Effects of increased energy intake and/or physical activity on energy expenditure in young healthy men

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Goran, Michael I., Jorge Calles-Escandon, Eric T. Poehlman, Maureen O'Connell, and Elliot Danforth, Jr. Effects of increased energy intake and/or physical activity on energy expenditure in young healthy men. J. Appl. Physiol. 77(1): 366-372, 1994. — This study was designed to examine effects of alterations in energy balance on adaptive changes in components of total energy expenditure (TEE). Nineteen young healthy males were studied during a 10-day sedentary energy balance baseline period and then randomly assigned to one of four 10-day treatment groups: 1) no change in energy intake (EI) or physical activity (PA; energy balance at low energy flux), 2) EI increased by 50% with no change in PA (positive energy balance), 3) TEE increased by 50% by increasing PA, matched by a 50% increase in EI (energy balance at high energy flux), and 4) TEE increased by 50% by increasing PA with no change in EI (negative energy balance). TEE was measured with doubly labeled water, resting metabolic rate (RMR) by indirect calorimetry, and thermic response to feeding (TFR) by indirect calorimetry. Energy expenditure of physical activity (EEPA) was estimated by subtracting RMR, TEF, and prescribed PA from TEE. TEE was significantly increased by PA (by design) but not EI. There was a significant main effect of intake and a significant intake-by-activity interaction for change in RMR. In post hoc analysis, RMR was significantly increased during positive energy balance and energy balance at high energy flux relative to change in RMR when energy balance was maintained at low energy flux. A significant increase in RMR was also noted during negative energy balance after adjustment for change in fat-free mass. There was no significant difference in change in RMR among the three treatment groups. There were no significant main effects of intake or activity on EEPA or thermic effect of a meal. These results suggest that in young healthy males living under tightly controlled conditions 1) adaptive changes in TEE in response to short-term alterations in energy balance are mediated primarily through changes in RMR, 2) RMR can be elevated during a state of energy balance when energy flux is increased, and 3) magnitude of adaptive change in RMR is similar in response to increased EI and/or PA; therefore simultaneous increases in energy intake and physical activity do not act synergistically to raise RMR.

energy intake; physical activity; overfeeding; energy metabolism

ALTERATIONS IN ENERGY balance occur through perturbations in energy intake and/or physical activity and are known to affect daily energy expenditure. However, there are discrepancies in the literature regarding the effects of increased energy intake or increased physical activity on adaptive changes in energy expenditure. For example, resting metabolic rate has been shown to be elevated in response to excess energy intake (13, 15, 21, 22, 24), although some studies explained this increase entirely by changes in body composition (6, 28). Similarly, as recently reviewed (20), resting metabolic rate has been shown to be elevated (9, 17, 19) or unaffected (2, 14) by physical activity. The discrepant findings may be explained by the difficulty in separating the simultaneous effects on resting metabolic rate that are induced by the increases in dietary intake and physical activity that occur in physically active people. Furthermore, interpretation of previously performed studies is often complicated because they have not been performed under controlled living conditions.

Previous studies from our laboratory (9, 17, 19) suggested that resting metabolic rate can be elevated in physically active individuals who are in energy balance but at an increased level of energy flux (i.e., increased daily energy expenditure matched by an increase in daily energy intake). However, we have not tested this hypothesis under controlled conditions, and it remains unclear whether the elevation in resting metabolic rate previously observed in physically active people (9, 17, 19) is due to the physical activity itself or the increased “energy flux” associated with the physically active lifestyle. We therefore designed a study to examine the independent effects of changes in energy intake and physical activity on resting metabolic rate. We hypothesized that resting metabolic rate can be increased when individuals are in energy balance but in a state of high energy flux.

Many of the studies that have examined the effects of alterations in energy balance on energy expenditure have been limited to measurements of resting metabolic rate. The availability of the doubly labeled water technique now makes it possible to measure total daily energy expenditure and its components in a noninvasive manner. In particular, physical activity-related energy expenditure, which is highly volitional in nature, is a major factor explaining individual variability in daily energy expenditure (7) and has recently been shown to be responsive to perturbations in physical activity (9) and energy intake (13). In the present study, we examined whether adaptive changes in physical activity-related energy expenditure play an important role in the overall regulation of energy balance in humans.

Thus the purpose of this study was to examine the effects of alterations in energy balance on the components of total daily energy expenditure, specifically resting metabolic rate, thermic response to a test meal, and the energy expenditure associated with physical activity. This objective was achieved by using a completely randomized full-factorial study design in which changes in energy expenditure were examined in response to various manipulations of energy balance induced through perturbations in energy intake and/or physical activity.
METHODS

**Subject information.** Twenty young healthy men were recruited to the study by newspaper advertisement from the Burlington, VT area, and one subject was dismissed from the study because of noncompliance. The subjects underwent a thorough medical and physical examination, and all met the following criteria before being accepted into the study: 1) no clinical signs of heart disease, as assessed by resting electrocardiogram recording and during a progressive stress test of maximal O2 consumption on a bicycle ergometer; 2) no resting blood pressure <140/90 mmHg; 3) no current use of any prescription or over-the-counter medication; 4) no family history of diabetes or obesity; and 5) no abnormal liver enzyme or lipid value from a routine blood chemistry screening. The nature, purpose, and possible risks of the study were carefully explained to each subject before consent to participate was obtained. The experimental protocol was approved by the Committee on Human Research of the Medical Sciences of the University of Vermont.

**Study design.** This study was designed to examine the effects of alterations in physical activity and energy intake on changes in the components of daily energy expenditure. The study was conducted on an in-patient basis, which afforded strict control over energy intake and physical activity. All subjects were initially studied during a 10 day sedentary baseline period at energy balance. After a 3-day break from the study, subjects were randomly assigned to one of four groups: 1) no change in energy intake or physical activity (energy balance at low energy flux, n = 5), 2) physical activity increased by 50% of estimated total energy expenditure at baseline matched by a 50% increase in energy intake (energy balance at high energy flux, n = 6), 3) energy intake increased by 50% with no change in physical activity (positive energy balance, n = 6), and 4) physical activity increased by 50% of estimated total energy expenditure at baseline with no change in energy intake (negative energy balance, n = 2).

Because of oxygen-18 isotope shortage halfway through the experiment, entry into one of the study groups (group 4) was curtailed, resulting in a sample size smaller than that for the other groups. This smaller sample size in group 4 did not compromise the overall power of detecting significant main effects in the two-way analysis of variance (ANOVA), because the effects of activity were eventually compared with a sample size of 11 at low activity (5 from group 1 and 6 from group 3) vs. 8 at high activity (6 from group 2 and 2 from group 4) and the effects of intake were examined by comparing 7 subjects at low intake (5 from group 1 and 2 from group 4) with 12 subjects at high intake (6 from group 2 and 6 from group 9).

**Protocol.** Subjects were admitted to the Clinical Research Center on the evening before the study and received a standard hospital meal. The subjects were awakened in the morning at -6 a.m., and after emptying their bladder they were weighed in a preweighed hospital gown. A sample of the second voided urine was collected each morning for assessment of stable isotope enrichment. On the mornings of days 7 and 8, resting metabolic rate was measured immediately upon awakening. On the morning of day 9, the final urine sample was collected to complete the 9-day study period for measurement of total energy expenditure with doubly labeled water. Thereafter, body composition was reassessed by underwater weight and isotope dilution after a second smaller dose of doubly labeled water, with sampling of plasma before and 4 h after the oral dose. On the following morning, the subjects were allowed to leave the Clinical Research Center, and then after a 3-day break they were randomly assigned to one of four treatment groups, as described above. On entering the study, all subjects agreed to accept any of the treatments. The protocol during the 10-day treatment period was identical to that described for the baseline period, except for the treatment interventions noted above.

**Dietary intake during the study.** Subjects were prescribed a diet that was designed to maintain body weight, which was estimated to be ~40 kcal/kg fat-free mass, as assessed by underwater weight on the morning of day 1 of the study. The level of metabolizable intake was different between individuals but was held constant for each individual for the duration of the experiment. The macronutrient content of the diet was constant, and the contribution to daily caloric intake from protein, carbohydrate, and fat was 15, 55, and 30%, respectively. The diet was fed in the form of three meals and an evening snack. The subjects consumed all meals in their rooms at the Clinical Research Center and were instructed to leave any food not consumed on their meal trays, and in this event the caloric content of the leftover food was estimated and added back in the next meal. Thus energy intake was accurately quantified in the study. For the intervention involving increased energy intake, the additional calories (50% of energy intake at baseline) were provided in the form of a liquid supplement with the same macronutrient content as the regular diet. The additional calories were consumed in three equal portions along with each main meal.

**Physical activity during the study.** Subjects were confined to their own rooms during the entire period of the study, and physical activity, other than that prescribed for the experimental intervention, was limited to movement to and from their private bathrooms and essential activities such as grooming, showering, and dressing. If subjects had to be moved (e.g., between rooms or to be weighed), they were transported by wheelchair. Thus physical activity was kept to an absolute minimum throughout the study. In the experimental groups where physical activity was increased, exercise prescriptions were tailored to expend ~50% of estimated total energy expenditure at baseline, which was assumed for this purpose to be equivalent to energy intake. The net energy cost of cycling at ~50% of maximal O2 consumption, as recorded during screening, was measured on the morning of day 1 of the treatment period while the subject cycled at a comfortable pace and work load. The pace and work load were then fixed for each subject, and the daily time required to consume an additional 50% of total energy expenditure at baseline was calculated. The duration of exercise was ~3 h/day. The energy cost of exercising at the prescribed level was checked every other day by recording O2 consumption for 20 min after a 10-min warm-up.

**Measurement of total energy expenditure.** Total energy expenditure was measured during the two in-patient test periods by the doubly labeled water technique, as previously described (11). Briefly, for this protocol, baseline urine and plasma samples (10 ml) were obtained after an overnight fast. Thereafter a mixed dose of doubly labeled water was orally administered at approximate doses of 1.5 g (first 12 subjects studied) or 1.0 g (last 6 subjects studied) per kilogram of body weight of a solution consisting of 10% enriched H218O (Cambridge Isotope Laboratories, Cambridge, MA) and 99.8% enriched 2H2O (Icon Services, Summit, NJ) mixed in a ratio of 90:1. The dose of oxygen-18 in the last six subjects was reduced because of a worldwide shortage of isotope. Second voided urine samples were collected daily for subsequent analysis for deuterium and oxygen-18. All samples were stored in sealed Vacutainers at ~70°C until analyzed by isotope ratio mass spectrometry at the Bio-
medical Mass Spectrometry Facility on the Clinical Research Center at the University of Vermont, as previously described (8). Turnover rates and time 0 enrichments of H$_2$O and H$_2$CO$_2$ were obtained from a multipoint approach utilizing isotope enrichments measured during the first and last 3 days of each study period, and CO$_2$ production rate was calculated using the revised equations of Speakman et al. (26), which are based on Eq. A6 of Schoeller et al. (22a) but uses a group mean value for the deuterium-to-oxygen-18 dilution space ratio. This revised equation has been shown to improve the accuracy and precision of previously performed comparisons of the doubly labeled water technique with chamber calorimetry (26). O$_2$ consumption was derived by dividing CO$_2$ production rate by the food quotient derived from the composition of the diet (3) and adjusted to take into account negative or positive energy balance, as previously described (13). During negative energy balance, it was assumed that the energy deficit was accounted for by oxidation of endogenous fat, and for positive energy balance we assumed that 87% of excess calories were deposited as fat (22), one-tenth of which was via de novo lipogenesis. Total energy expenditure was calculated according to Eq. 12 of de Weir (5).

**Measurement of resting metabolic rate.** Resting metabolic rate was measured twice during each of the two study periods on consecutive days in the early morning after an overnight fast. Respiratory gas was collected for 30 min after a 15-min equilibration period with use of a ventilated hood, and data were averaged every 5 min. In the first 10 subjects O$_2$ and CO$_2$ content of expired air were analyzed using a zirconium cell O$_2$ analyzer (Ametek, Pittsburgh, PA) and an infrared CO$_2$ analyzer (Ametek, Pittsburgh, PA), respectively, and flow rate was measured by a pneumotachograph (Vertek, Burlington, VT), as previously described (9). In nine subjects resting metabolic rate was measured using a Sensormedics metabolic monitor. The same experimental setup was used in each subject during baseline and treatment phases. Because within-subject change in resting metabolic rate was the main outcome variable, there was minimal concern for cross-calibration of the indirect calorimetry systems. Energy expenditure was calculated using the de Weir equation (5). Resting metabolic rate for each of the two periods was averaged from the two measurements within each period. All measurements of resting metabolic rate were performed 12–14 h after the previous exercise bout. An estimate of minimal resting metabolic rate was derived from the lowest 5-min average obtained during the 30-min measurement period.

**Measurement of the thermic effect of a meal.** Thermic effect of a meal was measured in all subjects during control and treatment phases. Baseline resting metabolic rate was first measured in a postabsorptive state, as described above. The subjects then consumed a liquid test meal representing one-third of the prescribed daily energy intake with the same macronutrient mixture as the prescribed diet. Metabolic rate was then measured continuously for the next 5 h. Subjects were allowed to watch television or read during this time, and occasionally the test was interrupted to allow the subjects to urinate. Thermic effect of a meal was calculated as the average metabolic rate during the 5-h postprandial period minus metabolic rate before consumption of the meal.

**Estimation of the energy expenditure associated with physical activity.** The average daily energy expenditure associated with physical activity, aside from that prescribed as part of the experimental protocol, was estimated by subtracting the sum of minimal resting metabolic rate (kcal/day), the thermic effect of meals (kcal/day), and the energy cost of prescribed physical exercise (kcal/day), when appropriate, from total energy expenditure (kcal/day), as measured by doubly labeled water.

**Measurement of body composition.** Body fat content was estimated from the three-compartment model of Siri that combines body density with total body water (25). Whole body density was estimated by averaging six measures of underwater weight, with simultaneous measurement of residual lung volume by helium dilution, as previously described (10). Total body water was estimated from oxygen-18 dilution in plasma 4 h after oral dosing according to the procedures described above. The values of body density (g/ml) and body water (as a percentage of body mass) were used to calculate body fat with the three-compartment model of Siri, and fat-free mass was calculated as body mass minus fat mass.

**Statistics.** Data are reported as means ± SD. Differences in physical characteristics between groups at baseline were examined using a one-way ANOVA. The main effects of experimental changes in physical activity and energy intake on the components of energy expenditure were examined using a two-way ANOVA. Post hoc testing using Fisher's least significant difference test was used to locate significant effects. Statistical analyses were performed using BMDF statistical software (Los Angeles, CA). *P* ≤ 0.05 was used to determine statistical significance.

**RESULTS**

Physical characteristics of the volunteers within each study group at baseline are shown in Table 1. The four groups were similar with respect to age, body weight, and fat mass, but height and fat-free mass were significantly lower in group 1. Energy intake and the components of energy expenditure at baseline are shown in Table 2. During the baseline period, the group as a whole was in energy balance, because there was no significant difference between energy intake (2,367 ± 275 kcal/day) and total energy expenditure (2,159 ± 466 kcal/day). There was no significant difference among the groups at baseline with regard to energy intake, total energy expenditure.
TABLE 2. Energy intake and energy expenditure at baseline in all subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Intake</th>
<th>TEE</th>
<th>RMR</th>
<th>Min RMR</th>
<th>TEM</th>
<th>EEPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n = 5)</td>
<td>2,143±285</td>
<td>1,970±346</td>
<td>1,720±287</td>
<td>1,594±319</td>
<td>250±111</td>
<td>126±208</td>
</tr>
<tr>
<td>2 (n = 6)</td>
<td>2,418±212</td>
<td>2,360±695</td>
<td>1,714±260</td>
<td>1,561±261</td>
<td>238±113</td>
<td>560±381</td>
</tr>
<tr>
<td>3 (n = 6)</td>
<td>2,494±137</td>
<td>2,202±231</td>
<td>1,792±200</td>
<td>1,644±239</td>
<td>274±44</td>
<td>284±332</td>
</tr>
<tr>
<td>4 (n = 2)</td>
<td>2,574±583</td>
<td>1,904±424</td>
<td>1,801±111</td>
<td>1,817±293</td>
<td>350±304</td>
<td>-263±27</td>
</tr>
<tr>
<td>All</td>
<td>2,367±275</td>
<td>2,159±466</td>
<td>1,760±232</td>
<td>1,625±285</td>
<td>264±114</td>
<td>272±464</td>
</tr>
</tbody>
</table>

Values are means ± SD expressed as kcal/day. TEE, total energy expenditure; RMR, resting metabolic rate; Min RMR, minimal RMR over 5 min during 30-min measurement period; TEM, thermic effect of a test meal; EEPA, energy expenditure associated with physical activity.

Changes in each of the various components of total daily energy expenditure in response to experimentally induced alterations in energy intake and physical activity are shown in Table 3. The specific changes in energy intake or physical activity were as follows. In group 1 there was no change in energy intake or physical activity. In group 2 energy intake increased by 1,109 ± 225 kcal/day (~50% increase relative to baseline), which was matched by an increase in activity by prescribing a total of 1,288 ± 323 kcal/day of exercise. In group 3 energy intake increased by 1,206 ± 61 kcal/day (~50% increase relative to baseline) with no change in activity. In group 4 there was no change in energy intake with an increase in activity by prescribing 1,185 ± 355 kcal/day of exercise.

There was a significant main effect of activity on adaptive changes in total energy expenditure (by design), but there was no effect of intake on change in total energy expenditure. There was a significant main effect of intake and a significant intake-activity interaction on change in resting metabolic rate (Table 3). In post hoc analysis, resting metabolic rate was significantly increased when intake and activity were increased (group 2) and when energy intake alone was increased (group 3) relative to when intake and activity remained unchanged (group 1, Table 3). In addition, when data were normalized for change in fat-free mass, resting metabolic rate was significantly increased when activity alone was increased (group 4, 82 ± 86 kcal/day) relative to when intake and activity remained unchanged (group 1). There was no significant difference in the magnitude of the change in resting metabolic rate when intake alone was increased (group 3), when intake and activity were increased (group 2), and when activity alone was increased (group 4) relative to when intake and activity remained unchanged (group 1). As shown in Table 3, there were no significant main effects of intake or activity on the thermic response to a test meal or the energy expenditure of physical activity.

There was no significant main effect of intake or activity on change in fat mass or relative percent body fat. However, there was a significant main effect of intake on fat-free mass (P = 0.05). In post hoc analysis, fat-free mass was increased by 0.1 ± 1.0 kg when intake and activity were increased (group 2) and by 0.4 ± 1.2 kg when activity alone was increased (group 3); fat-free mass was decreased by 1.5 ± 1.4 kg when activity alone was increased (group 4) and by 0.2 ± 0.7 kg when intake and activity were unchanged (group 1). The significant changes in resting metabolic rate listed in Table 3 persisted when change in resting metabolic rate was normalized for change in fat-free mass.

DISCUSSION

We performed a highly controlled study in which energy intake and physical activity were manipulated to create several states of altered energy balance and examined adaptive changes in energy expenditure. A major strength of this study is the randomization of volunteers to the various treatment groups and the subsequent comparison of changes in the dependent variables between baseline and treatment relative to change in subjects in whom intake and activity were maintained at baseline levels. The results suggest that in young healthy males living under controlled conditions 1) adaptive changes in total energy expenditure in response to short-term changes in energy intake and/or physical activity are small and are mediated primarily through changes in resting metabolic rate, 2) resting metabolic rate is significantly increased in a high energy flux state, in which an increase in energy intake is matched by a eucaloric in-

TABLE 3. Changes in energy expenditure components

<table>
<thead>
<tr>
<th>Intake</th>
<th>Group 1 (n = 5)</th>
<th>Group 2 (n = 6)</th>
<th>Group 3 (n = 6)</th>
<th>Group 4 (n = 2)</th>
<th>Main Effect of Intake</th>
<th>Main Effect of Activity</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribed exercise</td>
<td>0</td>
<td>1,109±225</td>
<td>1,206±101</td>
<td>0</td>
<td>P &lt; 0.05 (by design)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>TEE</td>
<td>-45±277</td>
<td>1,288±233</td>
<td>0</td>
<td>1,185±353</td>
<td>NS</td>
<td>P &lt; 0.05 (by design)</td>
<td>NS</td>
</tr>
<tr>
<td>RMR</td>
<td>-81±78</td>
<td>54±389</td>
<td>115±96*</td>
<td>48±85</td>
<td>P = 0.04</td>
<td>NS</td>
<td>P = 0.05</td>
</tr>
<tr>
<td>Min RMR</td>
<td>-78±116</td>
<td>77±247*</td>
<td>124±49</td>
<td>46±64</td>
<td>P = 0.01</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>TEM</td>
<td>-14±49</td>
<td>-17±71</td>
<td>-27±196</td>
<td>-43±17</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>EEPA</td>
<td>47±380</td>
<td>-311±336</td>
<td>-3±374</td>
<td>133±88</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values (means ± SD) are differences between baseline and treatment periods, expressed as kcal/day. * Significantly different from group 1 in post hoc analysis; † significantly different from group 3 in post hoc analysis; all other between-group post hoc tests were not significant.
increase in physical activity, and 3) the magnitude of adaptive changes in resting metabolic rate is similar in response to short-term increases in energy intake and/or physical activity, implying that increases in energy intake and physical activity do not act synergistically to raise resting metabolic rate.

In the high energy flux state, where eucaloric increases in energy intake and physical activity were sustained (group 2), resting metabolic rate was increased, whereas no changes in the other components of energy expenditure were noted (Table 3). This finding is the first clear indication that resting metabolic rate can be altered even under conditions of energy balance. The mechanism for the increased resting metabolic rate in response to physical activity is not clearly defined but is independent of increased fat-free mass (9) and appears to involve the sympathetic nervous system (1, 16, 27). In the present study, we found that in active subjects maintained in energy balance the increase in resting metabolic rate was similar in magnitude to the increase observed when energy intake alone was increased (positive energy balance) or when physical activity alone was increased (negative energy balance). Therefore simultaneous increases in energy intake and physical activity do not act synergistically to alter resting metabolic rate, suggesting a limited capacity of resting metabolic rate to adapt to altered states of energy balance.

In previous studies we showed that the energy expenditure associated with physical activity plays a key role in adaptive changes in energy expenditure in response to an increase in physical activity (9) and energy intake (13). Specifically, we showed that free-living healthy elderly persons decreased physical activity during the remainder of the day by ~60%, conserving 230 kcal/day during a period of vigorous endurance training. Conversely, healthy young men who were living within the confines of a Clinical Research Center with movement unrestricted increased their energy expenditure associated with physical activity by ~300 kcal/day in response to excess energy intake (13). Thus adaptive changes in the component of daily energy expenditure associated with physical activity may be a regulatory mechanism to dissipate or conserve energy.

We further examined this latter hypothesis in the present study but found no significant change in the energy expenditure of physical activity in any of the treatment groups. However, in the subjects subjected to a state of high energy flux (group 2), the energy expenditure of physical activity was reduced by 311 ± 336 kcal/day, although this was not statistically different from the change seen when intake and activity were unchanged. With the present sample size, the difference in response would have needed to be 589 kcal/day to reach statistical significance with a power of 0.8. In the present study, the potential for adaptive changes in physical activity-related energy expenditure was suppressed to a minimal level because of the imposed sedentary living conditions. Thus we cannot discount the possibility that compensatory changes in physical activity during the remainder of the day may offset the immediate caloric benefits associated with performing physical activity.

The elevation in resting metabolic rate in response to an increase in energy intake is in agreement with other overfeeding studies (13, 15, 21, 22, 24). The increase in resting metabolic rate in the overfeeding group was 6%, but the net increase was 11%, because resting metabolic rate was reduced by 5% when intake and activity were unchanged. The magnitude of this net response is similar to that in other studies (13, 21, 22, 24). Thus, in agreement with previous studies, the capacity of changes in resting metabolic rate to dissipate excess energy intake is small. Several other studies used the doubly labeled water technique to examine changes in energy metabolism in response to overfeeding. In healthy elderly males, Roberts et al. (22) found a 6% elevation in resting metabolic rate in response to overfeeding 1,000 kcal/day for 21 days, with no significant change in free-living total energy expenditure or energy expenditure associated with physical activity. Pasquet et al. (15) studied nine lean Cameroonian men during a traditional fattening season in which a doubling of energy intake was sustained for ~9 wk. The increase in resting 12-h postabsorptive metabolic rate was 40%, which is significantly higher than other overfeeding studies, but there was no significant increase in total energy expenditure by doubly labeled water (3,373 kcal/day before and during the last 10 days of overfeeding). These data suggest a 50% reduction (or 550 kcal/day decrease) in physical activity-related energy expenditure during the overfeeding. However, it is unclear how much of the suppression in physical activity was due to the overfeeding itself and how much was due to the altered activity patterns imposed by the traditional fattening season compared with activity during the agricultural season when the control data were collected.

We found no evidence that the thermic response to a meal changes in response to alterations in energy balance. Our laboratory previously showed that in healthy lean subjects the thermic response to a meal is unaffected by overfeeding 1,000 kcal/day for 18 days (12). Previous studies, however, showed that the thermic response to feeding over the course of the day increase during overfeeding in proportion to excess energy intake (21, 22). The thermic response to a meal has been shown to be elevated (18) or unaffected (23) by physical activity. We do not believe that the failure to detect a significant effect of intake on the thermic response to meals in the present study was a type II error, because power analysis calculations demonstrate that we had sufficient power to detect a 40 kcal/day difference in the thermic response to feeding with a power of 0.8. Rather the failure to detect any effects on the thermic effect of meals in the present study is explained by the fact that the caloric stimulus used to measure the thermic effect was the same during control and treatment phases. Overall our results suggest that the thermic effect of ingesting a fixed caloric load is unaffected by alterations in energy balance.

There are a number of limitations of this study that should be considered when the data are interpreted. First, we examined the adaptive response over a relatively short time period of 9 days. The disadvantage of this approach is that the time course of adaptive changes in energy metabolism in response to changes in energy intake and physical activity are unknown and longer-
term interventions, which may be more physiologically relevant, may be required in order to have any modulatory effects. On the other hand, the advantage of the short-term study is that the time period caused only minor changes in body composition, which enabled us to examine adaptive changes in energy metabolism independent of body composition changes. The second limitation relates to the significant decline in resting metabolic rate that was observed when intake and activity were unchanged from sedentary baseline levels (group 1), which may have amplified the net response observed in other groups. However, we specifically wanted to determine the effect of increasing activity and/or intake relative to a group of subjects in whom activity and intake were unchanged. Therefore the response seen in group 1 served as the control response that would have been expected if intake and activity were maintained at baseline levels. The decreased sample size of the group in which activity only was increased (group 4, n = 2) may also be seen as a weakness of the study. However, with the factorial design selected for this study, this effect was minimized, because the main effects of activity were eventually compared with a sample size of 11 at low activity vs. 8 at high activity, and the effects of intake were examined by comparing 7 subjects at low intake with 12 subjects at high intake. However, the smaller sample size in group 4 may have compromised the power of our post hoc analysis. If we had dropped group 4 from the analysis, we would not have been able to separately examine the main effects of intake and activity.

An important issue that we did not consider was the heterogeneity of the responses to manipulations in energy intake or physical activity. Previous studies showed that genetic factors, rather than environmental factors, seem to be involved in determining the magnitude of the adaptive changes in resting metabolic rate (4). Unfortunately an analysis of the heterogeneity of the adaptive response was limited in this study because of the small sample sizes within each of the subgroups.

In summary, we have examined the effects of short-term perturbations in energy intake and physical activity on energy metabolism using a randomized and controlled design. The results demonstrate that, in young healthy males living under controlled living conditions, adaptive changes in total energy expenditure in response to alterations in energy balance are mediated primarily through changes in resting metabolic rate. We have demonstrated that high energy flux states, characterized by eu- caloric increases in energy intake and physical activity, are associated with an elevation in resting metabolic rate. We have also shown that the magnitude of the adaptive change in resting metabolic rate is small and similar in response to increased energy intake and/or physical activity. Thus simultaneous increases in energy intake and physical activity do not act synergistically to raise resting metabolic rate.

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