Resting metabolic rate is associated with hunger, self-determined meal size, and daily energy intake and may represent a marker for appetite\(^1\text{-}^3\)

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ABSTRACT

Background: There are strong logical reasons why energy expended in metabolism should influence the energy acquired in food-intake behavior. However, the relation has never been established, and it is not known why certain people experience hunger in the presence of large amounts of body energy.

Objective: We investigated the effect of the resting metabolic rate (RMR) on objective measures of whole-day food intake and hunger.

Design: We carried out a 12-wk intervention that involved 41 overweight and obese men and women [mean ± SD age: 43.1 ± 7.5 y; BMI (in kg/m\(^2\))]: 30.7 ± 3.9] who were tested under conditions of physical activity (sedentary or active) and dietary energy density (17 or 10 kJ/g). RMR, daily energy intake, meal size, and hunger were assessed within the same day and across each condition.

Results: We obtained evidence that RMR is correlated with meal size and daily energy intake in overweight and obese individuals. Participants with high RMRs showed increased levels of hunger across the day (\(P < 0.0001\)) and greater food intake (\(P < 0.00001\)) than did individuals with lower RMRs. These effects were independent of sex and food energy density. The change in RMR was also related to energy intake (\(P < 0.0001\)).

Conclusions: We propose that RMR (largely determined by fat-free mass) may be a marker of energy intake and could represent a physiologic signal for hunger. These results may have implications for additional research possibilities in appetite, energy homeostasis, and obesity. This trial was registered under international standard identification for controlled trials as ISRCTN47291569. \textit{Am J Clin Nutr} 2013;97:7–14.

INTRODUCTION

The idea that a physiologic need state (energy expended in metabolic functions) could act as a stimulus for eating is a longstanding concept in the study of appetite control. However, the signals that drive eating are still being actively investigated, often within an approach termed energy homeostasis (1). Signals of need are often reported to arise from adipose tissue modulated by the gastrointestinal tract (2–4). However, an alternative approach to appetite control was generated by the study of human energy balance (5), which sought a relation between energy expenditure (EE)\(^4\) and energy intake (EI) and had “the desire to find out more about the mechanisms which relate intake to expenditure—what regulates appetite, in fact” (5). Indeed it was argued that “the differences between the intakes of food (of individuals) must originate in the differences in the expenditure of energy” (5). Edholm et al (5) could not find any relation between total energy expenditure (TEE) and EI within any one day, but there was a good relation over 2 wk (6). The lack of any relation within any one day is not surprising because a period of high EE (such as exercise or work) that occurs toward the end of a day would not leave time for the balancing effect of an increase in food intake. Moreover, TEE can fluctuate markedly from day to day according to the amount of volitional activity performed, and experiments have shown that this does not lead to any immediate compensation in food intake (7, 8). Consequently, there is no evidence for an effect of TEE on food intake within 1 d. Although TEE has a wide day-to-day variability, the resting metabolic rate (RMR), which is the largest component of daily EE, does not. Indeed, RMR is fairly uniform across the day and from day to day (9–11). Therefore, it is more plausible that EE from RMR could provide a tonic signal of energy demand and act as a driver of EI within the same day.

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\(^4\) Abbreviations used: DEI, daily energy intake; ED, energy density; EE, energy expenditure; EI, energy intake; FFM, fat-free mass; FM, fat mass; HED, high energy density; LED, low energy density; RMR, resting metabolic rate; TEE, total energy expenditure; VAS, visual analog scale.

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In keeping with this hypothesis, we have recently shown in overweight and obese subjects that fat-free mass (FFM), but not fat mass (FM) or BMI, is positively associated with daily energy intake (DEI) and average meal size (12). This relation was disclosed within a study designed to examine the medium-term impact of EE on EI. We postulated that FFM could drive appetite through the generation of some specific molecule that arises from nonfat tissues or through an increase in EE. The first postulate is not being considered in this article. The second postulate is plausible because FFM is the largest contributor to RMR (13, 14), which accounts for ~50–60% of the variance. In contrast, FM contributes in the order of 5–6% (10). Accordingly, we have investigated whether EE from daily RMR (which reflects the energy demand from bodily tissues and metabolism) could be associated with EI over the course of 1 d and at meals and could, therefore, be a source of hunger that would drive eating. However, we do not propose that RMR is independent of FFM. Indeed, RMR is influenced by contributions from FFM (large), FM (small), and sex and age (minor). We propose that RMR, which is heavily influenced by FFM, could act as a marker (or possibly a mediator) that reflects the relation between FFM and EI.

SUBJECTS AND METHODS

Subjects

Forty-one overweight and obese participants (14 men and 27 women) aged 43.1 ± 7.5 y, with a mean BMI (in kg/m²) of 30.7 ± 3.9 completed the study (see Table 1 under “Supplemental data” in the online issue). Subjects were recruited through poster advertisements, recruitment e-mails, and advertisements in local newsletters. These participants were predominantly members of staff from the University of Leeds and the General Infirmary at Leeds. Participants were informed of the general nature of the study (ie, an investigation into exercise and appetite) but not the precise aims. The time and physical commitments required from participants was made clear. Exclusion and inclusion criteria were assessed by using an initial contact form, which was completed during a screening visit. Exclusion criteria were as follows: weight change >3 kg within the previous 3 mo, any known medical condition or medication that could affect EE or appetite, current or recently abstinent smokers, aged <18 or >55 y, BMI <28 or >45, regular exercise or engagement in structured moderate-intensity exercise more than once per week, and nonacceptance of study foods. Informed written consent was obtained after the nature and possible consequences of the study were explained. Participants were informed of their right to withdraw themselves or their data from the investigation at any time. This research was granted ethical permission by the National Health Service Research Ethics Committee (Leeds West; number 09/H1307/7). The project was registered under international standard identification for controlled trials as ISRCTN47291569.

Design

The study design was based around a 12-wk supervised exercise intervention conducted in the Human Appetite Research Unit, University of Leeds, and designed to reveal associations among a number of relevant variables in a multilevel experimental platform (15). Body composition, RMR, objectively measured food intake, and appetite sensations were assessed within the same day (probe days) under experimental conditions of a sedentary or active state (before and after completion of the 12-wk intervention) and high or low dietary energy density (ED) foods during probe days (by using covert manipulation of fat and carbohydrate composition). The EE challenge took the form of an enduring period of imposed physical activity for which participants engaged in supervised and monitored exercise sessions 5 d/wk for 12 wk. The duration was set according to the individual requirement to expend 2.1 MJ at 70% of the maximum heart rate. This was assessed by maximal oxygen uptake tests every 6 wk and recalibrated if necessary. Subjects did not exercise on probe days, which were reserved for indirect calorimetry, body composition, EI, and appetite assessments. This procedure exerted a considerable impact on total daily EE and, therefore, provided a perturbation of energy balance against which the robustness of any relation between RMR and food-intake variables could be examined. The EI challenge took the form of a dietary intervention in which the carbohydrate and fat content of foods consumed during an entire day was manipulated. Therefore, at weeks 0 and 12 of the exercise program, subjects were assessed on 2 separate probe days separated by ≥2 d. On one probe day, the foods offered at each occasion were high in fat and relatively low in carbohydrate [high energy density (HED); >17 kJ/g], and on the other day, the foods offered at each occasion were low in fat and high in carbohydrate [low energy density (LED); <10 kJ/g]. The order of these days was systematically counterbalanced across the course of the study. The form of the meals on each probe day remained identical, and foods were similar in appearance and palatability so that the subjects could not detect that a nutritional manipulation was being performed. Taken together, these interventions were designed to test whether relations between RMR, meal size, and DEI were preserved under large challenges in TEE and ED.

Procedure

After screening and admission to the study, each subject took part in intensive sets of probe days at weeks 0 and 12. On each probe day, subjects arrived at the research unit after an overnight fast. To measure RMR, subjects were rested (laying supine) for 45 min during which expired air was collected by using the ventilated hood method (16). Subjects had body composition measured by using the procedure of air plethysmography (Bod-Pod 200A; COSMED). Afterward, subjects self-selected foods from a limited range of breakfast items with which they were familiar. They were instructed to select a breakfast that was consistent with their normal eating and sufficient to provide a state of comfortable fullness. Four hours later, subjects were given a standard lunch (~20% of the estimated daily intake). This method was designed to be consistent with a realistic lunch episode of working people in their normal lives. Four hours later, subjects were given an ad libitum evening meal (not a buffet) that consisted of a main course, side dish, and dessert. Subjects again self-selected their food to reach comfortable fullness. Afterward, subjects were free to leave the research unit and were given a snack box of food items to consume if necessary during the evening. Subjects were instructed to record all items eaten and to return remaining items the next morning. This eating procedure was designed to be sensitive to appetite requirements within a pattern of

For more information, please refer to the original source.
eating that was sympathetic to the natural local eating habits of the people recruited to the study. This procedure differed from a standard experimental form for the measurement of daily food intake on the basis of 4 ad libitum meals, which we believed was likely to lead to unnecessary overconsumption (the banquet effect). Consequently, the pattern of eating used for the measurement of meal size and daily food intake was consistent with the pattern normally followed by our subjects.

Measurements

Body composition and resting metabolism assessment

Body weight and body composition were measured by using air-displacement plethysmography (Bod-Pod 200A). This technique has been validated in both normal-weight (17) and obese adults (18) against underwater weighing. The procedure took place in the laboratory after an overnight fast. Subjects wore a bathing suit and swim cap and were weighed to the nearest 0.01 kg before being seated in the BodPod device. The BodPod uses air displacement to measure body volume, and body density is calculated as body weight divided by whole body volume. Once the overall body density was calculated, the proportions of fat and fat-free tissue were determined by using the equations of Siri (19). RMR was measured in the fasted state by using an indirect calorimeter fitted with a ventilated hood (GEM; Nutren Technology Ltd). The procedure followed the guidelines outlined by The American Dietetic Association, and the validity and reliability of this measurement technique have previously been established (20, 21). Participants were asked to remain awake but motionless in a supine position for 45 min, with RMR calculated from respiratory data averaged over the final 30 min of assessment. Oxygen uptake and maximal CO₂ were calculated from O₂ and CO₂ concentrations in inspired and expired air diluted in a constant airflow of ~40 L/min (individually calibrated for each participant) and averaged over 30-s intervals. Before use, the indirect calorimeter was calibrated according to the instructions of the manufacturer by using gases of known concentrations (1% CO₂, 20% O₂, and 79% N).

Food intake and appetite sensations

EI was assessed by using a laboratory test meal design that was consistent with the local natural eating habits of participants. This assessment involved the measurement of EI for 24 h on 4 separate probe days throughout the 12-wk intervention. The probe-day test meals were provided at 4-h intervals starting with an individualized fixed energy (but self-determined) breakfast, a fixed-energy lunch, an ad libitum dinner, and an ad libitum snack box. Participants were instructed to refrain from eating between meals; water was available ad libitum throughout the day. Food intake was assessed at weeks 0 and 12 on 2 separate probe days in each week ($±2$ d apart). Participants underwent 2 conditions whereby they were presented with covertly manipulated HED foods (>50% of energy provided from fat) for one full day and covertly manipulated LED foods (<25% of the energy provided from fat) on a separate day. All foods provided were carefully preselected, and the exact composition was known (see Table 2 under “Supplemental data” in the online issue). Each item was provided on a separate plate to enable the foods to be weighed before and after consumption to the nearest 0.1 g. Subjective sensations of hunger, fullness, and desire to eat were assessed by using visual analog scales (VASs) (22) presented on a modified personal digital assistant device [EARSII (electronic appetite ratings system) (23)]. The VAS method has satisfactory test-retest reliability (24, 25) and reproducibility (26). VASs are sensitive to experimental manipulations of appetite and frequently predict the amount eaten (27). In the current study, VASs were completed immediately before and after each test meal and at hourly intervals during probe days (eg, from 0800 to 1800).

Statistical analyses

Data are presented as means ± SDs unless otherwise specified. The contribution of body composition (FFM and FM), sex, and age to the observed between-subject variation in RMR (MJ/d) was assessed by using multiple linear regression analysis with the stepwise method (probability of $F$ to enter was <0.05).

RMR was tested for association (Pearson's correlation coefficient) with measures of EI at weeks 0 and 12 and under HED and LED dietary conditions. These analyses were repeated after sex and dietary ED were controlled for by using hierarchical multiple regression analyses. To further test for the influence of sex in the relation between RMR and EI, upper and lower tertiles ($n = 13$) of RMR that were stratified by sex were compared by using ANOVA (mixed-model procedure) with the RMR tertile as a between-subject factor and the intervention week (week 0 or 12) and ED (HED or LED) as within-subject factors. The effect of change in RMR (with baseline values) during the 12-wk intervention on EI at the end of the intervention was determined by using hierarchical multiple regression analyses.

RMR was tested for the association with daily profiles of hunger by calculating the AUC for all hunger ratings during probe days and for the ad libitum period only (ie, from postlunch to the end of the day) by using the trapezoid method. To further examine the effect of RMR on hunger ratings, 3-way repeated-measures ANCOVAs were conducted with the intervention week (week 0 or 12), ED (HED or LED), and probe-day time point (14 separate ratings) as within-subjects factors and RMR entered as a covariate. To test for the influence of sex in the relation between RMR and daily hunger profiles, upper and lower tertiles ($n = 13$) of RMR stratified by sex were compared by using ANOVA (mixed-model procedure) with the RMR tertile as a between-subject factor and intervention week (week 0 or 12), ED (HED or LED), and probe-day time point (14 ratings) as within-subject factors. In all analyses, both main effects and interactions were analyzed. Where appropriate, Greenhouse-Geisser probability levels were used to adjust for sphericity. Data were analyzed with SPSS for Windows (version 16; SPSS Inc), and significance was set at $P < 0.05$.

RESULTS

Characteristics of the participants before (sedentary state) and after the 12-wk period of exercise as well as the EI from the dietary manipulation are shown in Table 1. RMR was greater in men than in women ($P < 0.0001$) and stable across the 12-wk study period. There was a significant decrease in FM ($P < 0.0001$) and waist circumference ($P < 0.001$) and an increase in FFM ($P < 0.05$). EIls were greater during the HED condition than during the LED condition ($P < 0.0001$), and men
subject characteristics and objectively measured energy intakes in overweight and obese men (n = 14) and women (n = 27) in sedentary (week 0) and activated (week 12) states

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
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<tbody>
<tr>
<td><strong>Subject characteristics and objectively measured energy intakes in overweight and obese men (n = 14) and women (n = 27) in sedentary (week 0) and activated (week 12) states</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>42.6 ± 8.3</td>
<td>—</td>
<td>44.1 ± 5.9</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>82.4 ± 6.6</td>
<td>81.7 ± 10.2</td>
<td>98.4 ± 17.3</td>
<td>95.6 ± 17.2</td>
<td>—</td>
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<td>—</td>
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<tr>
<td>Fat mass (kg)</td>
<td>36.4 ± 7.1</td>
<td>34.9 ± 7.8</td>
<td>34.6 ± 12.9</td>
<td>32.1 ± 13.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>46.0 ± 5.8</td>
<td>46.7 ± 5.7</td>
<td>63.6 ± 6.4</td>
<td>63.8 ± 6.1</td>
<td>0.77</td>
<td>0.02</td>
<td>—</td>
</tr>
<tr>
<td>Percentage of body fat</td>
<td>44.0 ± 5.5</td>
<td>42.5 ± 5.8</td>
<td>34.3 ± 7.0</td>
<td>32.4 ± 7.6</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>99.6 ± 10.2</td>
<td>96.1 ± 10.2</td>
<td>106.7 ± 11.7</td>
<td>103.8 ± 11.5</td>
<td>2.8</td>
<td>2.9</td>
<td>—</td>
</tr>
<tr>
<td>Resting metabolic rate (MJ/d)</td>
<td>6.59 ± 2.00</td>
<td>9.04 ± 2.93</td>
<td>8.3 ± 2.93</td>
<td>12.77 ± 12.04</td>
<td>1.64</td>
<td>3.74</td>
<td>1.64</td>
</tr>
<tr>
<td>LED meal size (MJ)</td>
<td>4.18 ± 1.46</td>
<td>3.74 ± 1.52</td>
<td>5.70 ± 1.71</td>
<td>5.50 ± 1.79</td>
<td>1.89</td>
<td>11.24</td>
<td>1.89</td>
</tr>
<tr>
<td>HED meal size (MJ)</td>
<td>6.35 ± 2.22</td>
<td>5.55 ± 2.29</td>
<td>8.46 ± 2.46</td>
<td>9.40 ± 3.53</td>
<td>1.52</td>
<td>5.70</td>
<td>1.52</td>
</tr>
<tr>
<td>LED daily EI (MJ)</td>
<td>13.19 ± 2.93</td>
<td>12.77 ± 2.84</td>
<td>15.69 ± 3.04</td>
<td>16.63 ± 2.81</td>
<td>2.00</td>
<td>3.74</td>
<td>2.00</td>
</tr>
<tr>
<td>HED daily EI (MJ)</td>
<td>9.49 ± 2.00</td>
<td>9.04 ± 2.16</td>
<td>11.84 ± 1.89</td>
<td>11.24 ± 1.91</td>
<td>1.64</td>
<td>3.74</td>
<td>1.64</td>
</tr>
</tbody>
</table>

1 HED was defined as 17 kJ/g, and LED was defined as 10 kJ/g. 2 Mean ± SD (all such values). 3 Significant effect of time (pretraining compared with posttraining). 4 Significant effect of sex. 5 Significant time × sex interaction.

consumed more energy than women did overall (P < 0.0001). There were no differences in EI after the exercise compared with at week 0. See Table 1 under “Supplemental data” in the online issue for participant characteristics for men and women combined.

**Analysis of between-subject variation in RMR**

See Table 3 under “Supplemental data” in the online issue for bivariate correlations between body composition, RMR, and EI. As expected, RMR was strongly correlated with FFM (men: week 0, R² = 0.36 and P < 0.05; week 12, R² = 0.54 and P < 0.01; women: week 0, R² = 0.24 and P < 0.01; week 12, R² = 0.20 and P < 0.05), and overall, FFM accounted for ~57% of the variance in RMR. An additional unique variance in RMR was accounted for by FM (6%), sex (1.5%), and age (1%), although only FFM was significant (see Table 3 under “Supplemental data” in the online issue).

**Analysis of RMR and EI**

Analyses of resting metabolism and eating behavior indicated that RMR was significantly correlated with self-determined meal size and cumulative DEI under LED and HED conditions (Figure 1; all P < 0.0001). Consequently, because RMR and ED influenced meal size and DEI, we entered these variables in regression analyses at weeks 0 and 12 (Table 2). In the first step of each model, ED predicted meal size at weeks 0 (R² = 0.44, P < 0.0001) and 12 (R² = 0.37, P < 0.0001). In the second step, RMR significantly improved both models (week 0: ΔR² = 0.09, P < 0.0001; week 12: ΔR² = 0.16, P < 0.0001), which, overall, accounted for 53% of the variability in meal size (Table 2). This pattern of results was similar for DEI, with RMR adding significant unique variance to ED to predict DEI (week 0: ΔR² = 0.25, P < 0.0001; week 12: ΔR² = 0.39, P < 0.0001). To rule out the influence of sex in these relations, top and bottom tertiles of RMR (stratified by sex) were compared for differences in meal size and snack intake (Figure 2). This figure indicated that subjects with higher RMRs (8 women

![FIGURE 1](https://example.com/figure1.png)

**FIGURE 1.** Associations between resting metabolic rate and objectively measured food intake under LED (□) and HED (■) probe days in overweight and obese adults. All correlations were significant at P < 0.0001; n = 41. A: Ad libitum meal size. B: Meal and snack intake. C: Daily energy intake. The upper regression line is for HED, and the lower regression line is for LED. Data are mean values of measurement at weeks 0 and 12. HED, high energy density; LED, low energy density.
TABLE 2
Effect of RMR on objectively measured meal size and daily energy intake in overweight and obese adults in sedentary (week 0) and activated (week 12) states1

<table>
<thead>
<tr>
<th></th>
<th>Week 0</th>
<th>Week 12</th>
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<tbody>
<tr>
<td></td>
<td>B</td>
<td>β</td>
</tr>
<tr>
<td>Meal size</td>
<td>Constant</td>
<td>−639.3 ± 212.32</td>
</tr>
<tr>
<td></td>
<td>ED</td>
<td>570.3 ± 67.2 0.67**</td>
</tr>
<tr>
<td></td>
<td>RMR</td>
<td>0.42 ± 0.11 0.30**</td>
</tr>
<tr>
<td></td>
<td>R2 for step 1</td>
<td>0.44</td>
</tr>
<tr>
<td></td>
<td>ΔR2 for step 2</td>
<td>0.09</td>
</tr>
<tr>
<td>Daily EI</td>
<td>Constant</td>
<td>724.1 ± 381.5</td>
</tr>
<tr>
<td></td>
<td>ED</td>
<td>583.4 ± 120.8 0.45**</td>
</tr>
<tr>
<td></td>
<td>RMR</td>
<td>0.665 ± 0.194 0.325*</td>
</tr>
<tr>
<td></td>
<td>R2 for step 1</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>ΔR2 for step 2</td>
<td>0.105</td>
</tr>
</tbody>
</table>

1Regression coefficients show the effect of the RMR (after energy density was controlled for) on objectively measured meal size at weeks 0 and 12. *P < 0.0001; **P < 0.00001 (n = 41). ED, energy density; EI, energy intake; RMR, resting metabolic rate; Δ, change.

2Mean ± SE (all such values).

and 5 men) had significantly larger meal sizes and DEIs than did subjects with lower RMRs (8 women and 5 men). The data showed a clear effect of ED on meal size (P < 0.0001) and a clear effect of RMR (P < 0.0001), but these effects were independent.

Analysis of RMR and appetite (hunger) ratings

Bivariate correlations between RMR and AUC hunger across all probe days were r = 0.20 and P < 0.001 for the total-day AUC and r = 0.26 and P < 0.0001 for AUC during the period after the fixed lunch. The effect of RMR on the daily profile of appetite ratings was analyzed by using ANCOVA with RMR as a covariate and the time of rating, ED, and week of assessment as independent factors; there was a significant interaction between RMR and the time of rating (P < 0.05) but no interaction of RMR or the time of rating with the week or ED. To further examine these effects, the sample was divided into tertiles according to RMR values, and the daily profiles of hunger (average ratings across the 2 nutritional manipulations) for upper and lower tertiles at weeks 0 and 12 are shown in Figure 3. As before, each tertile (n = 13) was composed of 5 men and 8 women. As illustrated in Figure 3, subjects with high RMRs experienced significantly higher levels of hunger than did subjects with the lowest RMRs.

Analysis of change in RMR over 12 wk and EI

To go beyond cross-sectional associations, the change in RMR across the 12 wk of the study was examined as a potential predictor of EI at the end of the study (week 12) under conditions of high and low dietary ED (see Table 4 under “Supplemental data” in the online issue). These dependent measures were calculated as the value for RMR at week 12 after the effect of RMR at week 0 was controlled for by using linear regression. This analysis showed a significant positive relation between the change in RMR and DEI for LED (β = 0.60, P < 0.001) and a similar trend for HED (β = 0.42, P = 0.057) probe days, which showed that increases in RMR during the course of the intervention led to a greater intake at the end of the intervention.

DISCUSSION

The context of the current study was the relation between EE and EI and the interplay between variables that contribute to energy balance. These variables include components of body composition and metabolism, but the emphasis in the study was on the behavioral component of energy balance and the way in which a biological variable (RMR) might interact with behavioral variables (aspects of EI) and the associated drive for food. For a person who is weight stable and in energy balance, TEE will equal total EI. However, this balance does not apply to the majority of the adult population of most technologically advanced countries (and of many countries that are not so advanced), for whom total EI is greater than TEE, which leads to weight gain. This situation suggests that an increased EI is not compensated for by a corresponding increase in EE. In our current research program, we are investigating the converse scenario, namely, how does EE influence EI? In the study described in this article, we have reported how one component of the energy-balance budget, RMR (together with FFM, which exerts a major influence on RMR), is related to the drive to eat, the behavior of eating, and the consequent EI. We argue that a first step in this inquiry is to show robust and meaningful associations between variables with designs and methods that permit replication and confirmation. Such associations, in themselves, do not embody any necessary causal relation and do not provide any mechanism. If functional relations exist between molar components of body composition, metabolism, and behavior, a mechanism must exist in either pathways, cells, subcellular components, or molecules. It seems appropriate to investigate hypothesized potential mechanisms once firm associations have been established.

In this area of energy-balance research, adipose tissue is recognized as playing a dominant role in the control of appetite,
and this role is reflected in the adipostatic theory of energy-balance regulation. The relation is bidirectional, whereby EI influences adipose tissue that, in turn, influences EI. This effect is the essence of biology-behavior relations. Importantly, the hormones and neurotransmitters that form the mechanistic link between adipose tissue and the act of eating have been characterized, and the brain networks have been elegantly described (2–4). This mechanistic link is the core of the theory of energy homeostasis (28). One focus of the current study is a nonadipose tissue (FFM), which is the major determinant of the RMR, which, in turn, was shown in this study to be related to hunger and EI. It remains to be determined whether the molecular links with behavior arise independently from FFM and RMR and whether or not RMR exerts any additional action over and above that contributed by FFM. Also, if these associations do constitute an influence of biology on behavior, the hormones, transmitters, and their pathways that link FFM, RMR, and EI must be identified and can form the basis for legitimate scientific inquiry, as was the case for FM over the past 2 decades.

This study has shown that RMR (normally the largest component of daily EE) is correlated with self-determined meal size and daily EI. This finding may lead to additional investigations between EE and EI proposed by Edholm et al (5). The relation, within a single day, has been revealed because we have focused on RMR, which is relatively stable across the day, rather than on TEE or volitional physical activity, which can fluctuate markedly. Many studies have reported no effect of exercise-induced EE and EI within any one day (8). The relations between RMR and meal size and DEI were preserved under the 2 dietary challenges and at the end of the exercise intervention. The correlations were effectively the same both immediately before and at the end of the 12-wk period of supervised exercise and also when the ED of foods eaten was manipulated to change EI by ~30%. Consequently, the relation between RMR and meal size and DEI remains even when total EE and EI have imposed challenges on the energy-balance system. In the current study, the methodology ensured that this behavioral action was sensitively measured, in part by the use of an eating pattern that was consistent with the normal eating habits of the participants. In addition, the eating was carried out under quiet, scientifically controlled conditions that were free from disturbing or interfering stimuli of a turbulent environment. We believe that this procedure allowed the volitional intake of subjects to sensitively reflect the physiologic demand for energy that arose from individual differences in RMR. However, this association does not mean that RMR is an independent driver of food intake. In a previous study (12), we have shown that FFM (which has the largest influence on RMR) is associated with variables of EI. Our proposal is that RMR is a proportionate indicator of FFM and, therefore, can act as a marker or mediating signal for EI. Alternatively, the true signal for eating may arise from other actions of FFM, and RMR may simply be a correlate of EI. However, this remains an interesting association and should stimulate additional mechanistic investigations on this issue.

The demonstration that RMR is associated not only with EI but also with the profile of hunger offers possibilities for additional examination of several features of day-to-day appetite control. First, the association may promote additional research on the daily drive for food. In several descriptions of appetite regulation, it is often proposed that hunger arises from tissue depletion or imposed food restriction. Consequently, when people display daily hunger and experience a strong motivation to eat (without being food deprived or suffering depletion), the sensations are often ascribed to psychological states or to triggers in the environment. These ascriptions (although valid) may not always be necessary. The proposal that RMR represents a demand for energy is compatible with the idea of RMR as one component of physical hunger. This drive to eat influences the size of meals and contributes to the measured variance in meal size but does so independently of large differences in ED (Table 2). We propose that the function of any metabolic drive (for which RMR may be a candidate) would be to ensure that EI is driven so as to maintain a minimum EI to balance the requirements of obligatory EE. Our data certainly do not prove that RMR is a physiologic driver of hunger, but they suggest that the issue is worth exploring further.

An unmentioned problem for theories of energy homeostasis concerns the unexplained reason why obese people, who carry large amounts of stored energy, experience strong feelings of hunger and are driven to eat (29, 30). It is a paradox why people with sizeable stores of energy in the body should need to eat or to show a strong urge to eat. The recognition that obese people possess a large amount of adipose tissue and increased FFM with a proportionately raised RMR points to a correlation that may open ways to understand consistent hunger in obese people. Moreover, this correlation is quite compatible with, and
independent of, large fat stores. This account can also explain the apparent positive feedback that accompanies weight gain. The more that weight is increased, the greater is the increase in both FM and FFM. Consequently, a greater RMR will be associated with a corresponding increase in the drive to eat.

The data presented in this study are consistent with the observation that people with greater FFM and RMR have larger EI than do people with less FFM and RMR. We have been very careful to describe these plausible correlations without implying a causal relation. However, it is clearly tempting to envisage the possibility that RMR could act as a driver for EI. Therefore, to go beyond cross-sectional associations, we examined the change in RMR across the 12 wk of the study as a potential predictor of meal size at the end of the study. This analysis showed a significant positive relation between changes in RMR and DEI, and this observation goes some way toward providing evidence that there could be a causal aspect to the relation between RMR and EI (an increase during the course of the intervention that led to greater intake at the end of the intervention) and is not simply a static correlate. We recognize that this evidence is still rather weak, and any additional confirmation would require a deliberate experimental manipulation of RMR.

These findings about RMR add a degree of interest to the normal concept of energy balance and should be taken into account when the individual or population energy gap is computed (31–33). This is because RMR could be perceived as contributing to both sides of the energy-balance equation (34, 35), on one side adjusting the amount of energy expended while at the same time offering a proportionate measure of EI and the drive to eat. However such a view of RMR should not be seen as a biologically inevitable contribution to overconsumption or weight gain. As shown in this study, the drive to eat can remain within reasonable caloric limits or be transformed into overconsumption according to the ED of the foods eaten. With the use of the current study as an example, in the presence of an RMR signal that reflects the body composition (largely FFM) of the individual, the EI across the whole day was raised by 4.18 MJ or 39% (or by 2.24 MJ and 45% for a single meal) through the selection of foods that varied in ED (adjusted by varying the proportions of fat and carbohydrate). This effect represents a clear example of passive overconsumption identified by Swinburne et al (36) as a major feature of the obesogenic environment.

It is worth emphasizing that any proposed role for RMR (and its relation with FFM) does not exclude a role for FM. The evidence for the impact of adipose tissue on food intake is overwhelming. A parsimonious view is that FM should exert an inhibitory effect on food intake. However, as adipose tissue increases (in various species), it does not seem to exert a proportional downregulation of energy expenditure with a ventilated hood, face mask, and metabolic cart. Am J Clin Nutr 1987;45:1420–3.

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