Resting energy expenditure in reduced-obese subjects in the National Weight Control Registry

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ABSTRACT

Background: Weight loss in obese subjects is associated with a reduction in resting metabolic rate (RMR). Whether the reduction can be explained solely by a reduction in lean body mass remains controversial.

Objective: Our objective was to determine whether the reduction in RMR after weight loss was proportional to the decrease in lean mass alone or was greater than could be explained by body composition.

Design: We measured the RMR, fasting respiratory quotient (RQ), and body composition in 40 reduced-obese subjects (ie, 7 men and 33 women who had lost ≥13.6 kg (30 lb) and maintained the loss for ≥1 y) enrolled in the National Weight Control Registry and 46 weight-matched control subjects (9 men, 37 women).

Results: A stepwise multiple regression found lean mass, fat mass, age, and sex to be the best predictors of RMR in both groups. After adjusting RMR for these variables, we found no significant difference in RMR (5926 ± 106 and 6015 ± 104 kJ/d) between the 2 groups (P = 0.35). When we adjusted fasting RQ for percentage body fat and age, the reduced-obese group had a slightly higher (0.807 ± 0.006) RQ than the control group (0.791 ± 0.005, P = 0.05). This may have been due to the consumption of a diet lower in fat or to a reduced capacity for fat oxidation in the reduced-obese group.

Conclusion: These results show that in at least some reduced-obese individuals there does not seem to be a permanent obligatory reduction in RMR beyond the expected reduction for a reduced lean mass.


KEY WORDS Obesity, weight loss, body composition, weight maintenance, respiratory quotient, energy expenditure, humans, National Weight Control Registry

INTRODUCTION

Long-term maintenance of weight loss appears to be a true obstacle for many people. Despite the success of many individuals in losing a significant amount of excess weight at some time in their life, the long-term maintenance of that loss evades most obese individuals (1). Weight cycling of the same 10 kg is a common theme in many weight histories. This has led many researchers to speculate that metabolic efficiency develops after significant weight loss that predisposes individuals to regain the weight they have lost (2, 3). The 2 most commonly reported metabolic consequences of weight loss are 1) a reduction in energy requirements below that expected from the loss of body mass, and 2) a reduced capacity for fat oxidation.

Although most experts agree that a proportional decrease in metabolic rate is expected with a loss in fat-free mass (4–8), some studies have found a greater than expected reduction in metabolic rate (2, 3, 8–11). Leibel et al (2) reported a reduction in resting metabolic rate (RMR) of 12.6–16.7 kJ/kg fat-free mass in obese subjects maintaining a 10% reduction in body weight. This finding could represent a compensatory change by the body to try to return to a previous weight and resist further weight loss. Others, however, found RMR to be appropriate for the new reduced lean mass, a finding that does not support the hypothesis of a greater metabolic efficiency in a reduced state (5, 7, 12–17). Most of the studies to date have been conducted in small, homogeneous groups of obese individuals who had lost weight and measurements of RMR were often made relatively soon after weight loss (2, 9–13). Measurements of RMR taken during or immediately after weight reduction may reflect a metabolic adaptation to an acute negative energy balance, the reduced cost of substrate trafficking due to reduced energy intake (not to the reduced body weight itself), or both.

In addition, some investigators have reported a reduced capacity to oxidize fat after weight loss (15, 18–21). Larson et al (15) reported a higher adjusted 24-h respiratory quotient (RQ) in formerly obese subjects than in age- and weight-matched control subjects who had no history of weight loss in the previous year. Astrup et al (20) found a significant difference in fat oxidation between formerly obese subjects and control subjects while they were consuming a high-fat diet (50% of energy). The ratio of fat to carbohydrate oxidation increased in the control subjects, but not in the formerly obese subjects. A low capacity for fat oxida-
tion could predispose a formerly obese individual to be in a positive fat balance, especially when consuming a fat-rich diet.

The National Weight Control Registry (NWCR) is a registry of >2,000 reduced-obese subjects across the United States (22–25). Members must have maintained a weight loss of ≥13.6 kg (30 lb) for ≥1 y to qualify for membership. The NWCR provides the opportunity to investigate energy metabolism in a large heterogeneous group of weight-stable, reduced-obese subjects and to follow this group prospectively.

SUBJECTS AND METHODS

Subjects

Forty reduced-obese subjects (7 men, 33 women) were recruited to participate in the study. Existing members of the NWCR that lived in the Denver area were sent letters asking for volunteers to participate in the study. In addition, other subjects (n = 9) meeting the NWCR criteria [a weight loss ≥13.6 kg (30 lb) for ≥1 y] were identified. The only additional eligibility criterion was that subjects weighed the same, within 2.3 kg (5 lb), as they did in the 6 mo before the study began.

A control group (9 men, 37 women) was selected retrospectively from our database for participation in the study. Although the control subjects were not paired individually with the reduced-obese subjects, they were chosen to provide a similar range in age and body weight to the reduced-obese group (Table 1). Therefore, within both groups there was a wide variety of body weights, with some subjects being classified as obese and others as lean. Control subjects were contacted by phone and asked to return to our center for body-composition and metabolic testing according to the same protocol followed for the reduced-obese subjects. The control subjects were within 2.3 kg (5 lb) of their lifetime maximum weight and weighed within 2.3 kg (5 lb) of their weight in the 6 mo before the study began.

The protocol was approved by the Colorado Multiple Institutional Review Board at The University of Colorado Health Sciences Center in Denver. All volunteers gave written consent after the procedures were explained orally and in writing on the consent form. Subjects came to the laboratory once for measurement of body composition and RMR. Neither group was paid for their participation in the study and both groups received copies of their individual testing results after completion of the study.

Body composition

Body composition was assessed by using dual-energy X-ray absorptiometry (DXA). All subjects reported to The Center for Human Nutrition at the University of Colorado Health Sciences Center after a 12-h fast; subjects were allowed to have water up until 1 h before the test. Tests were performed with subjects in the supine position by using a Lunar DPX-IQ bone densitometer (Lunar Corp, Madison, WI). The scan mode was determined by the subjects’ sagittal diameters. The fast (150 μA) mode was used for subjects with a sagittal diameter ≤22 cm and the medium (150 μA) mode was used for subjects with a sagittal diameter >22 cm. A total body scan provides bone mineral content (g), bone mineral density (g/cm²), fat mass (g), and lean mass (kg). Lunar software version 4.3c (extended research analysis option) was used for all subjects.

Resting metabolic rate

RMR was measured by ventilated-hood, indirect calorimetry with a SensorMedics 2900 oxygen uptake system (Yorba Linda, CA). Subjects reported to The Center for Human Nutrition after a 12-h overnight fast. Subjects were told not to engage in physical activity for 24 h before testing. After lying quietly for 30 min, oxygen consumption and carbon dioxide production were measured continuously over 15–20 min. RMR was calculated from these values by using standard equations (26). In our laboratory, the daily variability in RMR is 4–5%.

Statistical analyses

Data analyses were performed by using the SAS statistical package (release 6.12; SAS Institute Inc, Cary, NC) and the SPLUS statistics package (version 4.0; MathSoft, Seattle). Independent sample t tests were used to compare mean values for subject characteristics for the reduced-obese and control groups. Univariate linear regression for continuous variables or one-way analysis of variance for categorical variables (group and sex) was used to study relations between RMR and RQ and other variables individually. General linear models were used to assess and quantify differences in RMR and RQ between the reduced-obese and control groups when the effects of other variables were adjusted for. At all stages, graphic exploratory analysis was done to examine the data for extreme cases or other irregularities.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reduced-obese subjects (n = 7 M, 33 F)</th>
<th>Control subjects (n = 9 M, 37 F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>46 ± 11.2</td>
<td>47 ± 11.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167 ± 7.5</td>
<td>168 ± 7.6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.3 ± 12.0</td>
<td>69.0 ± 17.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.3 ± 3.6</td>
<td>24.5 ± 5.8</td>
</tr>
<tr>
<td>Percentage body fat (%)</td>
<td>31.3 ± 9.1</td>
<td>30.6 ± 10.6</td>
</tr>
<tr>
<td>Lean mass (kg)</td>
<td>43.2 ± 9.1</td>
<td>43.8 ± 9.0</td>
</tr>
<tr>
<td>Bone mineral content (kg)</td>
<td>2.7 ± 0.5</td>
<td>2.7 ± 0.4</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>21.3 ± 8.0</td>
<td>22.1 ± 13.0</td>
</tr>
<tr>
<td>Weight/IBW (%)</td>
<td>115.9 ± 17.2</td>
<td>116.7 ± 27.8</td>
</tr>
<tr>
<td>Weight loss (kg)</td>
<td>24.1 ± 11.7</td>
<td>—</td>
</tr>
<tr>
<td>Duration (y)</td>
<td>9.8 ± 9.7</td>
<td>—</td>
</tr>
</tbody>
</table>

1 Estimates ± SEM.
2 Adjusted for lean mass, fat mass, age, and sex.
3 Adjusted for percentage body fat and age.
4 Not significantly different from reduced-obese subjects, P = 0.05.
RESULTS

The characteristics of study participants are shown in Table 1. There were no significant differences in any variable between the groups. The reduced-obese subjects had lost between 13.62 and 61.47 kg weight, with a mean weight loss of 24.13 kg. The duration of weight loss for the reduced-obese group was calculated based on the time the subject had maintained the minimum weight loss (13.6 kg) necessary for eligibility in the NWCR. The study participants had maintained the minimum weight loss from 1 to 43 y, with the average duration of weight loss maintenance being 9.79 y.

The mean unadjusted RMR for reduced-obese subjects was not significantly lower than that of control subjects (5728 – 151 compared with 5869 – 124 kJ/d; P = 0.52; Table 2). The associations between RMR and physical characteristics of the study population are shown in Table 3. RMR was highly correlated with lean mass, bone mineral content, height, and fat mass, and RMR differed significantly between men and women. Age and percentage body fat were not correlated with RMR. Lean mass showed the strongest correlation and explained 69% of the variation in RMR. The relation between RMR and lean mass did not differ significantly between the 2 groups (Figure 1). The same regression equation \[ RMR (kJ/d) = 1767.4 + 92.65 \text{ (lean mass, in kg)} \] fits both groups and estimates an increase in RMR of 92.65 – 6.79 kJ/d for every kilogram of lean mass.

A stepwise multiple regression analysis was performed to determine whether use of a combination of the variables in Table 3 would give a better correlation with RMR than would lean mass alone. The best-fitting multiple regression included lean mass, fat mass, age, and sex (as a categorical variable), which together explained 80.5% of the variation in RMR (Table 4). Height and bone mineral content were significant in a univariate

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intercept</th>
<th>Coefficient</th>
<th>SEM</th>
<th>R²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean mass (kg)</td>
<td>1767</td>
<td>92.65</td>
<td>6.79</td>
<td>0.689</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>–7127</td>
<td>77.23</td>
<td>11.9</td>
<td>0.333</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sex</td>
<td>7186</td>
<td>1698.7</td>
<td>210.2</td>
<td>0.438</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMC (kg)²</td>
<td>1692</td>
<td>1526.3</td>
<td>165.9</td>
<td>0.502</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>5047</td>
<td>34.80</td>
<td>9.34</td>
<td>0.142</td>
<td>0.9904</td>
</tr>
<tr>
<td>Group</td>
<td>5869</td>
<td>140.48</td>
<td>218.1</td>
<td>0.005</td>
<td>0.52</td>
</tr>
<tr>
<td>Age (y)</td>
<td>5649</td>
<td>3.32</td>
<td>9.81</td>
<td>0.0004</td>
<td>0.74</td>
</tr>
<tr>
<td>Percentage body fat (%)</td>
<td>5696</td>
<td>3.47</td>
<td>11.08</td>
<td>0.0012</td>
<td>0.76</td>
</tr>
</tbody>
</table>

1 Higher in men than in women.
2 Bone mineral content.
3 Higher in control than in reduced-obese subjects.

FIGURE 1. Regression of resting metabolic rate (RMR) on lean mass in reduced-obese subjects (+) and control subjects (o). The line has the following regression equation: \[ RMR (kJ/d) = 1767.4 + 92.65 \text{ (lean mass, in kg)} \]. The same regression equation fit both groups.
TABLE 4
Stepwise multiple regression coefficients for resting metabolic rate (RMR; kJ/d)\(^1\)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient(^2)</th>
<th>SEM</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean mass (kg)</td>
<td>71.90</td>
<td>10.39</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>33.10</td>
<td>4.99</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age (y)</td>
<td>-17.27</td>
<td>4.95</td>
<td>0.0009</td>
</tr>
<tr>
<td>Sex</td>
<td>541.48(^3)</td>
<td>248.60</td>
<td>0.03</td>
</tr>
</tbody>
</table>

\(^1\) The stepwise multiple regression with use of the above variables had an \(R^2\) value of 0.805, an intercept of 2608, and a \(P\) value of 0.0001.
\(^2\) Coefficients are the regression coefficients for the linear model parameters.
\(^3\) Higher in men than in women.

regression analysis but did not contribute anything additional to the multiple regression. No significant differences in the effects of any of the variables (interactions) were noted between the 2 groups or between the sexes.

After being adjusted for lean mass, fat mass, sex, and age, RMR was not significantly different between the reduced-obese and control groups (5926 ± 106 and 6015 ± 104 kJ/d, respectively; \(P = 0.38;\) Table 2). A 95% CI for the adjusted mean difference in RMR between reduced-obese and control subjects indicated that the RMR could be as much as 287 kJ/d lower or as much as 110 kJ/d higher for reduced-obese subjects than for control subjects. On the basis of a post hoc power analysis, our study had a power of \(\approx 50\%\) to detect a difference of 200 kJ/d, a power of \(\approx 80\%\) to detect a difference of 280 kJ/d, and a power of \(\approx 95\%\) to detect a difference of 360 kJ/d.

We also compared the groups in terms of the variation about the multiple regression prediction. We found no differences between reduced-obese and control subjects in the proportion of subjects falling outside prediction limits and no difference in the SD of the residuals of the regression. There was not more variation among the reduced-obese group than could be explained by chance.

Respiratory quotient

The unadjusted fasting RQs for both groups are shown in Table 2. The reduced-obese group tended to have a slightly higher RQ (indicative of a lower fat oxidation) than the control subjects; however, the difference was not significant. Univariate linear correlations between the RQ and variables of interest in the reduced-obese and control groups showed that only age was a significant predictor of RQ (\(P = 0.04;\) Table 5). A stepwise multiple regression using the same variables of interest found the best fitting regression to include age and percentage body fat in predicting RQ (Table 6). RQs adjusted for percentage body fat and age for both groups are shown in Table 2. Once again, the RQ for the reduced-obese group tended to be slightly higher (0.807 compared with 0.791), with the \(P\) value indicating near significance (\(P = 0.05\)).

DISCUSSION

We found no indication of increased energy efficiency in a group of individuals who have been successful in long-term weight maintenance. The RMR in this group of reduced-obese subjects was not significantly different from that in the control subjects. This suggests that an increased metabolic efficiency is not an obligatory consequence of weight reduction.

A low RMR has been suggested, in some populations, to be a predictor of weight gain and obesity (27). Whether or not reduced-obese individuals constitute such a population is controversial. Although some have found evidence of a lower than expected RMR (2, 3, 8–11), others have found RMR to be appropriate for body size and composition in these subjects (5, 7, 12–17). There are several possible reasons for these conflicting results. One obvious possibility is that reduced-obese subjects may be a heterogeneous group of subjects, some of whom may have an increased metabolic efficiency. It is certainly possible that by choosing subjects who have shown long-term success in maintaining weight loss we may have selected only those subjects without increased metabolic efficiency. However, many of these reduced-obese subjects (\(n = 12\) had maintained the minimum weight loss (13.6 kg) for only 1–2 y and would be expected to be at high risk of weight regain.

Another reason for conflicting results may relate to the timing of the RMR and body-composition measures relative to the active weight-loss period. Because of the difficulty of maintaining weight loss, it has been difficult to find large numbers of successful reduced-obese subjects. Thus, in many studies, RMR was measured soon after weight loss and may have precluded stabilization of both body weight and RMR.

One advantage of the NWCR is to provide access to a large group of reduced-obese subjects who have maintained their weight loss for \(\geq 1\) y. In this study, we assessed RMR in a large heterogeneous group of reduced-obese subjects. The amount of time that the subjects had maintained their reduction in body weight varied from 1 to 43 y and although the weight of all the subjects was lower than their maximum body weight over their lifetime, their current body weights varied, resulting in some subjects still being classified as obese and others as close to their ideal body weight. As we continue to evaluate RMR in a larger number of subjects in the NWCR, we hope to evaluate whether the amount of weight lost or duration of weight maintenance affects RMR.

It is important to note that our study had 80% power to detect a difference in RMR > 280 kJ/d. A difference in RMR

### Table 5

Univariate regression coefficients for respiratory quotient on variables of interest in the reduced-obese and control subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intercept</th>
<th>Coefficient</th>
<th>SEM</th>
<th>(R^2)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>0.76</td>
<td>0.00080</td>
<td>0.00037</td>
<td>0.052</td>
<td>0.04</td>
</tr>
<tr>
<td>Percentage body fat (%)</td>
<td>0.82</td>
<td>-0.00066</td>
<td>0.00043</td>
<td>0.028</td>
<td>0.13</td>
</tr>
<tr>
<td>Lean mass (kg)</td>
<td>0.77</td>
<td>0.00067</td>
<td>0.00047</td>
<td>0.024</td>
<td>0.16</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>0.81</td>
<td>-0.00052</td>
<td>0.00039</td>
<td>0.021</td>
<td>0.18</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>0.70</td>
<td>0.00061</td>
<td>0.00057</td>
<td>0.014</td>
<td>0.29</td>
</tr>
<tr>
<td>BMC (kg)(^1)</td>
<td>0.78</td>
<td>0.00618</td>
<td>0.00913</td>
<td>0.005</td>
<td>0.50</td>
</tr>
</tbody>
</table>

\(^1\) Bone mineral content.
dietary and physical activity patterns that are different from those weight loss do so primarily because they are not able to maintain modification. It is likely that many subjects who fail to maintain should be able to maintain weight loss with appropriate behavior after weight loss in some subjects, these results suggest that many inescapable consequence of weight loss. Although we cannot port the hypothesis that a lower than expected RMR is an A more definitive comparison of fat oxidation capability between

We reported previously that subjects in the NWCR were consum-
eses in usual dietary patterns as the explanation for this result. We reported previously that subjects in the NWCR were consuming diets very low in fat (22), which would produce a high fasting RQ (28). Furthermore, we only measured fasting RQ in this study. A more definitive comparison of fat oxidation capability between reduced-obese and control subjects will require measurement of 24-h fat oxidation after specified dietary manipulations.

In conclusion, the present study provides no evidence to sup-
port the hypothesis that a lower than expected RMR is an inescapable consequence of weight loss. Although this would be consistent with other reports of decreased fat oxidation in reduced-obese subjects (15, 18, 20, 21), we cannot rule out differences in usual dietary patterns as the explanation for this result. We reported previously that subjects in the NWCR were consuming diets very low in fat (22), which would produce a high fasting RQ (28). Furthermore, we only measured fasting RQ in this study. A more definitive comparison of fat oxidation capability between reduced-obese and control subjects will require measurement of 24-h fat oxidation after specified dietary manipulations.

<280 kJ/d may exist between the 2 groups. Negative studies in the past have not always reported their power to detect differ-
ences and thus their significance is not as easy to interpret. It is certainly possible that differences between groups of <280 kJ/d exist and could play a role in the tendency for the reduced-
obese subjects to regain weight.

We found some indication of a higher fasting RQ in reduced-
obese subjects than in control subjects. Although this would be consistent with other reports of decreased fat oxidation in reduced-obese subjects (15, 18, 20, 21), we cannot rule out differ-
ences in usual dietary patterns as the explanation for this result. We reported previously that subjects in the NWCR were consuming diets very low in fat (22), which would produce a high fasting RQ (28). Furthermore, we only measured fasting RQ in this study. A more definitive comparison of fat oxidation capability between reduced-obese and control subjects will require measurement of 24-h fat oxidation after specified dietary manipulations.

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REFERENCES

1. Wadden TA. Treatment of obesity by moderate and severe caloric restriction in weight loss and control: results of clinical research tri-
5. Amatruda JM, Statt MC, Welle SL. Total and resting energy expendi-
6. Welle SL, Amatruda JM, Forbes GB, Lockwood DH. Resting meta-
10. Elliot DL, Goldberg L, Kuehl KS, Bennett WM. Sustained depres-
12. Nelson KM, Weinsier RL, James LD, Darnell B, Hunter GR, Long CL. Effect of weight reduction on resting energy expenditure, sub-
20. Astrup A, Buemann B, Christensen NJ, Toubro S. Failure to increase lipid oxidation in response to increasing dietary fat content in for-
22. Klem ML, Wing RR, McGuire MT, Seagle HM, Hill JO. A descrip-
23. Klem ML, Wing RR, McGuire MT, Seagle HM, Hill JO. Psycho-
24. McGuire MT, Wing RR, Klem ML, Seagle HM, Hill JO. Long-term maintenance of weight loss: do people who lose weight through vari-