in NW and OW girls is unclear. Thirty-three NW and OW girls ages 8–18 yr old completed a peak aerobic capacity test on a cycle ergometer. FOR were calculated during progressive submaximal exercise. Body composition and Tanner stage were determined. For each participant, a best-fit polynomial curve was constructed using fat oxidation vs. exercise intensity to estimate max FOR. In a subset of the girls, IR derived from an oral glucose tolerance test ($n = 20$), and leptin and adiponectin levels ($n = 11$) were assessed in relation to FOR. NW pre-early pubertal girls had higher max FOR [6.9 ± 1.4 mg·kg−1·min−1] than NW mid-late pubertal girls [2.2 ± 0.9 mg·kg−1·min−1] ($P = 0.002$), OW pre-early pubertal girls [3.8 ± 2.1 mg·kg−1·min−1] and OW mid-late pubertal girls [3.3 ± 0.9 mg·kg−1·min−1] ($P < 0.05$). Bivariable analyses showed positive associations between FOR with homeostatic model assessment of IR ($P = 0.001$), leptin ($P < 0.001$), and leptin-to-adiponectin ratio ($P = 0.001$), independent of percent body fat. Max FOR decreased in NW girls during mid-late puberty; however, this decrease associated with puberty was blunted in OW girls due to lower FOR in pre-early puberty. The presence of IR due to obesity potentially masks the effect of puberty on FOR during exercise in girls.

fat oxidation; exercise; child; adolescent; obesity

THE PREVALENCE OF CHILDHOOD obesity has continued to increase worldwide with prevalence rates reaching 12.7% in Canadian youth (39). Several key risk factors for type 2 diabetes mellitus and cardiovascular disease, such as dyslipidemia, insulin resistance (IR), and hypertension, may already be present in obese youth at a young age. Therefore, there is a great demand for earlier intervention and treatment strategies for children. Studies that have implemented exercise programs in obese children have found significant improvements in a number of metabolic parameters, such as improved lipid profile and decreased IR and inflammatory cytokines (4, 5, 13). Determining exercise intensities to optimize fat oxidation in children across a range of ages could be of clinical benefit to guide exercise recommendations for management of obesity, and for promotion of healthy body weights.

Pubertal development is an important factor to consider when providing exercise recommendations for obese youth. Both lean and obese boys lower their maximal fat oxidation rates (max FOR) during exercise once they begin puberty (6, 36, 41, 51). Additionally, the exercise intensity at which max FOR occurs (known as FATmax) is less after puberty in boys (36). In girls, fat oxidation in early-pubertal (EP) and late-pubertal (LP) development has not been examined over a range of exercise intensities. Although past literature showed a greater reliance on fat utilization during exercise in prepubertal girls compared with women (24), and young girls compared with older girls (43) at select intensities, the mechanisms that lead to reduced max FOR and FATmax after puberty remain unclear. We hypothesize that lowered FOR in older girls may be related to differences in the rising IR occurring with puberty. To our knowledge, there has only been one study that has assessed the relationship between IR and substrate utilization in overweight women (8). These authors reported that IR led to decreased carbohydrate utilization during moderate-intensity exercise (i.e., walking at 45% maximal $O_2$ uptake) and to a greater reliance on lipid as fuel, when substrate utilization was expressed as a percentage of total energy expenditure (8). The association of IR on substrate metabolism during exercise has not been previously investigated in young girls, and it is unclear whether IR is also associated with increased lipid oxidation in obese girls.

Body adiposity may affect the capacity to oxidize fat during exercise. In obese boys, compared with lean boys, a reduced capacity to metabolize fat during exercise has been demonstrated (50). To the best of our knowledge, there is only one study reporting changes in max FOR and FATmax in normal-weight and obese females with a focus on pubertal stage; however, one of the limitations in that study is that it included measurements at three different walking speeds (4, 5.6, and 8 km/h) and not a wide range of standardized relative exercise intensities (27).

Increased adiposity also leads to alterations in the adipocyte-secreted hormones leptin and adiponectin. Studies in human and rodent models demonstrate that these hormones have insulin-sensitizing properties, which result in increased fatty acid oxidation and decreased lipid content of skeletal muscle (12, 14, 46). The enhanced fatty acid oxidation is explained, at least in part, by their regulation of AMP-activated protein kinase pathways (12, 28, 45). In obese and insulin-resistant individuals, adiponectin levels are reduced, and leptin levels are elevated (15, 29). However, similar to IR with obesity,
leptin resistance is also present, leading to the impairment of the insulin-sensitizing actions of these hormones (12, 40). How these adipokines interact during puberty to affect fat oxidation during exercise in girls has not been studied. Thus the objectives of our study were to explore the effect of puberty on max FOR and FATmax in normal-weight (NW) and overweight (OW) girls, and to examine the association of max FOR with measures of IR and leptin and adiponectin levels.

METHODS

Subjects. OW and NW girls, ages 8–18 yr old, were recruited for the study at the Hospital for Sick Children (SickKids) and York University. Participants were recruited from specialty care clinics, and by recruitment via posted flyers within SickKids and clinics within the Greater Toronto Area. Subjects attended two study visits separated by at least 10 days. The purpose, procedures, and possible risks of the study were explained to the children and parents in detail. Written parental or guardian consent and child assent were obtained for children under 16 yr of age. Written informed consent was obtained for participants 16 yr and older. Participants did not take medications related to glucose metabolism, participate in 3 or more days of physical activity per week, and were not previously diagnosed with type 2 diabetes mellitus or developmental delays that would interfere with the completion of the testing. The study was approved by the Research Ethics Board (REB) at SickKids and at York University.

General study design. Subject anthropometric measurements were recorded at the initial study visit. A standard stadiometer and calibrated scale were used to measure height and weight. Body mass index (BMI) was calculated as weight/height$^2$ (kg/m$^2$) and converted to BMI z-scores for age and sex using the World Health Organization BMI growth charts (10). Blood pressure was measured in the right arm using a Dinamapp device. The above measurements were taken three times each, and the means were recorded. Pubertal stage was determined by a physician’s exam according to the Tanner method (42). Girls were categorized as Tanner I and II (pre- and early pubertal; EP) or Tanner III–V (mid- and late pubertal; LP) for the statistical analyses. The four groups compared in the study included: OW EP girls, OW LP girls, NW EP girls, and NW LP girls. Bioelectrical impedance analysis was also completed to estimate body composition using equations provided by Horlick and colleagues (19).

Cardiorespiratory fitness. During visit 1, participants completed a maximal, incremental cycle ergometer test [peak aerobic capacity (\(\dot{V}O_2\)peak) test] according to the Godfrey protocol (16). This was completed 1 h following a light meal. The participant’s sex, height, and physical activity level were considered when determining work load increments for an 8- to 10-min test to exhaustion. Subjects were asked to pedal at ~60 revolutions/min. \(\dot{V}O_2\)peak was considered to have been reached when respiratory exchange ratio $\geq$ 1.05 and age-predicted heart rate (HR) was obtained. The exercise test was stopped if systolic blood pressure and diastolic blood pressure went above 220 and 110 mmHg, respectively, for safety reasons. Singlelead HR electrocardiogram and breath-by-breath volume and gas analysis were recorded using a SensorMedics metabolic cart (Vmax Encore).

Fat oxidation protocol. During the second visit to the exercise laboratory, subject’s performed an incremental, submaximal exercise test on an electromagnetically braked cycle ergometer with continuous gas collection and HR monitoring, as described above. Subjects performed the exercise testing at the same time of the day in the afternoon, 3 h after eating, and were asked to refrain from any intense physical activity the day before. Cycling started at a workload of 10 W and increased by 10 W every 3 min, modified from the protocol used by Riddell et al. (36). The test was stopped when a respiratory exchange ratio $\geq$ 1.00 was reached, indicating carbohydrate as the predominant fuel source. \(\dot{V}O_2\) uptake and \(\dot{V}CO_2\) production were averaged over the final 20 s of each stage and used to calculate FOR over a wide range of exercise intensities for each subject. Fat oxidation was calculated using the following equation from Peronnet and Massicotte (34): \(\text{FOR (g/min)} = 1.69 \cdot \dot{V}O_2 \ (\text{l/min}) - 1.70 \cdot \dot{V}CO_2 \ (\text{l/min})\). To estimate max FOR from the incremental exercise test, the highest 20 s average for FOR was recorded. For each individual, a best-fit second-order polynomial curve was then constructed with FOR [expressed as milligrams per kilogram of fat free mass (FFM) per minute] vs. exercise intensity (expressed as %\(\dot{V}O_2\)peak). Each individual curve was used to determine the max FOR and the FATmax. Polynomial curves that had a $R^2 \leq 0.50$ were excluded from the analysis. Individuals with negative FOR due to variability in the data were also excluded. Based on the FOR curves, we also identified FOR at relative intensities, including 20, 30, 40, 50, and 60% \(\dot{V}O_2\)peak.

Oral glucose tolerance test and hormonal measurements. Following an overnight fast on visit 1, subjects arrived at the Clinical Investigation Unit at SickKids at 8:00 AM. An intravenous catheter was placed in the antecubital fossa for blood draws. Subjects completed an oral glucose tolerance test (OGTT) with Glucodex (1.75 g/kg to a maximum of 75 g). Venous blood samples were obtained at fasting and then 30, 60, 90, and 120 min following ingestion of Glucodex. Insulin and glucose concentrations were measured at each time point. Insulin was measured by chemiluminescence using the Siemens Immuline 2500 [range of assay 15–2,165 pmol/l, intra- and interassay coefficient of variation (CV) <7.6%]. From the OGTT, homeostatic model assessment of IR (HOMA-IR) was calculated: HOMA-IR = fasting insulin $\times$ fasting glucose/22.5 (26). Whole body insulin sensitivity index (WBISI) was determined using the Matsuda model, where WBISI = 10,000/[square root of (fasting glucose $\times$ fasting insulin) $\times$ (mean glucose $\times$ mean insulin during OGTT)]. WBISI has been previously validated against gold-standard measures of insulin sensitivity in adults and in children (25). Biochemical assays were completed to measure leptin (ELISA; Linco Research, range: 0.5–100 ng/ml, and intra- and interassay CV of 1.0–7.4% and 2.6–6.2%, respectively) and adiponectin (ELISA; Linco Research, range: 1.5–100 ng/ml, and intra- and inter-assay CV of 1.0–7.4% and 2.4–8.4%, respectively). A total of 10.5 ml of blood was drawn, which is within REB guidelines for research in children.

Statistical analysis. The statistical analysis was conducted using SPSS statistical analysis software 19.0 and GraphPad PRISM 5 software. Categorical variables were presented as counts and percentages. Continuous variables were presented as means $\pm$ SD. Pearson’s correlation analysis was used to examine the association of max FOR with HOMA-IR, WBISI, leptin, adiponectin, and leptin-to-adiponectin ratio. Correlation analysis was also conducted with adjustment for percent body fat (%BF). The ratio of leptin to adiponectin is supported as a useful index for IR (20, 33).

RESULTS

Subject anthropometric characteristics and fitness data for the four groups of volunteers are summarized in Table 1. Participants involved in the study were excluded from the analysis if they did not attend their second exercise test ($n = 1$), were incapable of completing the exercise tests due to weight ($n = 2$) and other medical restrictions ($n = 2$), or were unable to reach \(\dot{V}O_2\)peak based on our criteria ($n = 1$) or due to technical issues with equipment ($n = 1$). In the entire group,
the curve-fitting method failed to identify an estimated value for max FOR and FATmax in subjects due to variability in the data; $R^2 < 0.50$ ($n = 2$) and negative values for FOR ($n = 1$). Thus the total number of subjects with valid fat oxidation curves was 33 out of 42 participants (79%).

Two-way ANOVA results showed a significant group $\times$ puberty interaction for max FOR ($P = 0.013$) and FATmax ($P < 0.001$) (Fig. 1). Post hoc analysis indicated max FOR during exercise ($6.9 \pm 1.4$ mg·kg·FFM$^{-1}$·min$^{-1}$) NW EP vs. $2.2 \pm 0.9$ mg·kg·FFM$^{-1}$·min$^{-1}$ NW LP, $3.8 \pm 2.1$ mg·kg·FFM$^{-1}$·min$^{-1}$ OW EP, and $3.3 \pm 0.9$ mg·kg·FFM$^{-1}$·min$^{-1}$ OW LP; $P < 0.05$) and FATmax were significantly higher in NW EP girls than in all of the other groups ($54.9 \pm 4.6\%$ $V_O^{\text{peak}}$ NW EP vs. $34.8 \pm 7.3\%$ $V_O^{\text{peak}}$ NW LP, $42.7 \pm 4.0\%$ $V_O^{\text{peak}}$ OW EP, and $42.8 \pm 5.4\%$ $V_O^{\text{peak}}$ OW LP; $P < 0.001$). Moreover, max FOR in NW EP girls was almost threefold greater than that in NW LP girls (Fig. 1A). NW LP girls had optimal (higher) fat oxidation at a lower exercise intensity than all groups, including OW EP girls and OW LP girls. Max FOR was reached at similar exercise intensities in OW EP and OW LP girls, whereas NW LP girls reached max FOR at an exercise intensity that was reduced by 25% $V_O^{\text{peak}}$ compared with NW EP girls. Since max FOR (i.e. the capacity to burn fat) was not significantly different for NW LP girls compared with OW LP girls, only the FATmax was shifted to lower intensities of exercise (Fig. 1B).

FOR was assessed while controlling for relative exercise intensity in each participant according to their fat oxidation curve (Fig. 2). This analysis showed that there were no significant interactions for group $\times$ puberty at 20% $V_O^{\text{peak}}$ and 30% $V_O^{\text{peak}}$ on FOR. However, there was a significant pubertal effect showing that EP girls had higher FOR than LP girls at 30% $V_O^{\text{peak}}$ ($3.7 \pm 1.9$ mg·kg·FFM$^{-1}$·min$^{-1}$) EP vs. $3.1 \pm 1.1$ mg·kg·FFM$^{-1}$·min$^{-1}$ LP; $P = 0.03$). At exercise intensities at and above 40% $V_O^{\text{peak}}$, results showed significant pubertal effects ($4.2 \pm 2.6$ mg·kg·FFM$^{-1}$·min$^{-1}$ EP vs. $3.5 \pm 1.3$ mg·kg·FFM$^{-1}$·min$^{-1}$ LP; $P = 0.009$) and group $\times$ puberty interactions ($6.4 \pm 1.4$ mg·kg·FFM$^{-1}$·min$^{-1}$ NW LP, $2.0 \pm 1.1$ mg·kg·FFM$^{-1}$·min$^{-1}$ NW LP, $3.7 \pm 2.0$ mg·kg·FFM$^{-1}$·min$^{-1}$ OW EP, and $3.4 \pm 0.8$ mg·kg·FFM$^{-1}$·min$^{-1}$ OW LP; $P = 0.02$) (Fig. 2). Therefore, it appears that obesity and puberty have greater influences on fat oxidation at higher exercise intensities. NW EP girls had higher FOR than NW LP girls at all exercise intensities above 40% $V_O^{\text{peak}}$. At 50% $V_O^{\text{peak}}$, NW EP girls also had a greater capacity to metabolize fat compared with OW LP girls, and NW LP girls had the poorest ability to metabolize fat during exercise compared with all groups. At the highest exercise intensity examined (60% $V_O^{\text{peak}}$, NW EP girls also had a greater capacity to metabolize fat compared with OW LP girls, and NW LP girls had the poorest ability to metabolize fat during exercise compared with all groups. At the highest exercise intensity examined (60%

### Table 1. Subject characteristics

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<td>$n$</td>
<td>7</td>
<td>16</td>
<td>5</td>
<td>5</td>
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<tr>
<td>Age, yr</td>
<td>11.1 ± 1.6</td>
<td>14.4 ± 1.5</td>
<td>9.3 ± 0.7</td>
<td>15.2 ± 1.8</td>
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<td>Weight, kg</td>
<td>54.8 ± 10.3</td>
<td>90.0 ± 22.5</td>
<td>30.4 ± 3.3</td>
<td>51.0 ± 5.7</td>
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<td>Height, cm</td>
<td>146.6 ± 5.6</td>
<td>164.6 ± 6.4</td>
<td>137.5 ± 5.7</td>
<td>161.9 ± 3.6</td>
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<td>BMI z-score (CDC)</td>
<td>1.71 ± 0.63</td>
<td>2.02 ± 0.50</td>
<td>−0.27 ± 0.97</td>
<td>−0.24 ± 0.58</td>
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<tr>
<td>Body fat, %</td>
<td>35.4 ± 5.8</td>
<td>42.0 ± 9.4</td>
<td>17.5 ± 4.3</td>
<td>23.2 ± 4.6</td>
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<tr>
<td>FFM, kg</td>
<td>35.0 ± 4.5</td>
<td>50.6 ± 6.9</td>
<td>25.1 ± 3.1</td>
<td>39.1 ± 4.2</td>
</tr>
<tr>
<td>$V_O^{\text{peak}}$, ml·kg·body mass$^{-1}$·min$^{-1}$</td>
<td>31.1 ± 6.1</td>
<td>25.4 ± 5.2</td>
<td>44.8 ± 7.3</td>
<td>35.7 ± 7.0</td>
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<tr>
<td>Maximum workload, W</td>
<td>48.8 ± 7.2</td>
<td>43.1 ± 6.3</td>
<td>54.2 ± 5.5</td>
<td>46.6 ± 7.6</td>
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<tr>
<td>Maximum heart rate, beats/min</td>
<td>106 ± 28</td>
<td>140 ± 28</td>
<td>93 ± 12</td>
<td>132 ± 17</td>
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<tr>
<td>Maximum RER</td>
<td>1.14 ± 0.07</td>
<td>1.19 ± 0.08</td>
<td>1.04 ± 0.08</td>
<td>1.23 ± 0.12</td>
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Values are means ± SD; $n$, no. of subjects. EP, early puberty; LP, late puberty; BMI, body mass index; CDC, Centers for Disease Control and Prevention; FFM, fat free mass; $V_O^{\text{peak}}$, peak aerobic capacity; RER, respiratory exchange ratio.
These findings for NW girls, max FOR and FATmax did not significantly change during puberty in the OW girls, likely because the oxidation rate of lipid was already impaired in EP.

To our knowledge, only one other research group has reported values of max FOR and FATmax in NW girls using a similar protocol (47, 48). Although there were different study objectives, our values for max FOR and FATmax were comparable to the values reported by Zakrzewski and Tolfrey (48). Few studies have compared FOR during exercise in NW and OW girls. Lazzer et al. (21) did not find any significant differences in max FOR during exercise between severely obese adolescents and nonobese sedentary adolescents ages 14–16 yr at 30, 40, 50, and 60% \( \dot{V}O_{2\text{peak}} \). However, there was a trend showing FOR were greater in the obese youth compared with nonobese adolescents <40% \( \dot{V}O_{2\text{peak}} \) and reduced at intensities >40% \( \dot{V}O_{2\text{peak}} \) (21). In contrast, our study showed that OW LP girls had higher fat oxidation at 40% \( \dot{V}O_{2\text{peak}} \) and 50% \( \dot{V}O_{2\text{peak}} \) than NW LP girls. Two important limitations to note in the study conducted by Lazzer and colleagues (21) include the absence of data presented as FOR normalized for FFM and data on pubertal stage. McMurray and Hosick (27) observed the interaction of obesity, sex, and puberty on substrate utilization at rest and at 4, 5.6, and 8 km/h on a treadmill. In girls, there were no differences in FOR per kilogram FFM between the prepubertal and pubertal groups. However, FOR were highest in the 4 km/h exercise trial, which suggests that the girls may not have been exercising at the same relative intensity or at a FATmax. In addition, there were no differences in FOR during exercise between the NW and OW boys or NW and OW girls at different speeds (27). This was inconsistent with the findings presented by Zunquin et al. (50), showing that NW boys had higher fat oxidation than OW boys. The different protocols between studies have made it difficult to fully clarify the influence of puberty and obesity on FOR during exercise.

In our study, decreasing FOR across puberty in NW but not OW may be explained by the effects of IR in these girls. There is a well-described transient rise in IR that occurs at the onset of puberty during normal growth and development, which is believed to be secondary to elevations in growth hormone (GH), a counterregulatory hormone that raises blood sugar (9, 17, 18, 32). The administration of GH during insulin-stimulated conditions results in suppression of insulin-stimulated glucose uptake into skeletal muscle (7, 35), but with no effect on insulin action on FFA concentration or circulating branched.

**DISCUSSION**

Our study is the first to examine max FOR in NW and OW EP and LP girls and to examine the potential associations between FOR and markers of insulin sensitivity in females. Our findings showed that NW EP girls have the greatest capacity to oxidize fat compared with NW LP or OW girls in general. In NW girls, we found that max FOR during exercise decreases as puberty progressed, and the FATmax was also lower during and after puberty. When FOR was examined at 20, 30, 40, 50, and 60% \( \dot{V}O_{2\text{peak}} \), NW EP girls had the highest FOR at 40% \( \dot{V}O_{2\text{peak}} \) and above, whereas the capacity to oxidize fat was reduced in NW LP girls at exercise intensities >40% \( \dot{V}O_{2\text{peak}} \). This suggested that the window of exercise intensities that elicits max FOR in NW girls is not as wide for older females compared with younger females. This is similar to what has been reported for NW boys (36). In contrast to

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**Table 2. Bivariate correlations with maximal fat oxidation rate with blood parameters related to insulin resistance**

<table>
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<tr>
<th></th>
<th>Pearson’s ( r ) Correlation</th>
<th>Partial Correlation Adjusted for %Body Fat</th>
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<tr>
<td></td>
<td>( r )</td>
<td>( P ) value</td>
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<tr>
<td>HOMA-IR</td>
<td>0.431</td>
<td>0.058</td>
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<tr>
<td>WBISI</td>
<td>−0.047</td>
<td>0.858</td>
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<tr>
<td>Leptin</td>
<td>0.690</td>
<td>0.019*</td>
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<tr>
<td>Adiponectin</td>
<td>−0.318</td>
<td>0.314</td>
</tr>
<tr>
<td>Leptin-to-adiponectin ratio</td>
<td>0.579</td>
<td>0.062</td>
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HOMA-IR, homeostatic model assessment of insulin resistance (n = 20); WBISI, whole body insulin sensitivity index (n = 17); leptin, adiponectin, and leptin-to-adiponectin ratio (n = 11). *Significant difference.
amino acids (35). Therefore, IR mediated by GH appears to be specific to glucose metabolism during puberty. Several studies have reported a positive association between pubertal IR and 24-h mean GH levels (2), as well as IGF-I levels and greater lipolysis (2, 3, 9, 31). In the OW girls, however, there was no significant difference found in max FOR between EP and LP. We suspect this is related to the fact that IR associated with obesity masked the expected decline in FOR associated with puberty.

Studies on substrate utilization at rest have shown higher FOR in OW children than in NW children (22, 23, 30, 37, 44). Our results demonstrate parallel results over exercise in LP girls, which appears to be associated with metabolic inflexibility defined by an inability to match fuel utilization with fuel availability. This is related to reduced adipose tissue lipolytic regulation, shown by higher plasma FFA in obese youth than lean youth and lean adults with hyperinsulinemia (37). As a result, fat oxidation is not suppressed in obese youth in insulin-stimulated conditions, as much as it is suppressed in lean youth or adults (37). In support of this finding, we found a positive correlation of HOMA-IR, a measure of fasting IR, with max FOR adjusted (P = 0.001) and unadjusted (P = 0.058) for %BF. Since a majority of the girls who completed blood work were in the OW group, we suspect that the greater IR was associated with greater FOR because of poor suppression of lipolysis at rest. Furthermore, a previous study in overweight sedentary women reported enhanced fat oxidation during exercise in insulin-resistant individuals compared with insulin-sensitive individuals (8). This provides additional support for the positive relationship we found between fat oxidation during exercise and IR in our OW girls. The authors suggested that one of the benefits of exercise in obese insulin-resistant individuals might be to oppose the impaired ability to utilize fat in the resting state in adults and promote the utilization of excess adiposity (8). In contrast, we did not find a significant correlation between WBISI, a measure of dynamic whole body insulin sensitivity following an oral glucose load, and FOR (P = 0.530). These findings suggest a greater influence of fasting IR with impaired suppression of hepatic glucose output compared with dynamic measures of insulin response to a glucose load on max FOR during exercise.

Unique to our study, we explored the relationship of the hormones leptin and adiponectin to FOR. These hormones play important roles in energy balance and IR and are known to change throughout puberty and with body fat accretion (1, 15, 38). Leptin is a satiety-inducing signaling hormone secreted by adipose tissue, which has a role in energy balance by decreasing food intake and/or increasing energy expenditure (49). With progressing obesity, leptin levels increase, and the action of leptin is disrupted, resulting in both leptin resistance and IR in obese patients (15, 29). Adiponectin is an insulin-sensitizing hormone also secreted by adipocytes and inversely related to the level of adiposity. With transition to puberty, adiponectin levels decline by ~50% in children, paralleling the increase in IR seen during this developmental period (18). The ratio of leptin to adiponectin has also been shown to demonstrate a stronger relationship to IR than either hormone independently (33). We found a positive correlation between leptin and the leptin-to-adiponectin ratio with max FOR during exercise when adjusted for %BF, and we speculate that these hormones are influencing max FOR. In support of this, studies in a mouse model characterized by obesity and hyperlipidemia, adiponectin administered to the rodent reduced plasma concentrations of fatty acids and triglycerides by accelerated fat oxidation in muscle cells (14, 46).

There are other potential mechanisms than increased IR that may contribute to reduction in FOR from prepuberty to puberty in girls. Studies comparing NW girls and women during exercise (treadmill running at 70% \( V_{\text{O2peak}} \)) resulted in a higher relative contribution of fat to total energy during exercise with lower lactate concentrations in girls than the women, suggesting a greater anaerobic energy contribution related to maturation (24). Timmons et al. (43) also reported higher fat oxidation when normalized to body mass during exercise at 70% \( V_{\text{O2peak}} \) in young girls (12 yr) compared with older girls (14 yr), despite lower serum estradiol levels in the young girls. Although we do not have data concerning lactate and estradiol concentrations in our population, these require further study as contributors to FOR during exercise.

The above results should be considered in the context of some important limitations. According to Zakrzewski and Tolfrey (48), max FOR and FATmax may have been higher conducted on a treadmill instead of on a cycle ergometer. However, for the OW groups, cycling exercise was preferred because it provided safer testing conditions. Another common limitation in research related to pubertal development is the inability to control for menstrual cycle phase in girls who have already reached menarche. In women, menstrual cycle phase may have slight effects on substrate utilization during exercise (11). Although information on the participant’s last menstrual period was recorded in the study, it was difficult to quantify because menses is often irregular in adolescent girls in the first 2 yr following menarche. Despite these limitations, the study provided novel insight into the interaction between obesity and puberty on max FOR and FATmax in girls, demonstrating that OW girls lack metabolic flexibility to substrate utilization during exercise, particularly in the EP ages. A major strength of our study is that we have evaluated these measures over a wide range of exercise intensities in NW and OW girls while controlling for puberty. This has not previously been done. Additionally, the measurements from the OGTT and other biochemical markers provided the unique ability to investigate the association of HOMA-IR, WBISI, leptin, and adiponectin with max FOR in OW girls, despite the fact that samples were not available for all subjects, as those who refused blood work were not excluded from participation. No studies have considered these important parameters in the past, while examining substrate metabolism during exercise in youth.

The rising prevalence of childhood obesity emphasizes the urgent need for effective prevention and intervention strategies. Research on fuel metabolism in NW and OW children may provide clinical applications for improving metabolic health and reducing obesity-related complications with exercise training. We showed a decline in the capacity to utilize fat during exercise in NW girls after puberty, which was not seen in OW girls, likely due to the effects of IR related to obesity and preferential use of lipid as a fuel source. In addition, OW girls do not need to exercise at as high of an intensity to achieve max FOR, which is relevant for clinical recommendations for OW youth. Further research into the physiological factors contributing to FOR during exercise across the spectrum of growth of development in childhood will be valuable.
to optimize the benefits of exercise and inform physical activity recommendations.

ACKNOWLEDGMENTS

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