Sustained depression of the resting metabolic rate after massive weight loss[1–3]

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ABSTRACT To assess potential long-term effects of weight loss on resting metabolic rate (RMR), the RMRs of seven obese women were measured by indirect calorimetry before weight loss, during a protein-sparing modified fast, and for 2 mo while at a stable reduced weight. Body composition was also determined at each interval. RMR significantly decreased 22% ($p < 0.01$) with initiation of the modified fast. RMR values during the modified fast and during the maintenance diet at stable reduced weight were not different and all were significantly lower than the prediet RMR. Loss of lean tissue could not account for the decrease because changes in RMR per fat-free mass paralleled the total RMR reduction. A sustained decrement in RMR accompanied weight loss and persisted for ≥ 8 wk despite increased caloric consumption and body weight stabilization. *Am J Clin Nutr* 1989;49:93–6.

KEY WORDS Resting metabolic rate, obesity, protein-sparing modified fast

Introduction

Obese individuals who achieve significant weight loss often return to their original obese state (1). The factors that impede sustained weight loss are not well understood. A major component of total caloric expenditure is the resting metabolic rate (RMR)(2). RMRs of obese individuals, when normalized for the amount of fat-free body weight, are comparable to those of nonobese individuals (3–5). However, previous studies have not adequately assessed potential RMR modifications after weight reduction. Changes in metabolic rate may develop during caloric restriction and contribute to the inability of individuals who have lost weight to maintain their weight loss.

A supervised protein-sparing modified fast was shown to be a safe and effective method for weight reduction (6, 7). Caloric restriction of that severity decreases the RMR (8–13). We sought to evaluate the hypothesis that the RMR remained depressed after discontinuation of a modified fast that achieved massive weight reduction.

Subjects and methods

Seven obese women, aged 31–55 y (40 ± 10 y, $\bar{x} \pm SD$) with body mass indices of 29.1–48.4 (37.6 ± 6.3) were recruited from clients enrolling in a medically supervised protein-sparing modified fast. The subjects all met the following criteria: positive childhood and family history of obesity, euthyroidism, normal fasting glucose (P) (5.8 ± 1.3 mmol/L), and no alteration during the study in medications that could affect RMR. All individuals reported stable weights preceding the study and none had attempted weight loss for a minimum of 2 mo before enrollment. After their informed consent had been obtained, 10 individuals began the study, 7 of whom completed it. Three women dropped out; one began medication for asthma, one was noncompliant with the modified fast, and social issues prevented a third from complying with testing.

The protein-sparing modified fast consisted of ~300 kcal/d, with 45 g of protein. Potassium and multivitamin supplements were provided. After the modified fast, subjects were gradually realimented over several weeks. A month after discontinuation of the diet individuals were consuming a low-fat (< 30% of total calories) diet at an estimated maintenance caloric intake (~1100–1400 kcal/d).

Body composition and RMR were determined before the diet began and monthly during the modified fast. In addition, each individual had RMR measured 4 and 8 wk after the modified fast ended while she was on a maintenance diet. The study was approved by the Committee on Human Research at our institution and informed consent was obtained from all subjects.

RMRs were assessed by indirect calorimetry by use of resting oxygen-uptake and resting carbon dioxide–production measurements. Subjects were not hospitalized overnight but reported directly to the laboratory on rising. All determinations were performed after a 10-h fast at 0630 and at an ambient temperature of 26 °C. After they were familiarized with the test-

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TABLE 1
Subject characteristics before the protein-sparing modified fast and after weight loss during caloric maintenance*

	Prediet	4 wk postdiet	8 wk postdiet
Total weight (kg)	106 ± 25	77 ± 14†	79 ± 16
Fat-free weight (kg)	55 ± 8	50 ± 8†	53 ± 8‡
Fat (kg)	50 ± 18	27 ± 8†	27 ± 9
Percent fat (%)	47 ± 6	35 ± 5†	33 ± 5

* $\bar{x} \pm$ SD.
† $p < 0.001$ for 4 wk postdiet vs prediet.
‡ $p < 0.01$ for 8 wk postdiet vs 4 wk postdiet.

ing procedures and equipment used, subjects rested supine while an occlusive facial mask with a low-resistance valve was used to continually collect expired gases. Minute ventilation was measured with a dry rolling-seal spirometer and analog potentiometer, with flow obtained by electronic differentiation of the volume signal. O_2 concentration was measured with a paramagnetic analyzer and CO_2 concentration was determined by infrared analysis; volume and concentration measurements were used to calculate uptake and production values (Gould 9000 IV metabolic cart, Dayton, OH). After a 5-min equilibration period, values were obtained at 20-s intervals and integrated over 20 min. After recalibration, the same procedure was repeated and the mean values for the two 20-min periods were averaged. Caloric consumption was calculated from the values obtained (14). Body composition was determined by hydrostatic weight and densitometry (15) and residual volume was estimated from the measured vital capacity (16).

Data were analyzed by repeated-measures ANOVA (17) with post-hoc comparisons by the two-tailed *t* test. Simple correlations were determined using Pearson's correlation coefficient (18). Statistical significance was set at the 0.05 level.

Results

Characteristics of subjects before and 4 wk after the modified fast are shown in **Table 1.** Each individual participated in the diet for ≥ 10 wk, with a range of 10–23 wk. Significant weight reduction occurred during the modified fast ($p < 0.001$), with a mean individual loss of 28.3 ± 11.4 kg. A significant decrease in both fat and fat-free mass was observed ($p < 0.001$ for each). The majority of weight lost was fat; overall, the weight loss averaged 82% fat and 18% fat-free mass. Between 4, and 8 wk after the modified fast, no significant change in total body weight or fat mass occurred (Table 1). However, during this maintenance interval, fat-free mass increased an average of 3 kg ($p < 0.01$).

RMR changed significantly during the modified fast ($p < 0.001$) **(Fig. 1)**, with a 22% decrease between the prediet and initial-diet-phase measurement. Posthoc comparisons revealed that the difference between values was limited to the prediet determination, which was significantly greater ($p < 0.01$) than each of the other measurements. RMR values during the modified fast and at 4

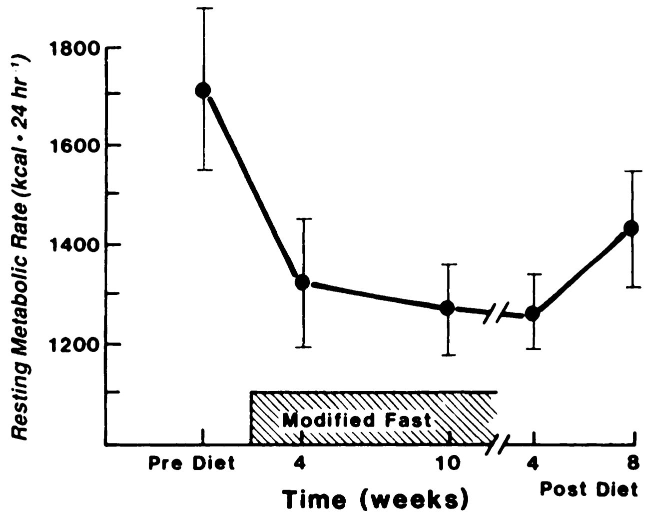

FIG 1. Changes in RMR (kcal·24 h^{-1}) observed in obese women before, during, and after a protein-sparing modified fast. The time effect is significant at $p < 0.001$ by ANOVA. ($\bar{x} \pm$ SEM.)

and 8 wk after weight loss at a stabilized body weight were not significantly different.

Fat-free mass correlated significantly with RMR ($p < 0.01$), accounting for 80% of its variability. Although subjects lost an average of 5 kg of fat-free mass during the modified fast, RMR per kg fat-free mass was also reduced ($p < 0.01$) **(Fig. 2)**. The RMRs per fat-free mass while on the modified fast and during maintenance caloric intake were not significantly different and all were significantly lower ($p < 0.01$) than the prediet measurement. The individual values for each subject's RMR per kg fat-free mass are shown in **Figure 3.** All values at 8 wk were lower than prediet measures and mean values at 4

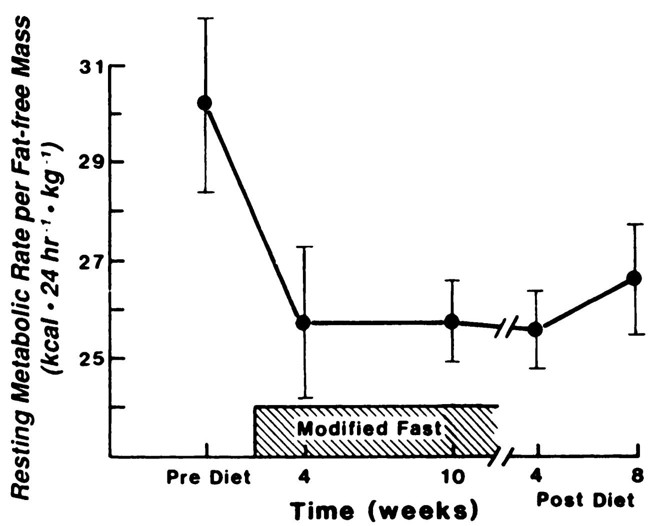

FIG 2. Changes in RMR per fat-free mass (kcal·24 h^{-1}·kg^{-1}) observed in obese women before, during, and after a protein-sparing modified fast. The time effect is significant at $p < 0.01$ by ANOVA. ($\bar{x} \pm$ SEM.)

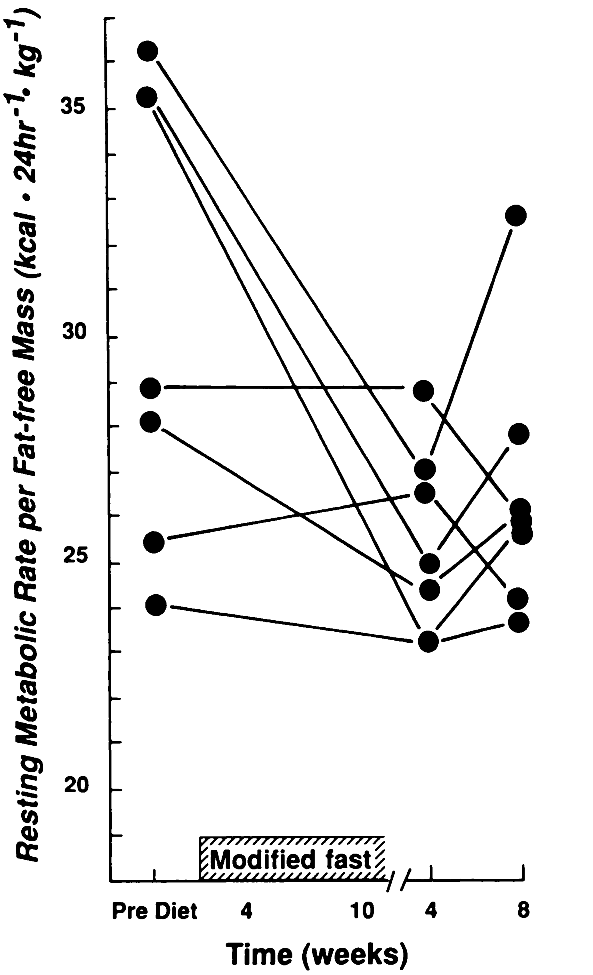

FIG 3. Individual subject's RMR per fat-free mass (kcal·24 h^{-1}·kg^{-1}) before and after a protein-sparing modified fast.

and 8 wk were not significantly different. During that last interval, values of five subjects' RMR per kg fat-free mass increased whereas two decreased. The change in RMR per fat-free mass during this maintenance interval did not correlate with the coincident change in total weight, lean body mass, or percent body fat.

Discussion

We found that the RMR of obese individuals decreased during a protein-sparing modified fast and remained depressed for 2 mo after its discontinuance. Severe caloric restriction was reported to lower the RMR of individuals with normal body composition and those who are obese, with the reductions' magnitude similar to that which we observed (8–13). In addition, previous studies established that fat-free mass is highly correlated with RMR (19, 20) and the relationship is similar for both obese and nonobese individuals (3–5). Although participants' fat-free mass decreased significantly during the study the metabolic rate decrement persisted when RMR per fat-free mass was calculated at each interval. Both total RMR and the metabolic rate per kg lean tissue were reduced during and after the modified fast.

Refeeding experiments with lean individuals suggested that the RMR decrement associated with severe caloric limitation reverses within days of resuming maintenance caloric consumption (8). However, the RMR of our obese subjects remained depressed after massive weight loss despite increased caloric consumption to a level that allowed body weight stabilization.

We attributed the change in RMR to weight loss but recognize that other factors may have contributed to the findings. Despite reported stable weights before the modified fast, subjects may have been consuming more than maintenance caloric needs. Caloric intake in excess of requirements in lean individuals has been associated with an increase in RMR (11, 21). Thus, a component of the initial RMR decrease may have been due to relative overeating before the diet started. In addition, a RMR increase has been associated with non-insulin-dependent diabetes mellitus (22). None of our subjects met criteria for the diagnosis of diabetes but more sensitive indices of insulin resistance were not assessed.

The sustained effect of physical exertion on metabolic rate is not well defined (23–25). Although the subjects did not report changes in their exercise patterns, each lost weight during the modified fast and their physical exertion with normal daily activities may have been less after weight loss. Finally, only one base-line measurement was obtained. Efforts were made to ensure that subjects were comfortable with the procedures and the mean (±SD) variability in our laboratory during repeat daily tests of the same individual by techniques similar to those used in this study was 2.2 ± 1.3%. However, none of these factors would explain the failure of RMR to increase when caloric intake was liberalized to allow weight stabilization after the modified fast.

Because we failed to find a difference between values during and after the modified fast, we calculated confidence intervals around the observed difference. At 4 and 8 wk of maintenance, 90% confidence limits included a 7% increase in RMR per kg fat-free mass. Thus, we can not reject small RMR increases but these limits exclude an increase equal to the original decrement.

Previous studies revealed conflicing results concerning the RMR of obese individuals after weight reduction. Some investigators reported that the relative RMR was unchanged with weight loss because the observed decrease was proportional to the loss in fat-free mass (26, 27). Recently, Barrows and Snook (13) determined metabolic rate 5 wk after a modified fast and compared these measurements with values before and at the conclusion of the diet. They found that despite significant weight loss, at 5 wk after the modified fast the metabolic rate had returned to prediet levels. However, the magnitude of RMR reduction that they observed during the diet was ~6%, which is less than our findings. In addition, in that study body composition was not assessed 5 wk after the diet to determine wehter the RMR per fat-free mass was unchanged.

Other investigators found an RMR decrement after weight loss (28, 29). However, these studies did not examine metabolic rates after weight stabilization. Leibel and Hirsch (30) reported that the RMR of reduced-obese individuals, when extrapolated from metabolic balance studies, was less than lean subjects with comparable fat-free body mass. This finding suggested that a prolonged reduction in RMR may follow weight loss. Although sequential body composition and metabolic measurements were not performed, the results are consistent with our findings.

Our data indicate that a sustained decrement in RMR per fat-free mass follows massive weight loss achieved with a modified fast. The RMR remained depressed for ≥ 2 mo after weight reduction despite an increase in caloric consumption to a level that allowed weight stabilization. Whether this observation relates to the method used to achieve weight loss or its magnitude has not been established. However, the decrement that we observed may contribute to the propensity to regain lost weight and suggests that variables other than caloric intake and body weight, as they relate to traditional desirable levels, may influence the RMR.

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