Long-term changes in energy expenditure and body composition after massive weight loss induced by gastric bypass surgery

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ABSTRACT

Background: Little is known about the determinants of individual variability in body weight and fat loss after gastric bypass surgery or about the effects of massive weight loss induced by this surgery on energy requirements.

Objectives: The objectives were to determine changes in energy expenditure and body composition with weight loss induced by gastric bypass surgery and to identify presurgery predictors of weight loss.

Design: Thirty extremely obese women and men with a mean (±SD) age of 39.0 ± 9.6 y and a body mass index (BMI; in kg/m²) of 50.1 ± 9.3 were tested longitudinally under weight-stable conditions before surgery and after weight loss and stabilization (14 ± 2 mo). Total energy expenditure (TEE), resting energy expenditure (REE), body composition, and fasting leptin were measured.

Results: Subjects lost 53.2 ± 22.2 kg body weight and had significant decreases in REE (−2.4 ± 1.0 MJ/d; P < 0.001) and TEE (−3.6 ± 2.5 MJ/d; P < 0.001). Changes in REE were predicted by changes in fat-free mass and fat mass. The average physical activity level (TEE/REE) was 1.61 at both baseline and follow-up (P = 0.98). Weight loss was predicted by baseline fat mass and BMI but not by any energy expenditure variable or leptin. Measured REE at follow-up was not significantly different from predicted REE.

Conclusions: TEE and REE decreased by 25% on average after massive weight loss induced by gastric bypass surgery. TEE changes were predicted by loss of body tissue; thus, there was no significant long-term change in energy efficiency that would independently promote weight regain. Am J Clin Nutr 2003;78:22–30.

KEY WORDS Obesity, weight loss, energy expenditure, fat mass, fat-free mass, body water, gastric bypass surgery, energy requirements

INTRODUCTION

The prevalence of extreme obesity has increased 3-fold over the past 4 decades, and as many as 6 million Americans are now classified as being extremely obese, ie, having a body mass index (BMI; in kg/m²) ≥ 40 (1). A more recent report suggests that the prevalence rates of this population continue to rise (2). Persons this severely obese often have a long history of excess weight, of repeated failures with traditional weight-loss methods, or both, and gastric bypass surgery is increasingly being viewed as a useful treatment option for achieving sustainable weight loss. However, relatively little is known about the long-term effects of weight loss induced by gastric bypass surgery on energy requirements or about the reasons for the observed substantial variability in weight loss between patients.

Studies that examined changes in energy requirements with moderate weight loss showed that active weight loss is associated with decreases in total energy expenditure (TEE) (3–8) and resting energy expenditure (REE) that are disproportionately large relative to the loss of body tissues (3, 7, 9–12). However, the extent to which these changes persist after weight restabilization remains controversial. Some studies have suggested that there is a persistent decrease in energy expenditure after moderate weight loss (9, 13, 14), whereas other studies showed no such changes (15–19). The question of whether there is a persistent decrease in energy expenditure after substantial weight loss is also controversial, primarily because most of the studies of this issue (8, 20–23) have had a very small number of subjects, failed to adequately account for the expected decrease in energy expenditure due to losses of fat, fat-free mass (FFM) (24–28), or both.

There is also a lack of information on why gastric bypass surgery causes some patients to lose much more weight than others (29, 30) and on whether it is possible to identify presurgical predictors of weight loss that could help identify those patients who are likely to obtain the maximum benefit from gastric bypass surgery. The potential predictors of weight loss are TEE, REE, and leptin, which have been suggested to predict weight loss in several (29, 30), although not all (17, 37), previous studies.
We therefore conducted a study to determine the magnitude of changes in TEE and components of energy expenditure with massive weight loss and subsequent weight restabilization in subjects undergoing gastric bypass surgery. We also examined the utility of several baseline variables—including body composition, energy expenditure (TEE, REE, and substrate oxidation), and fasting leptin concentrations—for predicting body weight and fat loss in individual subjects.

SUBJECTS AND METHODS

Subjects

The subjects were 30 adults (24 women and 6 men aged 39.0 ± 9.6 y; \( \bar{x} \pm SD \)) who underwent gastric bypass surgery for weight reduction at the Tufts–New England Medical Center Hospital and participated in both baseline and follow-up (after weight loss and weight restabilization) investigations. Persons were ineligible for the study if they had diabetes, cancer, coronary heart disease, endocrine disorders, or other acute or chronic diseases or if they were using medication known to influence energy expenditure. The ratio of women to men admitted to the study (5:1) was similar to the ratio of those seeking gastric bypass surgery. Of the 36 subjects studied at baseline, 6 subjects (all women) did not return for follow-up (1 did not undergo gastric bypass surgery, 2 became pregnant, 1 had burn injuries, and 2 relocated), which resulted in a study population of 30. Measurements were conducted at the Clinical Study Unit (CSU) of Tufts–New England Medical Center Hospital and at the Jean Meyer US Department of Agriculture Human Nutrition Research Center at Tufts University. The study was approved by the Human Investigation Review Committee of Tufts University and Tufts–New England Medical Center Hospital. All subjects gave written informed consent before participating.

Study protocol

All subjects were initially tested before gastric bypass surgery and then were retested after weight loss and weight restabilization. To determine weight stabilization, subjects weighed themselves at home or at other ambulatory sites 3 times/wk in the fasting state in the month before testing. Subjects who were not weight stable (defined as a weight within 2.3 kg of initial weight) during this period (at baseline and \( \approx 12 \) mo after gastric bypass surgery) were monitored further until the defined weight stability was achieved. The average time from gastric bypass surgery to weight stability was 14 ± 2 mo.

The study was conducted over a 15-d period at both time points, ie, at baseline and follow-up. Subjects were free-living, except for 3 overnight inpatient stays for measurements including REE and the thermic effect of food (TEF). The subjects were admitted to the CSU on the day before the start of the study. After the subjects fasted overnight, TEE was measured by using the doubly labeled water method and REE was also measured, which were followed by a 4-h TEF measurement. Body composition was also measured as described below. Subjects then returned home with instructions on how to collect daily urine samples for the measurement of TEE. They were readmitted on days 7–8 for additional body-composition testing and other measurements, after which they returned home for the rest of the week and continued the urine collections at home. Finally, subjects returned to the CSU on the evening of day 14, and a second REE measurement was made on the morning of day 15. Fasting blood samples were obtained on days 1 and 15, and food-frequency, physical activity, and other questionnaires were also completed as summarized below.

Total energy expenditure

A 15-d doubly labeled water study was conducted to measure TEE. On day 1, subjects were given a mixed dose of doubly labeled water (\( \text{H}_2\text{H}_2\text{O}^\text{18} \)) containing 0.1 g \( \text{H}_2\text{O}^\text{18} \) and 0.07 g \( \text{H}_2\text{O} \) per kg body weight. The dose was administered orally after the subjects had fasted overnight and collected a baseline urine sample early in the morning. Subjects remained in the CSU while the urine specimens were collected every hour for 5 h after administration of the doubly labeled water. Baseline and 5-h postdose urine samples were used for analysis and calculations.

The subjects were carefully instructed on how to collect and freeze the second void of the day while at home on subsequent days; the urine samples collected on days 1, 8, and 15 at the CSU were supervised. All urine samples were stored at \(-20^\circ C\) until analyzed.

Urinary isotope enrichment was measured with a Hydra gas isotope ratio mass spectrometer (PDZ Europa Ltd, Cheshire, United Kingdom) according to the method of Prosser and Scrimgeour (38) with a slight modification involving the use of a gas autosampler with a specially designed flushing needle (PDZ Europa Ltd) to introduce the equilibration gas. For the \( \text{H}_2\text{O} \) analysis, platinum was used as a catalyst. The tubes were filled with gas (carbon dioxide gas for \( \text{H}_2\text{O}^\text{18} \) and hydrogen gas for \( \text{H}_2\text{O} \)) by using a flushing needle and were then equilibrated (overnight for \( \text{H}_2\text{O}^\text{18} \) and 3 d for \( \text{H}_2\text{O} \)). After equilibration, the tubes were loaded on a second autosampler, on which gas from each tube was sequentially allowed to flow into a stream of helium gas (dried by magnesium perchlorate) and analyzed for isotopic abundance. \( \text{H}_2\text{O} \) and \( \text{H}_2\text{O}^\text{18} \) were analyzed in triplicate in urine samples collected at baseline, 5 h postdose, and 2, 4, 6, 8, 10, 14, and 15 d postdose.

TEE was calculated according to standard procedures (39), with a correction for isotopic fractionation in adults (40) and with the use of a constant dilution space ratio as suggested by Racette et al (41). In these calculations, the individual values for food quotient (FQ) used to convert measured carbon dioxide production \( \left( \text{CO}_2 \right) \) rates to TEE were obtained from a food-frequency questionnaire (42). It should be noted that, although underreporting of energy intake is a common concern in studies involving obese subjects, inaccurate FQ values introduce only very small errors into the calculation of TEE (43). Nonresting energy expenditure (NREE) was calculated as the difference between TEE and REE (described below). Activity energy expenditure (AEE) was calculated as the difference between TEE and the sum of REE and the group mean TEF (described below). Mean rather than individual TEF values were used to reduce the effect of variability in individual TEF measurements on subsequent calculations.

Resting energy expenditure and the thermic effect of food

REE was measured on 2 mornings (days 1 and 15) after the subjects had fasted overnight for 12 h at the CSU. Measurements were made by indirect calorimetry (DeltaTrac portable metabolic cart; SensorMedics Corp, Yorba Linda, CA) with subjects resting supine in comfortable thermoneutral conditions. The calorimeter was calibrated with a standard gas mixture (96% \( \text{O}_2 \) and 4% \( \text{CO}_2 \)) before each test, and standard alcohol burn tests were conducted periodically to ensure the accuracy of the calorimeter (±1%). Subjects were instructed to relax and avoid hyperventilating, fidgeting, and sleeping during measurements, and oxygen consumption.
(VO\textsubscript{2}) and \textit{VCO}\textsubscript{2} were measured every minute for 30 min. REE was calculated according to Weir’s equation (44) with the use of mean VO\textsubscript{2} and VCO\textsubscript{2} values. After the assessment of REE on day 1, TEF was measured for 4 h after the consumption of 400 mL of a mixed liquid meal (Pediasure, FQ = 0.88; Abbott Laboratories, Abbott Park, IL), which provided 1.67 MJ energy as 43.9 g carbohydrate (44% of energy), 12.0 g protein (12% of energy), and 19.9 g fat (44% of energy) over 20 min. TEF was calculated as the increase in energy expenditure above REE and was expressed as a percentage of the meal ingested. At follow-up, some subjects were not able to consume all 400 mL of the test meal during the allotted time period because of sensations of fullness or gastrointestinal discomfort. In these cases (\(n = 7\)), the actual amount of the meal that was consumed was used in the calculations. REE at follow-up was also predicted for each subject by using the standard equations adopted by the World Health Organization and US recommended dietary allowances (45, 46).

Body composition

The Siri 3-compartment model was used to estimate percentage body fat in most of the subjects at baseline and follow-up. The formula for the Siri 3-compartment model (47) incorporates total body water and body density, which was determined by air-displacement plethysmography (48, 49). This method has been validated for use in extremely obese subjects (50). Total body water was determined from \(H_2\text{H}_2\text{O}\) dilution, which was measured as part of the determination of TEE. FFM was calculated as the difference between body weight and fat mass. At baseline, air-displacement plethysmography measurements were not obtained in 6 subjects, and in these cases fat mass was predicted from \(H_2\text{H}_2\text{O}\) dilution values [the correlation between air-displacement plethysmography and \(H_2\text{H}_2\text{O}\) dilution for fat mass is \(r = 0.997\) (\(P < 0.001\)) and for FFM is \(r = 0.995\) (\(P < 0.001\)]. Height was measured to the nearest 0.1 cm with a wall-mounted stadiometer, and weight was measured to the nearest 100 g with a calibrated scale (model CN-20, DETECTO; Cardinal Scale Manufacturing Co, Webb City, MO). Waist circumference was measured at the level of the umbilicus, and hip circumference was measured as the maximal circumference at the level of the buttocks.

Fasting biochemical measures

Biochemical measures were determined in fasting blood samples collected at baseline and follow-up. Serum reverse triiodothyronine (rT\textsubscript{3}) was measured with the \(125\)I radioimmunoassay (RIA kit; BioChem ImmunoSystems, Cortland Manor, NY). Thyroxine and thyroid hormone binding ratio were analyzed with the Cloning Enzyme Donor Immuno Assay with the use of Beckman Synchrony LX Systems (Beckman Instruments Inc, Fullerton, CA). Thyrotropin and free thyroxine were analyzed with the Microparticle Enzyme Immuno Assay by using the AXSYM System (Abbott Laboratories). Fasting plasma leptin concentrations were measured with a sensitive commercial double-antibody RIA (Human leptin specific RIA kit; Linco Research, Inc, St Louis) that detects relatively low leptin concentrations (0.5 ng/mL).

Self-reported activity questionnaires (leisure and occupational)

The energy expenditure for leisure time activities during the previous 12-mo period was estimated via a structured interview by using the Minnesota Leisure Time Physical Activity (LTPA) questionnaire (51, 52). Occupational activity over the same period was assessed by using the self-administered Tecumseh Occupational Activity Questionnaire (53–55). Because the occupational activity questionnaire was used in conjunction with the LTPA, we used the modifications suggested by Montoye et al (56), which included eliminating questions on the LTPA that pertain to work-related activity. Self-reported physical activity from both questionnaires (expressed in min/d) was added and classified by METs [the ratio of energy expended to measured or estimated REE (56)] into light (\(\leq 3.9\) METs), moderate (4.1–5.9 METs), or heavy (\(\geq 6\) METs) categories.

Statistics

Statistical analyses were performed by using SPSS 10.0.7 and SYSTAT 9.0.1 (SPSS Inc, Chicago) and SAS (version 8; SAS Institute Inc, Cary, NC). Results are expressed as means ± SDs unless otherwise specified. Leptin was the only variable that needed log transformation. Changes in variables were calculated as follow-up values minus baseline values. Student’s \(t\) test for paired data was used to examine whether there were significant changes over time in body weight, body composition, energy expenditure, activity, and biochemical variables. In addition, the potential confounding effects of several aspects particular to the study sample [including surgical details such as length of the bypassed intestine (roux-limb) and protocol-related aspects such as sex and time until weight stability] were examined by using analysis of covariance. No confounding effects of any of these variables on the relations between energy expenditure and body-composition variables were observed. In addition, analyses were performed with data from men and women combined and from women only. However, the results remained the same with or without the inclusion of the 6 men; thus, data are presented for all subjects combined.

To determine whether the within-subject relation between changes in energy expenditure (ΔTEE or ΔREE and ΔNREE) and body composition (ΔFFM and Δfat mass) at follow-up were different from the cross-sectional relations at baseline between energy expenditure and body composition, a mixed-model regression analysis was performed by using SAS’s mixed procedure. All models included a baseline intercept, a change in intercept, and FFM (baseline values and changes from baseline); some models additionally included fat mass (baseline values and changes from baseline). The models show energy expenditure at follow-up, with significance terms for Δintercept and for each of the variables in the model. Details of the models used are given in Appendix A.

In addition, regression analysis was used to determine whether baseline variables [ie, TEE, REE, physical activity level (PAL), AEE, NREE, respiratory quotient (RQ), postprandial RQ (PPRQ), reported physical activity, and fasting leptin] were predictors of change in fat mass. In these analyses, values for TEE, REE, AEE, and NREE, and fasting leptin were expressed as a percentage of the value predicted from baseline body composition, and baseline BMI was also used as an independent variable. Baseline BMI was a strong predictor of change in fat mass (\(r = 0.79, P < 0.001\)). Student’s \(t\) test for paired data was used to compare the mean measured REE at follow-up with the mean REE predicted at follow up from the WHO equations (45, 46).

RESULTS

Subject characteristics at baseline are summarized in Table 1. The mean duration of weight loss after gastric bypass surgery was...
14 ± 2 mo. No significant trends in body weight were found during the measurement of energy expenditure at either baseline or follow-up, and mean changes within both study periods were relatively small (Δweight at baseline: -4 ± 144 g/d; Δweight at follow-up: 73.4 ± 13.6 g/d).

Body composition and energy expenditure data at baseline and follow-up and changes over time, including data on self-reported activity, are shown in Table 2. Gastric bypass surgery resulted in a substantial mean weight loss of 38 ± 19% of initial weight. There were large and significant changes in all body-composition variables and, on average, weight loss was 79% fat and 21% FFM. The proportions of weight lost as fat and FFM were not significantly related to the amount of weight loss. TEE, REE, and NREE were significantly lower at follow-up than at baseline. However, no significant changes in TEF, fasting RQ, or PPRQ (data not shown) were observed. Although there were large reductions in components of TEE, no significant changes in energy expenditure components were found when they were expressed as a fraction of TEE (Figure 1). In addition, there were no significant changes between baseline and follow-up in the reported time spent in all categories of activity.

Fasting biochemical measures are shown in Table 3. There were significant decreases in free serum thyroxine, rT3, and thyrotropin after weight loss, but mean values were within the normal range at both time points. Decreases in the thyroid hormone binding ratio and free thyroxine index were also found, but these decreases were not significant. The decrease in leptin concentration with weight loss was significant.

Different models for predicting energy expenditure at follow-up from baseline body composition and changes in body composition over time are shown in Table 4. As shown, models predicting follow-up REE, NREE, and TEE from intercepts and FFM variables consistently showed a decrease in energy expenditure at follow-up that was not fully accounted for after the decrease in FFM was included in the model, ie, the intercept term was significant in the model predicting REE from FFM alone. However, when fat mass variables (baseline fat mass and Δfat mass) were added

### Table 1

<table>
<thead>
<tr>
<th>Subjects characteristics</th>
<th>Women (n = 24)</th>
<th>Men (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>38.9 ± 9.0</td>
<td>39.2 ± 12.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.0 ± 7.0</td>
<td>183.0 ± 5.4</td>
</tr>
<tr>
<td>Baseline weight (kg)</td>
<td>127.4 ± 24.7</td>
<td>187.9 ± 29.5</td>
</tr>
<tr>
<td>Baseline BMI (kg/m²)</td>
<td>48.3 ± 8.2</td>
<td>57.3 ± 10.4</td>
</tr>
<tr>
<td>Baseline RQ</td>
<td>0.92 ± 0.12</td>
<td>0.94 ± 0.05</td>
</tr>
</tbody>
</table>

1±SD. 

### Table 2

<table>
<thead>
<tr>
<th>Summary of body-composition and energy expenditure data by phase of measurement</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Change over time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body composition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>139.5 ± 35.3</td>
<td>86.1 ± 20.6</td>
<td>−53.4 ± 22.2</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>50.1 ± 9.3</td>
<td>30.8 ± 5.7</td>
<td>−19.3 ± 6.7</td>
</tr>
<tr>
<td>Body fat (% of wt)</td>
<td>51.3 ± 4.6</td>
<td>33.9 ± 8.6</td>
<td>−17.4 ± 7.7</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>72.2 ± 23.0</td>
<td>30.1 ± 13.1</td>
<td>−42.1 ± 18.3</td>
</tr>
<tr>
<td>Energy expenditure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TEE (MJ/d)</td>
<td>14.8 ± 2.6</td>
<td>11.2 ± 3.1</td>
<td>−3.6 ± 2.5</td>
</tr>
<tr>
<td>REE (MJ/d)</td>
<td>9.3 ± 1.8</td>
<td>6.9 ± 1.1</td>
<td>−2.4 ± 1.0</td>
</tr>
<tr>
<td>NREE (MJ/d)</td>
<td>5.5 ± 1.3</td>
<td>4.3 ± 2.3</td>
<td>−1.2 ± 2.4</td>
</tr>
<tr>
<td>TEF (% of meal)</td>
<td>8.3 ± 4.1</td>
<td>9.9 ± 3.2</td>
<td>1.6 ± 6.0</td>
</tr>
<tr>
<td>Fasting RQ</td>
<td>0.77 ± 0.02</td>
<td>0.76 ± 0.04</td>
<td>−0.01 ± 0.05</td>
</tr>
<tr>
<td>PAL</td>
<td>1.6 ± 0.15</td>
<td>1.61 ± 0.28</td>
<td>0.002 ± 0.3</td>
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<tr>
<td>FQ</td>
<td>0.84 ± 0.02</td>
<td>0.85 ± 0.02</td>
<td>0.004 ± 0.005</td>
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<tr>
<td>Reported activity, leisure + occupational</td>
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<td></td>
</tr>
<tr>
<td>Light (min/d)</td>
<td>290 ± 205</td>
<td>230 ± 139</td>
<td>−60 ± 177</td>
</tr>
<tr>
<td>Moderate (min/d)</td>
<td>14 ± 31</td>
<td>22 ± 24</td>
<td>8 ± 40</td>
</tr>
<tr>
<td>Heavy (min/d)</td>
<td>11 ± 14</td>
<td>15 ± 12</td>
<td>4 ± 16</td>
</tr>
<tr>
<td>Total (min/d)</td>
<td>315 ± 220</td>
<td>267 ± 13.1</td>
<td>−48 ± 180</td>
</tr>
</tbody>
</table>

1/2 ± SD; n = 24 F, 6 M. FFM, fat free mass; TEE, total energy expenditure; REE, resting energy expenditure; NREE, nonresting energy expenditure; TEF, thermic effect of food; RQ, respiratory quotient; FQ, food quotient; PAL, physical activity level.

1/P < 0.001.

### Table 3

<table>
<thead>
<tr>
<th>Summary of biochemical variables by phase of measurement</th>
<th>Baseline</th>
<th>Follow-up after weight loss</th>
<th>Change over time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroxine (μg/d)</td>
<td>7.8 ± 1.3</td>
<td>6.7 ± 1.4</td>
<td>−1.1 ± 1.59</td>
</tr>
<tr>
<td>FT4 index (μIU/mL)</td>
<td>6.8 ± 1.1</td>
<td>6.6 ± 1.0</td>
<td>−0.2 ± 1.4</td>
</tr>
<tr>
<td>rT3 (ng/mL)</td>
<td>0.20 ± 0.01</td>
<td>0.17 ± 0.01</td>
<td>−0.03 ± 0.01</td>
</tr>
<tr>
<td>Thyrotropin (μIU/mL)</td>
<td>2.6 ± 1.5</td>
<td>1.6 ± 0.9</td>
<td>−1.0 ± 0.9</td>
</tr>
<tr>
<td>THBR</td>
<td>0.9 ± 0.1</td>
<td>1.2 ± 1.4</td>
<td>0.3 ± 1.5</td>
</tr>
<tr>
<td>Leptin (ng/mL)</td>
<td>52.6 ± 17.1</td>
<td>12.3 ± 7.6</td>
<td>−40.3 ± 15.2</td>
</tr>
</tbody>
</table>

1/2 ± SD; n = 24 F, 6 M. THBR, thyroid hormone binding ratio; rT3, reverse triiodothyronine; FT4, free thyroxine.

1/2 Significantly different from baseline (paired t test): 1/P < 0.001, 2/P < 0.01.
TABLE 4
Results of mixed-model regression analysis showing the changes in energy expenditure in relation to body composition
to the model predicting REE, there was no longer any significant decrease in REE that was independent of changes in body composition (the Δintercept coefficient was nearly significant, \( P = 0.07 \), but was quantitatively modest at \(-0.56 \text{ MJ/d} \approx -5\% \) of REE at follow-up). Models predicting NREE and TEE both had significant negative coefficients for the Δintercept, which were partially counterbalanced by significant positive Δfat coefficients (note that the negative value for Δfat had a positive effect on energy expenditure when multiplied by the negative fat mass change term). Unlike REE, models for TEE and NREE incorporating changes in FFM, fat mass, and the Δintercept suggested that the decreases in TEE and NREE were not completely predicted by changes in body composition. (There was a general decrease in ΔTEE and ΔNREE seen in the negative Δintercept term that was partially counterbalanced by some of the positive coefficients for body composition.)

Concerning the use of baseline indexes to predict weight loss and body-composition changes, baseline BMI was the best predictor of the change in BMI; change in body weight was best predicted by baseline body weight, and fat mass change was best predicted by baseline fat mass (as anticipated by regression to the mean effects). The results from an analysis of predictors of weight loss in models that adjusted for baseline BMI or body fat content showed that none of the examined energy expenditure variables (i.e., baseline TEE, REE, PAL, AEE, NREE, PPRQ, RQ, reported physical activity, and fasting leptin) were significant predictors of weight or fat loss. Some of the relations between change in fat mass and baseline TEE, REE, RQ, and fasting leptin—adjusted for baseline BMI—are shown in Figure 2.

A comparison of mean follow-up REEs with mean values for REE predicted from standard equations (45, 46) is shown in Table 5. No significant difference between mean measured REE

\[ \begin{align*}
\text{REE, with FFM only} & \\
\text{Intercept} & = 2.4210 \pm 0.65 & \text{0.0009} & \text{0.0007} \\
\Delta\text{Intercept} & = -1.0397 \pm 0.30 & \text{0.017} & \\
\text{Baseline FFM} & = 0.1020 \pm 0.01 & <0.0001 & \\
\Delta\text{FFM} & = 0.1177 \pm 0.03 & \text{0.0001} & \\
\text{REE, with FFM and fat mass} & \\
\text{Intercept} & = 2.4041 \pm 0.59 & <0.0004 & \\
\Delta\text{Intercept} & = -0.5652 \pm 0.30 & \text{0.0700} & \\
\text{Baseline FFM} & = 0.0757 \pm 0.01 & <0.0001 & \\
\Delta\text{FFM} & = 0.1177 \pm 0.03 & \text{0.0017} & \\
\text{Baseline fat mass} & = 0.0246 \pm 0.01 & \text{0.0044} & \\
\Delta\text{Fat} & = 0.0205 \pm 0.01 & \text{0.0044} & \\
\text{TEE, with FFM only} & \\
\text{Intercept} & = 3.6946 \pm 1.31 & 0.0272 & \\
\Delta\text{Intercept} & = -2.7148 \pm 0.99 & \text{0.0107} & \\
\text{Baseline FFM} & = 0.0757 \pm 0.01 & <0.0001 & \\
\Delta\text{FFM} & = 0.0698 \pm 0.09 & \text{0.4258} & \\
\text{TEE, with FFM and fat mass} & \\
\text{Intercept} & = 4.5925 \pm 1.63 & 0.0092 & \\
\Delta\text{Intercept} & = -3.9490 \pm 1.04 & \text{0.0014} & \\
\text{Baseline FFM} & = 0.0757 \pm 0.01 & <0.0001 & \\
\Delta\text{FFM} & = 0.1599 \pm 0.09 & \text{0.0897} & \\
\text{Baseline fat mass} & = 0.0013 \pm 0.02 & \text{0.9479} & \\
\Delta\text{Fat} & = -0.0525 \pm 0.02 & \text{0.0356} & \\
\text{NREE, with FFM only} & \\
\text{Intercept} & = 1.1981 \pm 1.31 & 0.3694 & \\
\Delta\text{Intercept} & = -1.5953 \pm 0.97 & \text{0.1104} & \\
\text{Baseline FFM} & = 0.0653 \pm 0.02 & \text{0.0022} & \\
\Delta\text{FFM} & = -0.0415 \pm 0.08 & \text{0.6199} & \\
\text{NREE, with FFM and fat mass} & \\
\text{Intercept} & = 2.1226 \pm 1.37 & 0.1333 & \\
\Delta\text{Intercept} & = -3.3136 \pm 1.04 & \text{0.0040} & \\
\text{Baseline FFM} & = 0.0756 \pm 0.03 & \text{0.0098} & \\
\Delta\text{FFM} & = 0.0648 \pm 0.08 & \text{0.4460} & \\
\text{Baseline fat mass} & = -0.0225 \pm 0.02 & \text{0.1708} & \\
\Delta\text{Fat} & = -0.0684 \pm 0.02 & \text{0.0051} & \\
\end{align*} \]

\[ n = 24 \text{ F, 6 M. REE, resting energy expenditure, TEE, total energy expenditure; FFM, fat-free mass; NREE, nonresting energy expenditure; Δ, change (follow-up − baseline).} \]

\[ ^a \text{Comparison of the coefficients at baseline with the coefficients for change.} \]

\[ ^b \text{P value for the global hypothesis that the coefficient for the Δintercept is 0 and the coefficients for baseline values are equal to the corresponding coefficients for change.} \]
and mean predicted REE values were observed for men and women separately or for all subjects combined.

DISCUSSION

This study showed that both TEE and REE decreased by 25% on average after massive weight loss and weight restabilization after gastric bypass surgery. We also found, in contrast with several previous reports (8, 20–23, 31, 33, 37), that the change in REE was explained by losses of both FFM and fat mass. In addition, we observed that mean REE after weight loss was not significantly different from REE predicted with the use of standard equations developed in nonobese persons (45, 46). Combined, these results suggest no energetic adaptation of REE toward increased efficiency after massive weight loss induced by gastric bypass surgery.

Previous studies that examined changes in REE with moderate weight loss resulting from conventional interventions (7, 9, 11, 57, 58) or massive weight loss in smaller groups of subjects (8, 20, 23) generally reported that REE was lower than expected on the basis of the changes in body composition. However, those studies only took into account changes in FFM, and indeed we found a similar result if changes in REE were predicted from FFM alone. Fat tissue is metabolically active and is a significant contributor to REE (24–28); therefore, it needs to be accounted for. Our data show that fat mass contributed significantly to the variability in REE, both in the extremely obese state and after weight loss and restabilization, and that failure to account for the changes in fat mass would have falsely indicated a relative decrease in energy expenditure that did not occur. An additional important feature of our study was that we measured body composition accurately with the use of a 3-compartment model, which accounts for shifts in body water compartments, whereas most other studies—with the exception of that by Westerterp et al (20)—used 2 compartment models only.

A substantial decrease in TEE with weight loss was also found, averaging 3.6 MJ/d on average. However, approximately 66% of this amount was accounted for by the change in REE (2.4 MJ/d) and was therefore predicted by body-composition change, leaving the calculated decrease in the NREE component of energy expenditure at only 1.2 MJ/d (which incorporates both the decrease in energy expenditure for physical activity and arousal and the change in TEF). Mean PAL values (TEE/REE) at follow-up were not significantly different from baseline, as were self-reported amounts of physical activity, which indicated that there was no decrease in NREE over and above that explained by the reduced energy costs of moving a smaller body. However, because energy expenditure ratios can be influenced by body weight as well as by physical activity (59, 60), we also conducted regression analyses to examine this issue. The analyses involved fitting a complex model to widely varying data and suggested both a decrease in NREE independent of body composition and an increase in NREE associated with loss of fat mass; the changes tended to counterbalance each other. One previous study reported no relative decrease in TEE with weight loss (16) and another reported a significant decrease in TEE that was greater than expected from body-composition change (7). The fact that we found only a small mean change in NREE despite massive weight loss and no change in mean PAL supports the suggestion of Amatruda et al (16) that energy expenditure is not abnormally low after weight loss.

With regard to identifying characteristics that might differentiate persons who are more successful at losing weight than are others, we found that baseline weight, fat mass, and BMI all significantly predicted changes in weight and body composition; initially more obese subjects had the greatest changes. This finding is consistent with the findings of several previous studies (17, 23, 31–37). However, caution must be used in the interpretation of this result because there is a regression to the mean effect in such analyses (61) that might obscure the quantitative role of biology. The biological mechanism by which initially larger subjects lose more weight has been suggested to be that they have initially higher energy intakes and thus have a relatively greater absolute restriction of energy intake with gastric bypass surgery [a similar-sized

TABLE 5

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 6)</th>
<th>Women (n = 24)</th>
<th>Total (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured REE</td>
<td>8.67 ± 0.5</td>
<td>6.52 ± 0.7</td>
<td>6.97 ± 1.1</td>
</tr>
<tr>
<td>Predicted REE</td>
<td>9.08 ± 0.8</td>
<td>6.52 ± 0.6</td>
<td>7.15 ± 1.4</td>
</tr>
</tbody>
</table>

$\bar{x} \pm$ SEM.

$^2$Predicted by using the equations of the World Health Organization (45).
gastric pouch is created in all surgical patients, which restricts the total quantity of food that can be consumed (62). However, if this were the case, TEE should predict weight loss better than does initial body weight because TEE is equivalent to energy intake during weight stability. The fact that baseline TEE did not predict weight loss as strongly as did baseline body weight in our study argues against initial energy intake being the primary determinant of weight loss and suggests that other factors may be important. Baseline variables—including TEE, REE, and PAL—were also unrelated to changes in body weight or fat mass in our study when adjusted for body composition and when included in models with baseline body weight or fat mass. Our finding that PAL did not predict weight loss conflicts with the findings of Westerterp et al (20), who unexpectedly reported greater fat loss in more sedentary subjects. However, that study had only a small group of subjects ($n = 6$) and did not account for the potential confounding effect of initial body fat.

A further result from this study is that measured REE after weight reduction was comparable with REE values predicted from standard equations developed from data obtained from normal-weight subjects (45, 46). This finding suggests that standard REE prediction equations are suitable for use in persons after weight loss and are consistent with the results from our study, suggesting that there is no disproportionate long-term decrease in REE with weight loss that would favor weight regain.

Our data suggest that fasting leptin at baseline (relative to body fatness) does not predict weight loss. This observation is contrary to the findings of previous studies in obese subjects, which examined the role of leptin as a predictor of weight-loss success (35, 36). The results of these studies suggest that persons with low leptin concentrations relative to fat mass (ie, greater leptin sensitivity) have greater weight losses. However, these studies examined diet-induced weight loss and smaller reductions in fat mass, which may explain some of the contrasting findings. A further finding related to leptin in the present study was that the leptin concentration was lower after weight reduction than it was at baseline, even after adjustment for changes in body fat. Although this relative decrease in leptin was not associated with measurable changes in energy expenditure, it might potentially help to explain the weight regain observed in some gastric bypass patients; further follow-up studies in this area are needed.

In summary, our results show that energy requirements and REE are significantly reduced after weight loss and weight stabilization after gastric bypass surgery but that the decreases appear to be largely or completely predicted by decreases in body FFM and fat mass. Further studies are needed to examine other potential explanations for the variability in weight loss between patients after gastric bypass surgery, including psychological or behavioral factors that may affect food intake. An appropriate and permanent reduction in energy intake appears to be critical for long-term weight management in patients who have undergone gastric bypass surgery.

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According to the model [resting energy expenditure (REE) and fat-free mass (FFM) for the k-th subject]

$$REE_k = c + b_0 + b_1 \text{FFM}_k + b_2 \Delta\text{FFM}_k$$

(A1)

where $b_0$ is multiplied by an indicator variable, which is 0 at baseline and 1 at follow-up, and $REE_k$ is the REE at time $i$ (1 at baseline and 2 at the follow-up visit), $\text{FFM}_k$ is FFM at baseline, $\Delta\text{FFM}_k$ is the change in FFM from baseline (time 1) to time $i$, and $c$ is a constant.

At baseline (time 1), because $\Delta\text{FFM}_k$ always = 0 and $b_0 = 0$, the model reduces to

$$REE_1 = c + b_1 \text{FFM}_1$$

(A2)

Thus, $b_1$ represents the between-subject regression coefficient of FFM at baseline. The difference between $REE_2$ and $REE_1$ is as follows:

$$REE_2 - REE_1 = b_0 + b_2 (\Delta\text{FFM}_2 - \Delta\text{FFM}_1)$$

(A3)

However, because $\Delta\text{FFM}_1$ is always 0

$$REE_2 - REE_1 = b_0 + b_2 \Delta\text{FFM}_2$$

(A4)

where $b_2$ is the expected change in REE per unit change in FFM. This model allows $b_1$ and $b_2$ to be compared directly. When fat mass is added as a second independent variable, the coefficients for fat mass and FFM at baseline and the coefficients for $\Delta$fat mass and $\Delta$FFM at the follow-up visit can be compared.