Regional body composition in adolescents with anorexia nervosa and changes with weight recovery

Madhusmita Misra, Leslie A Soyka, Karen K Miller, Steven Grinspoon, Lynne L Levitsky, and Anne Klibanski

ABSTRACT

Background: Studies of regional fat distribution in adults with anorexia nervosa (AN) have shown decreased extremity fat at baseline and increased trunk fat with weight recovery, resulting in truncal adiposity. Little is known about fat distribution in adolescents with AN, especially with weight recovery.

Objective: We sought to determine whether regional fat distribution in adolescents with AN is comparable with that in healthy adolescents and whether weight recovery results in increased truncal adiposity.

Design: In 21 adolescent girls with AN and 21 control subjects matched for age and pubertal stage, we measured body-composition variables with dual-energy X-ray absorptiometry at baseline, 6 mo, and 12 mo. Weight recovery was defined as a ≥10% increase in body mass index.

Results: At baseline, the girls with AN had a lower percentage of trunk fat than did the control subjects, whereas the percentage of extremity fat was not significantly different between the groups. Weight recovery in 13 subjects with AN resulted in an increased percentage of trunk fat and an increased ratio of trunk fat to extremity fat; however, this ratio did not exceed that of control subjects.

Conclusions: In adolescents with AN, trunk fat rather than extremity fat is reduced. Weight recovery is associated with increased trunk fat and an increased ratio of trunk fat to extremity fat. In contrast with previous findings in adults, this most likely represents normalization of fat distribution rather than development of truncal adiposity.


KEY WORDS Anorexia nervosa, body composition, lean body mass, fat mass, trunk fat, extremity fat, adolescents, eating disorders

INTRODUCTION

Anorexia nervosa (AN) is the third most common chronic disorder diagnosed in adolescent girls (1), and in the United States, 0.2–4% of all adolescent girls develop AN (1, 2). Although improved nutritional intake and weight recovery remain the goal for all patients with AN, the resulting changes in body composition, especially regional fat distribution, may make psychological and physical recovery difficult in a population so focused on body image. Nutritional recovery is essential, however, because medical and metabolic complications in this disorder commonly cause increased morbidity and mortality. In addition, bone loss and increased fracture risk are complications of the weight loss associated with AN (3–5), and therefore sustained weight recovery is encouraged for optimizing bone mass accrual.

Studies of adults with AN have shown abnormalities in fat distribution, both with acute refeeding (6–8) and with long-term weight recovery (9, 10). In women with AN, overall fat mass is lower than that in healthy, age-matched control subjects, and most of the fat mass is lost from the extremities. Weight recovery results in a significant increase in trunk fat and development of truncal adiposity (7–10) compared with control subjects. Because women and girls with AN have an intense fear of weight gain and becoming fat, these findings may have major implications for the ability of such patients to psychologically tolerate weight gain.

Several groups have examined body composition and regional fat distribution in adults with AN, but very few studies have been done in adolescents with this disorder. Adolescent physiology is substantially different from that of adults; thus, results from adult studies cannot be extrapolated to adolescents. Kerruish et al (11) reported lower trunk and leg fat and a lower ratio of trunk fat to leg fat in adolescents with AN than in control subjects, in contrast to findings in adults with AN. This study did not, however, assess the effects of weight recovery on regional fat distribution. Koo et al (4) reported an increase in fat mass without a change in lean body mass in a group of older adolescent girls with partial weight recovery; this study did not examine regional fat distribution.

In the current study, our objectives were 1) to determine body composition and regional fat distribution in adolescents with AN and in matched control subjects and 2) to measure changes in these parameters with weight recovery. To our knowledge, this is the first study to investigate the effects of chronic weight loss and also weight recovery on regional body composition and regional fat distribution in adolescents with AN compared with normal control subjects matched for age and pubertal stage.

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SUBJECTS AND METHODS

Subject selection

Twenty-one adolescent girls with AN (diagnosed by using criteria from the Diagnostic and Statistical Manual of Mental Disorders IV) and 21 healthy control subjects were studied. All subjects were white and ranged in age from 12.1 to 18.7 y. The mean duration since diagnosis of AN was 14.4 mo (range: 1–48 mo). Eight subjects with AN had not attained menarche and 13 had secondary amenorrhea (mean duration: 12.3 mo; range: 6–36 mo). Three control subjects had not reached menarche. All control subjects had a body mass index (BMI; in kg/m^2) between −1 and +2 SD scores for age (12). No subject had a medical condition (other than AN) or received hormonal or other medication known to affect body composition. Recruitment of AN subjects was carried out through referrals from primary care providers, nutritionists, psychiatrists, and therapists, and through collaboration with inpatient and day-treatment eating disorder programs in the New England area. Recruitment of healthy control subjects was carried out through mass mailings to local primary health care providers and advertisements in community newspapers. All AN subjects were enrolled in integrated treatment programs (involving pediatricians, nutritionists, and therapists) when the study began and remained in these programs for the duration of the study. The study was approved by the Subcommittee on Human Subjects of Massachusetts General Hospital, and informed consent was obtained from all subjects and their parents.

Experimental protocol

Eligibility for study participation was determined after an initial screening visit to the General Clinical Research Center of Massachusetts General Hospital. All subjects received detailed instructions for collecting a 24-h urine sample (to be tested for urinary free cortisol) and for completing 4-d food records (to be done using home measuring utensils). Exclusion criteria included elevated thyroid stimulating hormone concentrations, elevated gonadotropins, or hyperprolactinemia. Subjects were studied at baseline, 6 mo, and 12 mo. A complete history and physical examination was performed at each visit, and blood samples were drawn in the fasting state. Body composition was assessed in all subjects at each visit.

Anthropometric measurements

Height and weight were measured at all visits. For height, we used the average of 3 readings on a single stadiometer. Subjects were weighed on an electronic scale while wearing a hospital gown. BMI was calculated, and the BMI standard deviation score was determined from published charts (12). Rising concentrations of sex steroids in puberty cause changes in regional fat distribution and development of a gynecoid distribution of body fat. It is therefore important to control for pubertal stage in studies of body composition in adolescents. Tanner breast staging in girls with AN can be erroneous because excessive weight loss and hypoestrogenism may result in breast atrophy and make breast staging unreliable. In these circumstances, bone age is a better indicator of pubertal stage. Bone age was assessed with an X-ray of the left wrist and hand by using the methods described by Greulich and Pyle (13); the results were used to confirm that bone ages were similar in the AN and control groups. Tanner staging of pubic hair was also carried out. Menarchal status was different in the 2 groups. However, because there is much variation in the timing of menarche, even in girls of similar breast and pubic hair status, menarche was not used as an indicator of pubertal status.

Biochemical assessment

Urinary free cortisol was measured with the GammaCoat 125 radioimmunoassay (RIA) (Diasorin Inc, Stillwater, MN; detection limit of 1 μg/dL and CV of 7.0%) by using the extraction method. The concentration of free cortisol in the 24-h urine sample was multiplied by the total volume over 24 h to obtain the value for urinary free cortisol in μg/d. We measured estradiol concentrations by ultra-sensitive RIA (Diagnostic Systems Laboratories Inc, Webster, TX; detection limit of 8.1 pmol/L and CV of 6.5–8.9%). RIA was used to measure free testosterone (DiaSorin Inc; detection limit of 0.6 pmol/L and intra-assay CV of 3.7–6.2%), serum dehydroepiandrosterone sulfate (DHEAS) (Coated Tube RIA; DiaSorin Inc; detection limit of 0.03 μmol/L and intra-assay CV of 3.8–5.3%), and serum leptin (Linco Diagnostics, St Louis; sensitivity of 0.5 μg/L and intra-assay CV of 3.4–8.3%). An acid-alcohol extraction and RIA kit (Nichols Institute Diagnostics, San Juan Capistrano, CA) was used to measure serum insulin-like growth factor I (IGF-I) (detection limit of 0.06 μg/L and intra-assay CV of 2.4–3.0%). Serum insulin-like growth factor binding protein 3 (IGFBP-3) was measured with an immunoradiometric assay (Coated Tube IRMA; DiaSorin Inc) with a detection limit of 0.5 μg/L and an intra-assay CV of 1.8–3.9%. Values of DHEAS, leptin, and IGFBP-3 were available for 17 AN subjects and 14 control subjects.

Body composition

Body composition was determined by using both whole-body dual-energy X-ray absorptiometry (DXA) (Hologic Inc, Waltham, MA) and bioimpedance analysis. DXA has been validated for body-composition measurements (14, 15). The precision (SD) of DXA is 425 g for whole-body fat and fat-free mass (14), with correlations of 0.99 with a 4-compartment-model body-composition method for measuring fat-free mass and 0.93–0.97 with multi-slice computed tomography for measuring regional fat-free mass (15). We found a correlation of 0.88–0.91 between percentage body fat readings reported by DXA and by bioimpedence analysis in this group of patients; only the results from DXA are reported. Percentage trunk fat, percentage extremity fat, ratio of trunk fat to extremity fat, percentage trunk lean body mass (LBM), percentage extremity LBM, and trunk to extremity LBM were calculated from whole-body DXA by using the following formulas (16):

\[
\begin{align*}
\text{Percentage trunk fat} & = \frac{\text{total trunk fat}}{\text{total fat}} \times 100 \\
\text{Percentage extremity fat} & = \frac{(\text{right arm LBM} + \text{left arm LBM} + \text{right leg LBM} + \text{left leg LBM})}{\text{total LBM}} \\
\text{Ratio of trunk fat to extremity fat} & = \frac{\text{percentage trunk fat}}{\text{percentage extremity fat}} \\
\text{Percentage trunk LBM} & = \frac{\text{total trunk LBM}}{\text{total LBM}} \\
\text{Percentage extremity LBM} & = \frac{(\text{right arm LBM} + \text{left arm LBM} + \text{right leg LBM} + \text{left leg LBM})}{\text{total LBM}} \\
\text{Ratio of trunk LBM to extremity LBM} & = \frac{\text{percentage trunk LBM}}{\text{percentage extremity LBM}}
\end{align*}
\]

where LBM is lean body mass, total fat includes head fat, and total LBM includes head LBM.

Nutrition and activity assessment

Computer analysis of 4-d food records (Nutrition Data Systems, version 2, Minneapolis) was performed to provide an assessment of macronutrient and micronutrient intakes at each visit. Exercise
and activity of the subjects during the past year were determined by using a validated questionnaire (17).

Statistical analysis

Data were collected at baseline, 6 mo, and 12 mo; t tests were used to compare differences between the 2 groups at baseline and in the percentage change from baseline to 12 mo. For comparisons between recovered AN subjects, nonrecovered AN subjects, and control subjects, we first performed analysis of variance (ANOVA). If the ANOVA was significant, we also performed the Tukey-Kramer test for comparisons within all groups. Correlational and stepwise regression analyses were performed to determine the predictors of percentage trunk fat, percentage extremity fat, and ratio of trunk fat to extremity fat. These analyses were also performed to determine the predictors of percentage change in body-composition variables over the study period. All data are reported as means ± SDs. The data were analyzed by using the JMP program, version 4 (SAS Institute Inc, Cary, NC).

Weight recovery was defined as a ≥10% increase in BMI from baseline; this definition was selected on the basis of data from the JMP program, version 4 (SAS Institute Inc, Cary, NC).

RESULTS

Baseline characteristics

Baseline demographic and hormonal data, but not regional body-composition data, on 17 AN subjects and 14 healthy control subjects were reported previously by Soyka et al (19). The demographic characteristics of the study population are shown in Table 1. The groups were not significantly different in terms of chronologic age, bone age, or stature. The mean weight of the AN group was significantly lower than that of the control group, as was the mean BMI. Body-composition variables and regional fat distribution at baseline are shown in Table 2. Both LBM and fat mass were lower in AN subjects than in control subjects; fat mass was 57.7% lower and LBM was 8.9% lower. Percentage trunk fat was 16.8% lower in AN subjects than in control subjects. However, there was no significant difference between the 2 groups in percentage extremity fat. Thus, in girls with AN, fat mass was lost primarily from the trunk rather than from the extremities, and they did not have a central distribution of fat. There was a lower ratio of trunk fat to extremity fat in AN subjects compared with control subjects.

Analysis of food records showed no significant differences between the 2 groups in intakes of total energy, protein, or carbohydrates (1972 ± 658 kcal/d, 78.7 ± 30.0 g protein/d, and 292 ± 93 g carbohydrates/d for the entire group). However, girls with AN consumed significantly less fat than did control subjects (46.4 ± 29.1 and 71.8 ± 31.9 g, respectively; P = 0.01). The groups also differed in terms of the type of fat consumed. AN subjects consumed less saturated fat than did control subjects (17.2 ± 12.3 and 27.3 ± 13.4 g, respectively; P = 0.01) and also consumed less monounsaturated fat than did control subjects (15.5 ± 9.4 and 25.4 ± 12.1 g, respectively; P = 0.005). The 2 groups did not differ significantly on intake of polyunsaturated fat. No significant differences in activity level were found between the groups.

Hormonal measurements are shown in Table 3; data on 17 AN subjects and 14 control subjects were reported previously (19). Estradiol concentrations were significantly lower in AN subjects than in control subjects. No significant differences between groups were observed in mean DHEAS and urinary free cortisol values. However, positive correlations were observed between urinary free cortisol concentration and duration of AN (r = 0.51, P = 0.04) and DHEAS concentration and duration of AN (r = 0.44, P = 0.05).

Statistical analysis

Data were collected at baseline, 6 mo, and 12 mo; t tests were used to compare differences between the 2 groups at baseline and in the percentage change from baseline to 12 mo. For comparisons between recovered AN subjects, nonrecovered AN subjects, and control subjects, we first performed analysis of variance (ANOVA). If the ANOVA was significant, we also performed the Tukey-Kramer test for comparisons within all groups. Correlational and stepwise regression analyses were performed to determine the predictors of percentage trunk fat, percentage extremity fat, and ratio of trunk fat to extremity fat. These analyses were also performed to determine the predictors of percentage change in body-composition variables over the study period. All data are reported as means ± SDs. The data were analyzed by using the JMP program, version 4 (SAS Institute Inc, Cary, NC).

Weight recovery was defined as a ≥10% increase in BMI from baseline; this definition was selected on the basis of data from other studies (18, 19). All AN subjects who were weight recovered according to these criteria were also >85% of ideal body weight for height, with BMI greater than the 10th percentile and BMI standard deviation scores above −1.5 at study completion. On the basis of other studies (18), we expected 50% of our control subjects. However, there was no significant difference

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic data for adolescent girls with anorexia nervosa and healthy control subjects1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia nervosa group (n = 21)</td>
<td>Control group (n = 21)</td>
</tr>
<tr>
<td>Chronologic age (y)</td>
<td>15.9 ± 1.6&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bone age (y)</td>
<td>15.4 ± 1.6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.9 ± 6.2</td>
</tr>
<tr>
<td>BMI (kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>16.4 ± 1.0</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>−2.02 ± 0.18</td>
</tr>
</tbody>
</table>

<sup>1</sup>SDS, standard deviation score.  
<sup>2</sup>Mean ± SD.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Body-composition data at baseline in adolescent girls with anorexia nervosa and healthy control subjects2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia nervosa group (n = 21)</td>
<td>Control group (n = 21)</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>34.6 ± 3.1&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fat mass by DXA (%)</td>
<td>7.7 ± 3.1</td>
</tr>
<tr>
<td>Trunk fat (%)</td>
<td>17.2 ± 0.6</td>
</tr>
<tr>
<td>Fat mass by DXA (%)</td>
<td>30.2 ± 5.3</td>
</tr>
<tr>
<td>Extremity fat (%)</td>
<td>57.9 ± 6.7</td>
</tr>
<tr>
<td>Ratio of trunk to extremity fat</td>
<td>0.54 ± 0.15</td>
</tr>
<tr>
<td>Trunk LBM (%)</td>
<td>49.1 ± 1.4</td>
</tr>
<tr>
<td>Extremity LBM</td>
<td>43.0 ± 1.5</td>
</tr>
<tr>
<td>Ratio of trunk to extremity LBM</td>
<td>1.14 ± 0.07</td>
</tr>
</tbody>
</table>

<sup>1</sup>LBM, lean body mass; DXA, dual-energy X-ray absorptiometry.  
<sup>2</sup>Mean ± SD.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Hormonal data at baseline in adolescent girls with anorexia nervosa and healthy control subjects1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia nervosa group (n = 21)</td>
<td>Control group (n = 21)</td>
</tr>
<tr>
<td>Estradiol (pmol/L)</td>
<td>60.9 ± 24.8&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Urinary free cortisol (μg/d)</td>
<td>47.9 ± 34.0</td>
</tr>
<tr>
<td>Free testosterone (pmol/L)</td>
<td>6.2 ± 2.1</td>
</tr>
<tr>
<td>DHEAS (μmol/L)</td>
<td>4.3 ± 1.8</td>
</tr>
<tr>
<td>Leptin (μg/L)</td>
<td>3.1 ± 1.8</td>
</tr>
<tr>
<td>IGF-I (mg/L)</td>
<td>319.9 ± 135.9</td>
</tr>
<tr>
<td>IGFBP-3 (μg/L)</td>
<td>4224 ± 968</td>
</tr>
</tbody>
</table>

<sup>1</sup>DHEAS, dehydroepiandrosterone sulfate; IGF-I, insulin-like growth factor-I; IGFBP-3, IGF binding protein 3. Data for 17 anorexia nervosa subjects and 14 healthy control subjects shown in this table were reported previously (19).  
<sup>2</sup>Mean ± SD.
such that girls who had had AN for a longer period of time had higher urinary free cortisol and DHEAS values. No correlations were observed between urinary free cortisol value and either weight or BMI. AN subjects had significantly lower IGF-I and leptin concentrations than did control subjects, as would be expected because both are measures of nutritional status.

Regarding the correlational analyses, when AN and control subjects were analyzed together, percentage trunk fat was significantly correlated with IGF-I concentration ($r = 0.47$, $P = 0.002$) and IGFBP-3 concentration ($r = 0.44$, $P = 0.01$). In the stepwise regression analysis, IGF-I was a significant predictor of the variability in percentage trunk fat (accounting for 22% of the variability), whereas IGFBP-3 was not a significant predictor. The single most important predictor of percentage extremity fat was saturation free cortisol ($r = -0.34$, $P = 0.03$), which accounted for 12% of the variability. The ratio of trunk fat to extremity fat was not significantly correlated with urinary free cortisol ($r = 0.26$, $P = 0.09$), accounting for 7% of the variability. For the AN group, percentage extremity fat correlated with DHEAS concentration ($r = -0.67$, $P = 0.003$) and the ratio of trunk fat to extremity fat correlated with DHEAS ($r = 0.60$, $P = 0.01$); DHEAS accounted for 45% and 36% of the variability in these body-composition variables, respectively. Percentage trunk fat in the AN group at baseline was not correlated with any of the hormonal parameters.

### Effects of weight recovery

BMI increased by a mean of 2.3 in the adolescent girls with AN over the 12-mo study period (baseline to the 12 mo visit). BMI increased by a mean of 3.5 in the 13 AN subjects who met the criteria for weight recovery (defined as an increase in BMI of ≥10%); in this subgroup, BMI was 16.3 ± 0.3 at baseline and 19.8 ± 0.7 at 12 mo ($P = 0.0003$). At 12 mo, in weight-recovered AN subjects ($n = 13$), 55.6% of the weight gain was attributable to an increase in fat mass and 44.4% was attributable to an increase in LBM. However, even at 12 mo, weight-recovered AN subjects had a significantly lower BMI than did control subjects (19.8 ± 2.4 and 22.0 ± 3.1, respectively; $P < 0.05$ by Tukey-Kramer test).

In the AN subjects with weight recovery, marked increases were observed in fat mass, LBM, percentage trunk fat, and ratio of trunk fat to extremity fat (Table 4). However, even with these increases, these variables never exceeded those in the control subjects, who were normal, healthy adolescents. Specifically, at 12 mo, mean fat mass was 14.2 ± 4.8 kg in recovered AN subjects and 18.6 ± 5.6 kg in control subjects ($P < 0.05$). LBM was 39.3 ± 4.8 kg in recovered AN subjects and 39.3 ± 5.9 kg in control subjects (NS). Percentage trunk fat was 35.1 ± 2.9% in recovered AN subjects and 36.1 ± 4.7% in control subjects (NS). The ratio of trunk fat to extremity fat was 0.61 ± 0.08 in recovered AN subjects and 0.62 ± 0.13 in control subjects (NS). In addition, in recovered AN subjects, the rate of increase in percentage trunk fat and ratio of trunk fat to extremity fat (5.7% and 5.0%, respectively) between 6 mo and 12 mo was lower than that between 0 and 6 mo (13.3% and 15.2%, respectively, despite a steady increase in BMI over these periods. Also, in 6 AN subjects with an increase in BMI of ≥20% (mean BMI of 16.3 ± 0.5 at baseline and 21.6 ± 0.7 at 12 mo), percentage trunk fat and ratio of trunk fat to extremity fat were 36.0 ± 2.5% and 0.62 ± 0.07, respectively, at 12 mo. No increase occurred in percentage extremity fat with weight recovery.

Weight recovery was not associated with a significant increase in any particular dietary component. The intakes of saturated, monounsaturated, and polyunsaturated fat increased by 45.4 ± 155.6%, 145.3 ± 364.6%, and 107.8 ± 141.2%, respectively, in weight-recovered AN subjects compared with 0.2 ± 51.9%, 5.8 ± 48.7%, and 3.1 ± 48.6%, respectively in control subjects. The $P$ values when recovered AN subjects and control subjects were compared were not significant except for the percentage change in polyunsaturated fat intake ($P < 0.05$ by Tukey-Kramer test).

Among the nutritional variables, for the entire group of AN and control subjects, percentage change in fat content of the diet was the only significant predictor of percentage change in trunk fat and percentage change in the ratio of trunk fat to extremity fat (for both: $r = 0.49$, $P = 0.002$, and 24% of the variability was explained). Of the various hormonal variables, percentage change in IGF-I concentrations predicted percentage change in percentage trunk fat ($r = 0.61$, $P = 0.0005$, accounting for 37% of the variability) and percentage change in the ratio of trunk fat to extremity fat ($r = 0.54$, $P = 0.003$, accounting for 29% of the variability). In the AN group, percentage change in IGF-I concentrations predicted percentage change in trunk fat ($r = 0.66$, $P = 0.01$, accounting for 44% of the variability) and the ratio of trunk fat to extremity fat ($r = 0.64$, $P = 0.01$, accounting for 42% of the variability).

Baseline values of percentage trunk fat, percentage extremity fat, and the ratio of trunk fat to extremity fat correlated negatively with percentage change in these values over 12 mo (Figure 1). Thus, girls starting with the lowest percentage trunk fat and ratio of trunk fat to extremity fat had the largest increases in these 2 variables over time.

### DISCUSSION

In this study of adolescent girls with AN compared with healthy control subjects, we investigated body composition and regional

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**TABLE 4**

Percentage change in body-composition variables from baseline to 12 mo in adolescent girls with anorexia nervosa (AN) and healthy control subjects

<table>
<thead>
<tr>
<th>Percentage change from baseline to 12 mo</th>
<th>Nonrecovered AN group ($n = 8$)</th>
<th>Recovered AN group ($n = 13$)</th>
<th>Control group ($n = 21$)</th>
<th>$P$ (ANOVA)$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>2.5 ± 6.4$^2$</td>
<td>21.5 ± 12.5$^2$</td>
<td>1.5 ± 7.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lean body mass</td>
<td>4.7 ± 4.5</td>
<td>14.1 ± 8.7$^3$</td>
<td>5.1 ± 8.3</td>
<td>0.0006</td>
</tr>
<tr>
<td>Fat mass</td>
<td>24.1 ± 40.4</td>
<td>88.4 ± 62.8$^3$</td>
<td>2.4 ± 18.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Percentage trunk fat</td>
<td>−0.5 ± 12.8</td>
<td>24.6 ± 23.7$^3$</td>
<td>0.7 ± 6.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Percentage extremity fat</td>
<td>4.0 ± 15.7</td>
<td>−1.8 ± 6.9</td>
<td>0.2 ± 3.0</td>
<td>NS</td>
</tr>
<tr>
<td>Ratio of trunk to extremity fat</td>
<td>−0.3 ± 20.7</td>
<td>27.5 ± 31.4$^4$</td>
<td>−0.3 ± 8.2</td>
<td>0.0009</td>
</tr>
</tbody>
</table>

$^1$The Tukey-Kramer test was used for comparisons between groups if the ANOVA was significant.

$^2$$\pm$ SD.

$^3$Significantly different from control subjects and nonrecovered AN subjects, $P < 0.05$.
fat distribution at baseline and with weight recovery. As has been reported in adults with AN, adolescent girls with AN had less fat mass and LBM than did control subjects. However, in contrast to adults with AN, percentage extremity fat was not significantly different in AN subjects compared with control subjects. In addition, adolescent girls with AN had lower percentage trunk fat than did control subjects. Weight recovery led to an increase in trunk fat relative to extremity fat and thus led to central fat accumulation. However, in contrast to findings reported in adults with AN, trunk fat and the ratio of trunk fat to extremity fat did not exceed that of control subjects, indicating that changes in girls with AN most likely represented a normalization of body composition. Adolescent girls with AN who had the lowest trunk fat and ratio of trunk fat to extremity fat at baseline had the largest gains in these variables during the 12-mo study.

Although body-composition data for adults and adolescents with AN have been reported, there are few data on regional fat distribution. Decreased fat mass has been found in adult AN subjects with either normal LBM (7, 15) or decreased LBM (9, 10, 20). Studies in adolescents with AN have also reported decreased fat mass and LBM (4, 11, 21). Our results at baseline were similar in that fat mass and LBM were lower in AN subjects than in control subjects. The decrease in fat mass was greater than the decrease in LBM, suggesting a preferential loss of body fat. In adults with AN, fat mass is lost primarily from the extremities, with sparing of trunk fat (9). We showed in this study that adolescents with AN lose fat mass primarily from the trunk, with sparing of extremity fat. Therefore, adolescent girls with AN do not have the central fat distribution at baseline that is observed in adults with AN. These results are similar to those of Kerruish et al (11), who reported lower trunk fat in adolescents with AN. Unlike our study, marked decreases in leg fat were found, and body composition was not measured with weight recovery.

The pathophysiology underlying differences in fat distribution between adolescent AN and adult AN is unknown. One possibility is that the longer average duration of AN in adults results in higher cortisol concentrations, which exacerbates a central fat distribution. Studies of Cushing syndrome (22) and of hypercortisolism from impaired habituation to stress (23) have shown increased waist-to-hip ratios in comparison to those of control subjects. Omental (but not subcutaneous) adipose stromal cells generate cortisol from inactive cortisone as a result of increased expression of the type 1 isofrom of 11-β-hydroxysteroid dehydrogenase. Cortisol exposure further increases expression of this enzyme (24), suggesting an explanation for the central adiposity seen with hypercortisolism.

Data have shown marked hypercortisolism in adults with AN (9, 25, 26), and our group previously reported greater trunk fat in women with AN who had higher cortisol values (9). In contrast, studies in adolescents with AN reported no differences in cortisol values compared with those of control subjects (5, 27). In this study, although urinary free cortisol values were not significantly different between the 2 groups, we did find a positive correlation between urinary cortisol and duration of AN. We also observed a weak positive correlation between urinary free cortisol and ratio of trunk fat to extremity fat. These data are consistent with a more central fat distribution with higher cortisol values, as reported in adults with AN (9).

Lower DHEAS values were reported in adolescents with AN (28). A negative correlation was found between DHEAS and trunk fat in obese girls (29) and between DHEAS and fat mass in older men (30, 31). Taken together, these data suggest that lower DHEAS concentrations should result in increased fat mass and increased trunk fat. However, we found a positive correlation between DHEAS concentration and the ratio of trunk fat to extremity fat. Because DHEAS also correlated positively with the duration of AN, the association with fat distribution may merely reflect the effect of duration of AN.

Growth hormone deficiency causes central adiposity in children and adults (32, 33), and growth hormone replacement decreases fat mass and increases LBM (34, 35). Low IGF-I concentrations with high growth hormone values were found in adults (36–38) and adolescents (39, 40) with AN, suggesting an acquired, nutritional growth hormone resistance. This could contribute to the more central fat distribution in AN. However, in this study, when data from girls with AN and control subjects were combined,
baseline IGF-I values correlated positively, rather than negatively, with baseline trunk fat.

With weight recovery, AN subjects had increases in fat mass and LBM, as reported in another study of adolescents with AN (41). However, that study did not examine regional fat distribution. Increased weight in recovered AN was primarily a result of increased fat mass rather than increased LBM; this was similar to the findings of other investigators (6, 9, 10, 42).

In adults with AN, weight recovery results in increased trunk fat and truncal adiposity compared with control subjects (7–10). We found a marked increase in trunk fat and the ratio of trunk fat to extremity fat with weight recovery. However, percentage trunk fat and the ratio of trunk fat to extremity fat never exceeded that of control subjects, despite greater increases in BMI over the study period (3.5 in recovered AN) than those reported in adults with AN, who developed truncal adiposity after an increase in BMI of 1.4 during a 9-mo study (9). Thus, the lack of development of central adiposity (ie, a ratio of trunk fat to extremity fat greater than that of control subjects) could not be explained by a failure to increase BMI. However, despite significant increases in BMI from baseline, weight-recovered AN subjects continued to have a lower BMI compared with that of control subjects at 12 mo. Therefore, we cannot rule out that central obesity may develop in these girls with continued weight gain that approaches the weight of control subjects. The slower rates of increase in percentage trunk fat and ratio of trunk fat to extremity fat from 6 to 12 mo, despite a steady increase in BMI in weight-recovered AN subjects, suggests that a persistent increase in BMI may not cause truncal adiposity. Therefore, it appears that the increase in trunk fat represents a trend toward normalization rather than development of central adiposity. Further studies are needed to investigate long-term changes in body composition with full weight recovery in adolescents with AN.

Grinspoon et al (9) reported a negative correlation between baseline percentage trunk fat and change in percentage trunk fat in adult women with AN. In this study, we found similar negative correlations between baseline values and percentage change over 12 mo for percentage trunk fat, percentage extremity fat, and ratio of trunk fat to extremity fat, such that girls with the lowest baseline values had the largest gains over time. In contrast to studies in adult AN subjects (9), we found no correlations between urinary free cortisol values and changes in regional fat distribution during the 12-mo study. In our study, changes in IGF-I (a marker of nutritional status) strongly predicted changes in trunk fat and ratio of trunk fat to extremity fat.

In the present study, we showed decreases in percentage trunk fat and the ratio of trunk fat to extremity fat in adolescent girls with AN, in contrast to previously reported findings in adult women with AN, who had reduced extremity fat and a more central fat distribution. We also showed an increase in trunk fat with weight recovery, as has been reported in adult women. However, in our study, percentage trunk fat and the ratio of trunk fat to extremity fat in weight-recovered adolescents with AN did not exceed values in control subjects despite greater increases in BMI than were reported in adults with AN. Thus, weight recovery resulted in a tendency toward normalization of body composition rather than development of central adiposity. This concept is further supported by the finding that girls with the least trunk fat at baseline gained the most trunk fat over time. Regional fat distribution at baseline and changes with weight recovery are thus very different in adolescents with AN than in adult AN patients and may be related to the duration or severity of hypercortisolism in adolescents compared with adults. These findings may be important in that they will allow health care providers to convey to adolescents with AN that weight recovery is not likely to lead to central adiposity.

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