

## Weekly Changes in Basal Metabolic Rate with Eight Weeks of Overfeeding

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### Abstract

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**Objective:** The contribution of basal metabolic rate (BMR) to weight gain susceptibility has long been debated. We wanted to examine whether BMR changes in a linear fashion with overfeeding. Our hypothesis was that BMR does not increase linearly with 1000-kcal/d overfeeding in lean healthy subjects over 8 weeks. The null hypothesis states that BMR increases linearly with 1000-kcal/d overfeeding in lean healthy subjects.

**Research Methods and Procedures:** Initially, 16 lean healthy sedentary subjects completed 2 weeks of weight maintenance feeding at the General Clinical Research Center. The subjects were then overfed by 1000 kcal/d over 8 weeks. BMR was measured under standard conditions each week using indirect calorimetry.

**Results:** Baseline BMR was  $1693 \pm 154.5$  kcal/d. BMR increased from  $1711 \pm 201.3$  kcal/d at week 1 of overfeeding to  $1781 \pm 171.65$  kcal/d at the second week of overfeeding ( $p = 0.05$ ). BMR fell during the third week of overfeeding to  $1729 \pm 179.5$  kcal/d ( $p = 0.05$ ). After 5 weeks of overfeeding, BMR reached a plateau. Thereafter, there was no further change. Comparison of BMR with weeks of overfeeding was significantly different compared with the linear model ( $p < 0.05$ ).

**Discussion:** Increases in BMR in lean sedentary healthy subjects with 1000-kcal/d overfeeding are not linear over 8 weeks. There seems to be a short-term increase in BMR in the first 2 weeks of overfeeding that is not representative of longer-term changes.

**Key words:** basal metabolic rate, overfeeding, energy metabolism, indirect calorimetry

### Introduction

Basal metabolic rate (BMR)<sup>1</sup> is the energy humans require to maintain primitive bodily functions, including maintenance of cell metabolism, breathing, thermoregulation, and wakefulness. BMR accounts for ~60% of total daily energy expenditure (1). Thus, small fluctuations in BMR may result in important changes to overall energy balance. Furthermore, ~80% of the variability in BMR is predicted by lean body mass within and across species (2,3).

Obesity is a disease that has reached epidemic proportions in many developed countries. Obesity increases the prevalence of a multitude of diseases, increases mortality, and decreases quality of life (4–21). Changes in BMR with overfeeding and the contribution of BMR to obesity susceptibility have been discussed and researched for more than 100 years in order to better understand obesity (22–42). This extensive literature is contradictory but suggests, on balance, that BMR increases with positive energy balance. However, the pattern by which this increase occurs is unknown.

The primary goal of this paper is to address our hypothesis that BMR does not increase linearly with 1000 kcal/d of overfeeding in lean sedentary healthy subjects over 8 weeks. The null hypothesis is that a linear increase in BMR occurs with time of overfeeding.

### Research Methods and Procedures

#### Subjects

Sixteen healthy, non-obese volunteers (12 men and 4 women;  $29 \pm 4$  years;  $66 \pm 10$  kg;  $\text{BMI} = 21 \pm 3$  kg/m<sup>2</sup>) were recruited. They are detailed elsewhere (43). Subjects were excluded if they used any medication at the time of the study or within 6 months of the study, exercised more than

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<sup>1</sup> Nonstandard abbreviations: BMR, basal metabolic rate; GCRC, General Clinical Research Center; AUC, area under the curve; SD, standard deviation; FFM, fat free mass; TSH, thyroid-stimulating hormone.

twice per week, smoked, used alcohol, were pregnant, had any acute or chronic illness, or reported unstable body weight (>2 kg fluctuation for the 3 months before the study).

**Measurements of BMR**

We measured BMR weekly between baseline and week 8 of overfeeding. At baseline and at week 8 of overfeeding, BMR measurements were performed in triplicate to assess reproducibility. Each measurement was performed at ~6:30 AM. Subjects were not moved before measurements and had not eaten since 9:00 PM the night before. For each measurement, the calorimeter (Deltatrac; SensorMedics, Yorba Linda, CA) was calibrated using gases of known composition. Subjects were awake, semirecumbent (10° head bed tilt), lightly clothed, and in thermal comfort (68 to 74 °F) in a dimly lit, quiet room. Measurements were performed for 30 minutes, during which time subjects were not allowed to talk or move. For independent calorimeter validation, alcohol burns were performed twice weekly.

**Measurements of Body Composition**

Each volunteer was weighed each morning using the same calibrated scale under standard conditions by trained General Clinical Research Center (GCRC) personnel. Body fat and mineral mass were measured in duplicate on three occasions using DXA: at baseline (after 2 weeks of maintenance feeding), mid-overfeeding (week 4), and after completion of overfeeding (week 8).

**Experimental Protocol**

Subjects were studied as outpatients for 10 weeks. Meals were prepared in the metabolic kitchen at the Mayo GCRC and weighed to within 1 gram as described previously (43).

For the first 2 weeks, volunteers were fed so as to establish the dietary intake necessary to maintain steady-state body weight. For the remaining 8 weeks, each subject received 1000 kcal/d in addition to weight maintenance requirements. The diet composition throughout the study was 40% carbohydrate, 40% fat, and 20% protein.

Informed consent was obtained after the nature and possible consequences of the study were explained. The study was approved by the Mayo Institutional Review Board.

**Data Analysis**

**BMR.** For the second baseline week and week 8 of overfeeding, the average of the 3 consecutive days of data was taken to represent the BMR for that week. For weeks 1 to 7 of overfeeding, the average of the final 25 minutes of data collection was taken to represent the BMR for that week.

**Fat Free Mass.** Fat free mass was calculated as the difference between body weight and fat mass as calculated from DXA.

To address our hypothesis, that BMR does not increase linearly with 1000-kcal/d overfeeding in lean sedentary healthy subjects over 8 weeks, we compared the area under the curve (AUC) for the actual data with that predicted by the linear model. Where appropriate, week-to-week change was compared using ANOVA and post hoc paired Student's *t* tests. Data are expressed as mean ± standard deviation (SD), and statistical significance is defined as *p* ≤ 0.05.

**Results**

The subjects were 29 ± 4 years old (12 men and 4 women) and had a BMI of 21.4 ± 3.0 kg/m<sup>2</sup>. Baseline weight of the subjects was 53.3 to 91.9 kg.

**Table 1.** BMR, body composition, and leptin in 16 participants with overfeeding

Time (weeks)	BMR (kcal/d)	Weight (kg)	FFM (kg)	FM (kg)	Leptin (ng/mL)
Baseline	1693 ± 155	65.7 ± 10.3	54.8 ± 9.0	11.0 ± 5.2	4.4 ± 4.1
1	1711 ± 201	66.2 ± 10.5			
2	1781 ± 172	67.2 ± 10.3			
3	1729 ± 179	68.0 ± 10.2			
4	1778 ± 183	68.5 ± 10.1	56.4 ± 8.3	12.3 ± 5.0	5.4 ± 7.4
5	1800 ± 199	69.1 ± 10.0			
6	1791 ± 175	69.5 ± 9.9			
7	1801 ± 202	70.0 ± 9.7			
8	1772 ± 172	70.5 ± 9.7	57.1 ± 9.4	13.3 ± 5.2	6.6 ± 6.2

Results reported as mean ± standard deviation. BMR, basal metabolic rate; FFM, fat free mass; FM, fat mass.

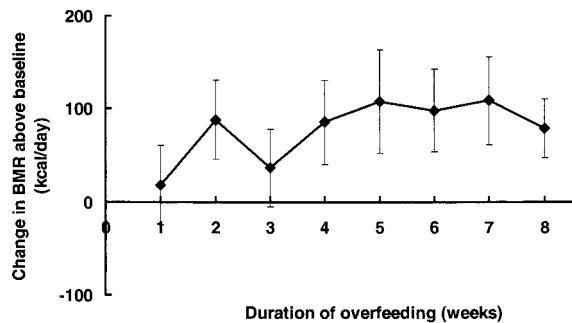


Figure 1: Change in BMR above baseline with overfeeding by 1000 kcal/d. Values are shown as mean  $\pm$  standard error of the mean for the 16 subjects.

For indirect calorimetry, repeated alcohol burn experiments yielded CO<sub>2</sub> and O<sub>2</sub> recoveries of >98%. The SD of the respiratory quotient for the last 15 minutes of these measurements was <1% of the mean. Test-retest differences for duplicate measurements of BMR were <3%.

Baseline data for the 16 subjects showed a BMR of 1693  $\pm$  154.5 kcal/d. We analyzed the AUC for the weekly BMR data compared with the linear model. The mean  $\pm$  SD AUC using a linear model from week 0 to 8 was 2205  $\pm$  3516.3 kcal compared with the actual weekly AUC, which was 4065.2  $\pm$  7739.5 kcal ( $p = 0.042$ ). BMR data for each week are shown in Table 1 and Figure 1. BMR increased by 5.2% ( $p = 0.05$ ) over the first 2 weeks of overfeeding, decreased to 2.1% above baseline in the third week ( $p = 0.05$  compared with the week prior), and increased again and plateaued in the 5th to 8th week.

Average weight for the 16 participants is shown in Table 1. Weight change with overfeeding is shown in Figure 2. Figure 3 shows the change in BMR as a proportion of weight. Using BMR/weight, we compared weeks 2 and 3,  $p = 0.034$ , week 3 and 4,  $p = 0.11$  and finally week 4 and 5,  $p = 0.78$ .

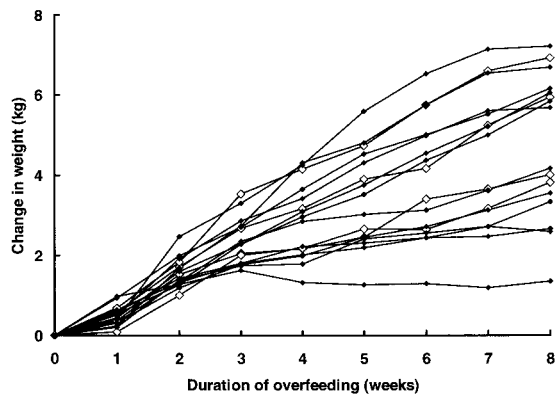


Figure 2: Weekly change in weight with overfeeding for the 16 subjects. Solid diamonds, men; open diamonds, women.

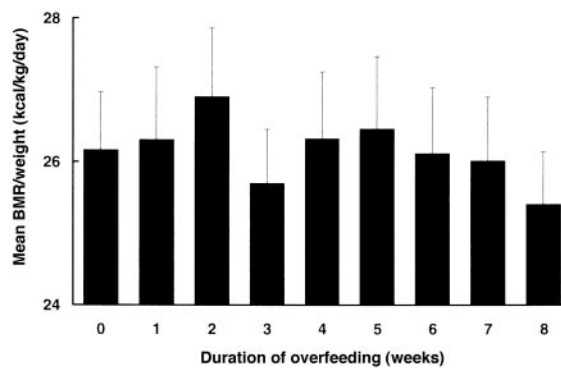


Figure 3: BMR/weight with 8 weeks of overfeeding by 1000 kcal/d. Values are shown as mean  $\pm$  standard error of the mean.

The body composition of subjects at time 0, 4 weeks, and 8 weeks of overfeeding is shown in Table 1. The change in fat free mass (FFM) at 4 weeks was 1.61  $\pm$  5.68 kg and at 8 weeks of overfeeding was 2.35  $\pm$  1.18 kg. These were not statistically different.

We compared how BMR/body composition changed with overfeeding. The baseline BMR/FFM was 31.4  $\pm$  3.8 kcal/d per kilogram FFM. The midpoint BMR/FFM was 32.0  $\pm$  4.7 kcal/d per kilogram FFM, and the week 8 BMR/FFM was 31.63  $\pm$  5.08 kcal/d per kilogram FFM. There is no statistical difference comparing the baseline, 4-week, and 8-week BMR/FFM. Thus, BMR/FFM did not change with overfeeding. It is regrettable that we did not have body composition data at weeks 2 and 3, where the accelerated increase in BMR occurred.

Baseline leptin was 4.4  $\pm$  4.1 ng/mL. At weeks 4 and 8 of overfeeding, leptin levels were 5.4  $\pm$  7.4 and 6.6  $\pm$  6.2 ng/mL ( $p = 0.01$  compared with baseline), respectively. Assessment of the thyroid function at baseline [thyroid-stimulating hormone (TSH): 2.7  $\pm$  1.8 mIU/liter; T4: 6.9  $\pm$  0.8  $\mu$ g/dL; T3: 90.2  $\pm$  16.3 ng/dL] and comparison with

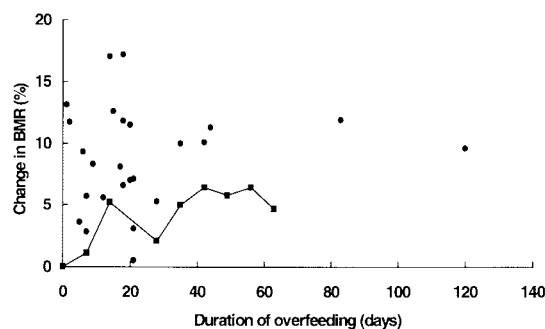


Figure 4: Change in BMR with overfeeding from the literature review studies and this study. The literature review data are presented as circles. The data from this study are presented as squares with a connecting line.

**Table 2.** Literature review of overfeeding studies performing BMR and body composition assessment (reference numbers are shown in parentheses in Study column)

Study	Subjects (men:women)	Overfeeding (days)	Mean change BMR (%)	Mean change weight (kg)	Mean change FFM (kg)	Mean change BMR/FFM (kcal/d/kg)
1 (27)	6	18	6.6	2.5		
2 (28)	5 (5:0)	14	17	7%*		
3 (29)	5 (3:2)	20	7			
4A (30)	4	83	11.9	11.2	3.6	
4B (30)	4	18	11.8	4.5	1.1	
4C (30)	5	18	17.2	4.3	2.3	
5 (31)	3 (3:0)	10–14	5.6	0.17		
6 (32)	7 (7:0)	20	11.5	3.3	1.4	2.6
7 (33)	8 (4:4)	1.2	13.1			
8 (34)	7 (7:0)	21	3.1	0.2		0.7
9 (35)	6 (6:0)	21	7.1	2.5	1.5	1.1
10 (22)	6 (6:0)	28	5.3	0.4	0.1	1.2
11A (36)	4 (0:4)	5	3.6	1.8		
11B (36)	4 (0:4)	2	11.7	1.7		
12 (37)	5 (5:0)	9	8.3	3.2	1.4	1.8
13A (38)	8 (8:0)	7	2.8	1.1		
13B (38)	8 (8:0)	7	5.7			
14 (25)	15 (2:13)	15–19	8.1	4.4	2.2	1.1
15 (39)	8 (0:8)	6	9.3	1.1		
16 (40)	6	21	0.5	2.4		
17 (23)	24 (24:0)	120	9.6	8.1	2.7	1
18 (41)	6	42	10.1	7.7	3.1	1.4
19 (24)	13	28–42	10	6.7	1.5	2
20 (26)	6 (6:0)	44	11.3	6	2.3	2.2
21 (42)	8	15	12.6	1.4		

BMR, basal metabolic rate; FFM, fat free mass.

\* No raw data available.

completion of overfeeding (TSH:  $2.5 \pm 1.3$  mIU/liter; T4:  $6.5 \pm 0.6$   $\mu$ g/dL; T3:  $99 \pm 18.2$  ng/dL) failed to identify any statistically significant difference in TSH, T4, or T3.

### Discussion

In humans, BMR encompasses the essential basic metabolism humans need for survival. BMR accounts for ~60% of daily energy expenditure (1). Given the proportion of total daily energy expenditure that BMR comprises, small changes in its quantitative value per day could make a marked impact on overall energy balance. This has led to extensive research into changes in BMR with overfeeding. In this paper, we delineated the weekly

changes in BMR that occur with overfeeding. We found that BMR does not change in a linear fashion with fixed overfeeding. Rather, BMR initially increases rapidly and then decreases, followed by a more gradual increment and plateau. We therefore wonder whether unidentified mechanisms exist to change BMR in response to excess energy supply.

To compare our results to those previously found in overfeeding studies, the change in BMR with duration of overfeeding from this study is compared with that found in 21 other studies (22–42) that examined positive energy balance and BMR (Table 2; Figure 4). Overall, the literature on overfeeding human subjects over 0.2 to

17 weeks suggests that the BMR response to overfeeding is variable and that BMR increases by ~10%. In our study, the mean increase in BMR with 8 weeks of overfeeding was  $5 \pm 8\%$ .

There is controversy in the literature as to whether changes in BMR track changes in FFM. Several studies (22–24) showed no statistically significant changes in BMR as a proportion of FFM after overfeeding compared with baseline as we found in our study.

The mechanism by which BMR changes with overfeeding is open to speculation. Possible factors that could be important include the sympathetic nervous system, which Kush et al. (44) noted to be decreased in Pima Indians and which, when knocked out in mice, is associated with obesity (45). Potential humeral mediators include thyroid hormone, which has been associated with increased BMR in animals and humans. The conversion of T4 to T3 is stimulated by overfeeding, particularly with carbohydrate overfeeding (46–48). Adipokine factors could be important, particularly ghrelin and leptin. We did not measure ghrelin or leptin during the critical upswing in BMR that occurred over the first 4 weeks. Future studies could address this. One interesting hypothesis would be that the increased caloric load could be associated with a delayed postprandial increase in energy expenditure that would “wash over” in BMR (49,50). This explanation, however, would not explain the variance in BMR from week-to-week because energy intake was constant over this time.

We found after week 1, BMR increased by 1.1%, whereas body weight increased by 0.76%. From week 1 to week 2, BMR increased by 4.1%, whereas body weight increased by only 1.51%; the BMR increment cannot be explained by the increase in body weight/FFM alone. Thus, the change in BMR is likely to relate to overfeeding. Over the 8-week period, BMR increased by 4.7%, whereas body weight and FFM increased by 7.3% and 4.2%, respectively; therefore, the increase in BMR looks reasonable based on the increase of body weight/FFM at the conclusion of the study. Is it possible that, in the beginning, the body needs to adapt to the overfeeding pattern by increasing BMR, and then, after certain weeks, the body becomes used to the overfeeding pattern; thus, the increase of BMR can be explained by the increase of body weight/FFM?

Finally, another potential source of type II error might be the stated precision of the indirect calorimeters. Although our calorimeters are carefully maintained and validated against quantitative alcohol burns, precision is not perfect. However, this imprecision is more likely to contribute to type I error, which would have resulted in our incorrectly concluding that BMR increases in a linear fashion with overfeeding. Thus, although the biological mechanism of short- vs. long-term modulation in BMR is poorly defined, these studies allow mechanistic hypotheses to be generated and tested.

In conclusion, BMR does not seem to increase linearly with 8 weeks of overfeeding in lean healthy subjects. Our data suggest that short-term changes in BMR may occur that are not sustained in the longer term. This may be important in understanding the mechanisms of weight gain and obesity with positive energy balance.

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