Rate and extent of compensatory changes in energy intake and expenditure in response to altered exercise and diet composition in humans


We assessed the effect of no exercise (Nex; control) and high exercise level (Hex; ~4 MJ/day) and two dietary manipulations (a high-fat diet (HF; 50% of energy, 700 kJ/100 g) and low-fat diet (LF; 20% of energy, 300 kJ/100 g)] on compensatory changes in energy intake (EI) and energy expenditure (EE) over 7-day periods. Eight lean men were each studied four times in a 2 x 2 randomized design. EI was directly quantified by weight of food consumed. EE was assessed by heart rate (HR) monitoring. Body weight was measured daily. Mean daily EE was 17.6 and 11.5 MJ/day (P < 0.001) on the pooled Hex and Nex treatments, respectively. EI was higher on HF diets (13.4 MJ/day/pooled) compared with the LF diets (9.0 MJ/day). Regression analysis showed that these energy imbalances induced significant compensatory changes in EB over time of ~0.3–0.4 MJ/day (P < 0.05). These were due to changes in both EI and EE in the opposite direction to the perturbation in energy balance. These changes were significant, small but persistent, amounting to ~0.2 and ~0.35 MJ/day for EI and EE, respectively.

It has been suggested that humans appear to control energy balance over a period of ~1 wk, although this relationship is difficult to detect over the course of 1 or 2 days (6). The two phenomena most commonly cited as risk factors for body weight gain are a lack of physical activity (5) and the consumption of an energy dense, high-fat diet (30). A number of studies have shown that an increase in physical activity due to exercise has little effect on energy intake (EI) and so precipitates a negative energy balance (EB) in studies of 7 days or less (for review, see Ref. 19). Studies lasting 1–2 wk are also notable in their apparent lack of compensation of EI for increases in energy expenditure (EE) due to imposed exercise (15, 34, 45). Compensation of EI is often slight (46). These studies suggest that over periods ranging from ~1 to 20 days, EI does not accurately track changes in EE. Fewer studies have examined how decreases in physical activity within the sedentary range influence EB (22). In a recent study we assessed the effect of an imposed sedentary routine on appetite, EI, EB, and nutrient balance in lean men continually resident in a calorimeter for 7 days (32). EE differed by ~3.0 MJ/day between the sedentary and active treatments, respectively. Despite this, EI was not significantly different across treatments. By day 7, cumulative EB was 26.3 and 11.1 MJ, respectively. Over the course of the study there was no tendency to compensate EI over time for alterations in physical activity.

Studies that manipulate dietary fat and energy density tend to show similar effects (3). Specifically, increases in the energy density of the diet by adding fat appear to lead to little/no change in food intake and so EI rises with the energy density of the diet (3). These effects are apparent over time periods ranging from 1 day (22) to 2 wk (20, 31). Interestingly, a 3-mo study that used medium vs. low-fat (LF) diets did show incipient but significant compensation of EI for the energy deficit on the LF, less energy-dense diet over the course of 11 wk (17). Taken together these studies tend to suggest that when using systematic manipulations of diet composition and energy density, or of EE by altering physical activity, it is remarkably easy to induce considerable energy imbalances in human subjects (3). This raises the critical question: what is the time course over which humans begin to compensate for energy imbalances induced by systematic manipulations of EI (through manipulations of the diet) or of EE (through manipulations of activity patterns) and can this be detected over 7 days? This is a difficult question to answer because the majority of studies do not track EI and EE on a day-by-day basis. The most precise means of objectively measuring EE in free-living humans is the doubly labeled water method, which tends to estimate EE over periods of 10–20 days (24). Daily EE can be estimated using heart rate (HR) monitoring (1, 28), but this technique is widely regarded as relatively low in precision and accuracy, especially in sedentary people (23). However, it is in studies that employ within-subject comparisons and where most changes in EE occur through the same exercise activities that were used to individually calibrate the HR monitors, that this approach is most efficacious. We combined this means of measuring EE with our covertly manipulated diet design to monitor EI (31, 33) to examine the combined effects of increases in dietary fat content (and energy density) and increases in exercise-induced EE on EB. We then examined evidence for the day-to-day rate of compensation of either EI or EE over 7 days for these initial perturbations of EB. The choice of a 7-day interval was made on the basis of the scheduling constraints of the 2 x 2 design and the fact that in previous studies we had begun to see evidence for changes in EE over time (15, 34).

**MATERIALS AND METHODS**

*Subject recruitment.* Eight lean men [(mean ± SD) age 29.5 ± 6.0 yr; weight 77.0 ± 13.9 kg; height 1.79 ± 0.09 m; body mass index 0.67 ± 0.04 kg/m²] were recruited for the study and provided written informed consent, with the protocol approved by the local ethical committee. The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Address for reprint requests and other correspondence: R.J. Stubbs, Rowett Research Institute, Greenburn Road, Bucksburn, Aberdeen, AB21 9SB (E-mail: J.Stubbs@ri.sari.ac.uk).
(BMI) 23.9 ± 2.2 kg/m²), were recruited by advertisement. Mean resting metabolic rate (RMR) amounted to 7.22 MJ/day (SD = 0.93) and daily energy requirements (estimated as 1.6 × RMR) amounted to 11.6 MJ/day (SD = 1.58). Mean baseline extrapolated \( V_{02 \text{max}} \) was 42.25 ml·min\(^{-1}\)·kg\(^{-1} \) (SD = 9.88). They were nonsmokers, aged 18–40 yr, not taking any medication, BMI between 19 and 26 kg/m², not consuming any type of specialized diet, sedentary to moderately active lifestyle (i.e., not training), and not highly restrained eaters. Subjects underwent a medical examination before the study, and their family physician was also informed of their participation and asked to confirm their recent medical and medication status. The study was approved by the Joint Grampian Health Board and University of Aberdeen Ethical Committee.

Subjects were resident in but not confined to the Human Nutrition Unit. They were not overtly informed that the true purpose of the study was to specifically assess feeding responses to exercise and dietary manipulation until they had completed the protocol. Instead emphasis was placed on metabolic adaptations and changes in body composition due to exercise. Subjects were asked not to monitor their weight or consume alcohol during the course of the study. With the exception of the deemphasis on feeding responses to exercise, subjects gave their written informed consent.

Height, weight, and RMR were recorded as described previously (16). In this study, body fat was estimated at the start of the study using skinfold calipers (Holtain, Dyfed, Wales) as described previously (34). Mean ± SD %body fat was 20.8% ± 4.2. Dietary restraint was assessed using the Dutch Eating Behaviour Questionnaire (DEBQ; 40) and the Three Factor Eating Inventory (35). The DEBQ showed that subject’s restraint ranged between 0.6 and 3.6 with a mean of 2.06 (SD = 1.0). The Eating Inventory scores for restraint ranged from 2 to 18 with a mean of 6.00 (SD = 5.4). On average, values on the DEBQ over –2.9 indicate greater restraint. Corresponding values for the Eating Inventory would be ~8 (data taken from our reference population).

**Experimental design.** The eight men were each studied four times in a 9-day protocol (2 day maintenance diet, followed by a 7-day treatment period), using a 2 × 2 design corresponding to each of the four treatments: 1) high-fat diet with exercise (HFHex), 2) high-fat diet, no exercise (HFNex), 3) low-fat diet with exercise (LFHex), and 4) low-fat diet, no exercise (LFNex). The sedentary routine required no additional exercise [control (Nex); 0 MJ/day]. On the high exercise treatments, subjects were assigned three 40-min exercise sessions per day [Hex: 42.8 kJ·kg\(^{-1}\)·day\(^{-1}\) (giving 3.5 MJ/day for a 77-kg subject)]. The average (±SD) relative intensity of the exercise on the Hex treatment was 65.1 ± 9.0% of \( V_{02 \text{max}} \). The range of relative intensity across subjects was on average (±SD) 50.3 ± 0.23 to 79.3 ± 4.8% of \( V_{02 \text{max}} \). The low-fat diet contained ~25% energy from fat and the high-fat diet, 50% energy from fat. Energy density increased with percent fat. The order of the four treatments was randomized across subjects and each study period was separated by at least 1 wk, where subjects followed their usual dietary and exercise regimens at home. On days –2 and –1 of the study, subjects consumed a mandatory maintenance diet (estimated at 1.6 × RMR). The purpose of the maintenance diet was to standardize energy and nutrient intakes before each run, so that subjects began their treatments at the same nominal point. Thus, whereas EI did not necessarily match EE across these conditions and this timeframe, body weight only gives a very approximate estimate of EB. Subjects also completed hourly hunger ratings during waking hours to record subjective sensations of hunger and appetite, using a specifically designed program for the Newton Message Pad (29), as previously described (12, 29).

**Estimation of total EE using HR monitoring.** HR monitoring can be used to determine EE because increases in HR during physical activity are associated with a linear rise in oxygen consumption (\( V_{02} \)) and CO\(_2\) production (\( V_{CO2} \)) (4, 23, 28). This means that an increase in HR can be used to estimate EE. The correlation between HR and \( V_{02} \) and \( V_{CO2} \) is very poor (4, 23, 28). The critical cut-off point, below which a poor relationship between HR and \( V_{02} \) occurs, is termed the FLEX HR. This is defined as the mean of the highest HR during rest and the lowest HR during the lightest imposed exercise during the calibration procedure. FLEX HR has to be determined separately for each subject (4, 28).

**Calibration of HR monitors and determination of FLEX.** To equate HR to EE, a regression line of HR vs. EE was established individually for each subject by simultaneously measuring HR, breath-by-breath \( V_{02} \) and \( V_{CO2} \) at incremental workloads in the morning after an overnight fast. The test was done twice before the study began and at the beginning and end of each treatment period. The test comprised sedentary routines and incremental workloads on a bicycle ergometer in the following sequential steps with no break between them: 5 min sitting, 5 min standing up, 5 min cycling at the lowest possible resistance (55 W), and a further 3 × 5 min blocks increasing resistance and maintaining 60 rpm. Pedal speed remained constant at 60 rpm throughout the test, and resistance was gradually increased to elevate HR. Every 5 min the resistance was increased to the next level. Resistance was increased by 50 W for each block of the submaximal test. This was done within a few seconds and the subjects then cycled at the higher resistance but the same cadence for the remainder of the 5 min. The criteria for ending the test was that subjects had cycled for four of these incremental stages. The same power (watts) and intensity was repeated at each and every fitness test. During the last 3 min of each step when the HR was adjusted to the workload and was stable, breath-by-breath \( V_{02} \) and \( V_{CO2} \) were measured with indirect calorimetry (Vmax29 metabolic cart, Sensor Medics) using a mouthpiece and noseclip. Data derived from sedentary routines were used in the determination FLEX HR.

**Estimation of total EE from HR.** Total EE from HR was calculated using the modified FLEX HR method of Ceesay et al. (4) and the calorimetric equations of Elia and Livesey (7). Total daily EE was estimated according to the following equation: TEE = \( \text{SEDEE} + \text{SEE} + \text{AE} \) (4, 28).
where SEE is sleeping EE, SEDEE is sedentary EE, and AEE is activity EE. SEE was calculated as 95% of RMR (10) and was applied to the time when the HRM was not worn (i.e., during sleep). SEDEE was assumed to be equal to the mean EE from the RMR, sitting, and standing measurements during the calibration (28). For HR exceeding the FLEX, HR was calculated using the treatment-specific regression equation (AEE) for each individual. Unphysiological high pulse rates (>220 beats/min, which indicated interference) and zero values were removed and replaced by the average of the previous and subsequent values (41). It should be noted that there are considerable limitations to the use of HRMs to estimate daily EE (4, 23, 28) and it is therefore important to verify through post hoc analysis that there was a reason-
able relationship between HR and EE (see RESULTS).

Data derived from the calibration procedure were also used to predict the subjects’ $\dot{V}_O_2$max by extrapolation of the regression of $\dot{V}_O_2$ against HR to the subjects’ maximum HR. This was calculated as 220 – age. The $\dot{V}_O_2$ that coincides with maximal HR was assumed to be the $\dot{V}_O_2$max and was expressed in milliliters per minute per kilogram body weight (25). There are considerable limitations to the use of submaximal exercise tests to estimate $\dot{V}_O_2$max (see DISCUSSION) and these ancillary data are presented with this in mind.

**Formulation and preparation of the diets.** The composition of each dish in terms of energy, fat, carbohydrate, protein, and nonstarch polysaccharide was calculated from McCance and Widdowson’s *The Composition of Foods*, 5th edition and supplements (21). The diets for days 1–2 and 1 were formulated to be of a very similar energy content and density so that differences in amount of food ingested did not influence ad libitum food intake on the subsequent days. The ad libitum diet was formulated so that every item on the menu comprised approximately the same percentage of energy from protein, fat, carbohydrate and energy density (ED). The composition of the two diets in terms of percent energy from protein:fat:carbohydrate and ED was 13:25:62, 350 kJ/100 g for the LF diet; and 13:50:37, 700 kJ/100 g for the HF diet (contact corresponding author for composition per 100 g of each food). This was done so that within each dietary treatment, food intake directly paralleled EI. The food was prepared by the dietary research assistant in the metabolic kitchen. The ad libitum diets were formulated to contain, as far as possible, normal every-day ingredients and to contain recognizable food that varied little in composition (for example, prepared foods were not used). They had to be palatable and appealing to the volunteers. Diets were pilot tested (33) and altered accordingly to resemble familiar food items yet have the appropriate composition. The 3-day rotating menu was also randomized across treatments to reduce the possible effect of menu day preferences on food intake.

**Presentation of the diets and measurement of food intake.** Subjects were resident in (but not confined to) the Human Nutrition Unit for the duration of the study. Throughout days 1–7, meals or food items were placed in a labeled fridge and freezer for subjects to consume in the volunteer dining room. Food from the ad libitum diets was presented to the subjects in the following amounts: breakfast, 600 g; main courses, 400 g; sweets, 150 g; milkshakes, 300 g; hot drinks, 350 g; milk allowance, 200 g; salad garnish, 100 g; fruit juice, 2,000 g; with an additional bread roll and 5 g butter (HF) or very low fat spread and milk allowance, 200 g; salad garnish, 100 g; fruit juice, 2,000 g; with two pieces of fruit. Extra portions were readily available on request. They had to be palatable and appealing to the volunteers. Diets were pilot tested (33) and altered accordingly to resemble familiar food items yet have the appropriate composition. The 3-day rotating menu was also randomized across treatments to reduce the possible effect of menu day preferences on food intake.

**Statistical analysis.** Total EE, RMR, exercise EE, and EE excluding the cost of exercise were analyzed by ANOVA, with exercise level, diet, and day as treatment factors and subject and run (within subject) as blocking factors.

Changes in $\dot{V}_O_2$max pre- and posttreatment, were analyzed by ANOVA with subject and run as blocking factors and diet and exercise as treatment factors.

Food eaten, EI, and protein, carbohydrate, and fat intakes were analyzed by ANOVA with exercise level, diet, and day as treatment factors and subject and run (within subject) as blocking factors. In addition, to examine temporal trends in EE, EI, and EB, simple linear regression analysis was conducted using study day as predictor and EE, EI, or EB as the outcome variable; significant differences from zero were examined using t-tests.

Changes in body weight from day 1 to 7 were analyzed by ANOVA to test for treatment effects. For each treatment, t-tests were used to test for significant changes in weight over the period.

Visual analog scales were analyzed by ANOVA, with block and treatment factors as above.

Also examined were the relationship between HR and $\dot{V}_O_2$ for each subject at the beginning vs. the end of each of the four runs, the impact this has on the Hex vs. Nex conditions, RMR, and estimates of daily EE, using factorial ANOVA with pre- and posttreatment measures (here termed a time effect) and condition (Hex vs. Nex) as factors and subject as a blocking factor (Table 1).

All analyses were performed using the Genstat statistical program (Genstat 5 Committee, Rothampstead Experimental Station, Harpenden, UK).

**RESULTS**

**Validation of the use of HR to predict EE.** Each subject underwent an HR-$\dot{V}_O_2$ calibration before and after each of his four experimental runs. Table 1 shows that, on average, there was no effect of time (i.e., pre- vs. posttreatment calibrations) on resting HR, but there was an effect of treatment. Specifically, time × treatment interactions were significant because, whereas resting HR did not change from the beginning to the end of the Hex condition (65 vs. 64 beats/min), there was a significant increase in resting HR (from 66 to 69 beats/min) from the beginning to the end of sedentary routine \( F(1,181) = 10.66, P = 0.001, \) SE of the difference between the means \( (S E D) = 0.96 \).

In addition, similar patterns were seen for FLEX HR (Table 1). Thus, whereas there was a slight decrease in FLEX, on average, between the HR calibrations at the beginning and the end of the exercise runs (79 to 77 beats/min), this was not significant. However, the rise in FLEX between the beginning and the end of the Nex treatments was significant \( [78 to 82 \text{ beats/min}; F(1,181) = 12.67, P = 0.001, \text{SED} = 1.43] \).

Thus the change in the relationship between HR and $\dot{V}_O_2$ at the calibration before and after each run systematically differed

<table>
<thead>
<tr>
<th>Measure</th>
<th>Hex Pre</th>
<th>Hex Post</th>
<th>Nex Pre</th>
<th>Nex Post</th>
<th>Time F</th>
<th>Treatment F</th>
<th>$T \times T$ SED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting HR, beats/min</td>
<td>65.6</td>
<td>68.6</td>
<td>64.9</td>
<td>63.5</td>
<td>0.541</td>
<td>0.027</td>
<td>0.083</td>
</tr>
<tr>
<td>HR FLEX, beats/min</td>
<td>77.8</td>
<td>82.4</td>
<td>79.4</td>
<td>76.8</td>
<td>0.590</td>
<td>0.287</td>
<td>0.059</td>
</tr>
<tr>
<td>BMR, MJ/day</td>
<td>7.26</td>
<td>7.24</td>
<td>7.29</td>
<td>7.56</td>
<td>0.114</td>
<td>0.034</td>
<td>0.078</td>
</tr>
<tr>
<td>Estimated EE, MJ/day</td>
<td>13.09</td>
<td>11.94</td>
<td>13.28</td>
<td>13.25</td>
<td>0.138</td>
<td>0.065</td>
<td>0.165</td>
</tr>
</tbody>
</table>

Factorial ANOVA was conducted with pre and post treatment measures (here termed a time effect) and condition (high exercise (Hex) vs. no exercise (Nex)) as factors and subject and diet as a blocking factor. HR, heart rate; BMR, basal metabolic rate; EE, energy expenditure; $T \times T$, time × treatment.
between the exercise and nonexercise treatments. However, the effect was only significant as a consequence of the Nex rather than the Hex condition.

In the HR-\(\dot{V}O_2\) calibrations, the lack of significant time (pre- vs. post), treatment (Hex vs. Nex) effects, or time \(\times\) treatment interactions indicates that in general the changes in resting HR and FLEX did not influence the relationship between HR and \(\dot{V}O_2\) to a significant degree during the exercise session. We estimated whether a change in the relationship between HR and \(\dot{V}O_2\) at the calibration before and after each run, significantly affected estimates of daily EE. To do this we used the HR data for 3 specific days for each subject to calculate daily EE using the data from the pre- and postrun calibrations for each treatment. This was done to examine whether changes in resting HR, FLEX HR, or the HR-\(\dot{V}O_2\) relationship significantly influence estimates of daily EE. If the relationship did change this would be apparent as significant differences in daily EE estimates using the different HR-\(\dot{V}O_2\) calibrations (i.e., pre- vs. post-, Hex vs. Nex, or time \(\times\) condition). There was no significant time (i.e., pre vs. post), condition (Hex vs. Nex), or time \(\times\) condition interaction for the prediction of daily EE. On the Hex condition, the estimate from the pretreatment relationship was 13.3 MJ/day, whereas that for the posttreatment was 13.2 MJ/day. Corresponding values for the Nex conditions were 13.1 and 11.9 MJ/day \([F(1,178) = 3.69, P = 0.068]\). The EE calculated from HR during the exercise sessions was 4.9 and 4.6 MJ/day \((SED = 0.105)\) on the HFHex and LFHex treatments, respectively. Regression analysis showed that EE due to exercise did not change as each run progressed on each of the exercise conditions. Total daily EE was regressed against study day. On average subjects showed a significant decline in EE during the course of the study on the Hex \([mean\ slope = -0.423\ MJ/day; t = -3.224; P = 0.015\ (SE = 0.131)]\), but not on the Nex condition \([mean\ slope = 0.020\ MJ/day; t = 0.220; P = 0.832\ (SE = 0.091)]\; Fig. 2B\). A \(t\)-test indicated that the difference between the two exercise conditions was significant \((P = 0.030)\). Interestingly, when dietary treatments were examined (Fig. 2A), subjects showed a decline in EE over time in the LF group \([mean\ slope = -0.266\ MJ/day; t = -2.439; P = 0.045\ (SE = 0.109)]\). However, the change was not significant in the HF condition \([mean\ slope = -0.137\ MJ/day; t = -1.983; P = 0.088\ (SE = 0.069)]\). The mean difference between the groups was not significant \((P = 0.211;\ Fig. 2)\).

Figure 2 shows that when data for exercise treatments were combined, looking at Hex vs. Nex condition, there was a significant difference in the change in nonexercise EE over time \((P = 0.049)\). On the Hex conditions, EE minus exercise decreased over time \([mean\ slope = -0.346\ MJ/day; t = -2.748; P = 0.029\ (SE = 0.126)]\). On the Nex condition, there was no significant change in daily EE (excluding exercise) over time \((P = 0.832)\). The regression slopes for the components of EE that changed on each treatment are given in Table 3. From this it can be seen that the major change in EE occurred through changes in nonexercise activity.

**Aerobic fitness.** The mean estimated \(\dot{V}O_{2\max}\) \((\pm SD)\) for the six subjects was 46.46 \pm 6.77, 41.28 \pm 9.87, 45.29 \pm 7.73, and 42.91 \pm 7.89 ml/kg\(-1\) min\(-1\) at the end of the HFHex, HFNex, LFHex, and LFNex treatments, respectively. The change in estimated \(\dot{V}O_{2\max}\) (postintervention \(-\) preintervention value) was 3.91, \(-3.63, -1.72, -0.78\) \((SED = 2.34\ ml/min\(-1\)kg\(-1\)) on the HFHex, HFNex, LFHex, and LFNex treatments.
Thus carbohydrate intake was higher on the Hex condition than the Nex condition (due to the larger amount of fruit drink consumed). Average values were 5.9 and 5.5 MJ/day (SED = 0.184) \( F(1,21) = 6.36; \ P = 0.020 \).

Total daily EI was regressed against study day for each condition (Fig. 3). Subjects on average showed a significant decrease in daily EI as the study progressed on the HF condition [mean slope = -0.217 MJ/day; \( t = -2.370; \ P = 0.050 \) (SE = 0.092)], whereas there was no change over time detected in the LF condition [mean slope = -0.067 MJ/day; \( t = -0.983; \ P = 0.358 \) (SE = 0.068)]. The differences between the dietary conditions were not significant (\( P = 0.172 \)). As can be seen from Fig. 3A, slopes, \( t \)-statistics, and probability values for change across time for the exercise conditions were not significant, Hex [mean slope = -0.060 MJ/day; \( t = -0.904; \ P = 0.396 \) (SE = 0.067)]; Nex [mean slope = -0.224 MJ/day; \( t = -1.677; \ P = 0.137 \) (SE = 0.134)]. There was no significant difference between the exercise conditions (\( P = 0.362 \)).

Body weight. Looking across dietary condition gave significant average losses over the 7-day treatment period of -0.06 and -0.51 (SED = 0.16) kg on the HF and LF conditions, respectively \( F(1,21) = 7.94 \ P = 0.010 \). The weight loss on LF condition was significantly different from zero \( P = 0.021 \), but not on the HF treatment \( P = 0.698 \). Average change in body weight was not significantly different between the exercise conditions. Average weight change over the Hex and Nex conditions, respectively. Comparing \( \dot{V}O_2 \) to prestudy measurements, there were no significant differences between separate diet conditions \( F(1,21) = 0.04; \ P = 0.845 \). However, the exercise conditions showed a significant change \( F(1,21) = 2.31; \ P = 0.007 \), with subjects gaining 2.82 ml\( \cdot \)kg\(^{-1}\)\( \cdot \)min\(^{-1}\) on the Hex condition and losing -2.21 on the Nex condition (SE = 1.66). Diet \( \times \) exercise interactions were not significant \( F(1,21) = 2.31; \ P = 0.145 \).

**Food, energy, and nutrient intake.** The higher weight of food and drink consumed on the Hex compared with the Nex condition (Table 1) was due to higher fluid (fruit drink) intake.

Table 3. Average change, between days 1 and 7 of each treatment, in total EE and its components (Exercise EE, non-exercise EE, and BMR)

<table>
<thead>
<tr>
<th></th>
<th>HF/Nex</th>
<th>HF/Hex</th>
<th>LF/Nex</th>
<th>LF/Hex</th>
<th>SED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total energy expenditure, MJ/day</td>
<td>0.063</td>
<td>-0.338</td>
<td>-0.023</td>
<td>-0.503</td>
<td>0.201</td>
</tr>
<tr>
<td>Exercise energy expenditure, MJ/day</td>
<td>0</td>
<td>-0.085</td>
<td>0</td>
<td>-0.076</td>
<td>0.05</td>
</tr>
<tr>
<td>Nonexercise energy expenditure, MJ/day</td>
<td>0.063</td>
<td>-0.254</td>
<td>-0.023</td>
<td>-0.437</td>
<td>0.197</td>
</tr>
<tr>
<td>RMR, MJ/day</td>
<td>0.047</td>
<td>-0.020</td>
<td>0.052</td>
<td>0.032</td>
<td>0.056</td>
</tr>
</tbody>
</table>

While RMR did not significantly change during the course of the study, only 2 measures per subject per treatment (beginning and end) were made. Thus no regression analysis was possible for BMR. Diet-induced thermogenesis was not measured and was assumed to have not changed significantly during each treatment. RMR, resting metabolic rate.
conditions was $-0.32$ and $-0.24$ kg (SED = 0.16), respectively [$F(1,21) = 0.22; P = 0.641$]. The weight loss on Hex and Nex conditions were not significantly different from zero. There was a significant diet $\times$ exercise interaction [$F(1,21) = 7.08; P = 0.015$] for weight change over days 1–7, with average change in body weight of $-0.31, -0.19, -0.33$, and $-0.68$ kg on the HHex, HNex, LFHex, and LFNex conditions, respectively.

**EB.** Average daily EB was regressed against study day to assess temporal trends in EB (Fig. 4). The mean slopes, $t$-statistics, and probability values for differences from zero were [mean slope = 0.362 MJ/day; $t = 3.616; P = 0.009$ (SE = 0.100)] for the Hex condition [mean slope = $-0.244$ MJ/day; $t = -2.103; P = 0.074$ (SE = 0.116)] and Nex condition (Fig. 4B). A $t$-test between conditions revealed that there was a significant difference between the groups ($P = 0.013$). Also, for the dietary treatment groups, the LF group showed a significant increase in EB over time [mean slope = 0.199 MJ/day; $t = 2.914; P = 0.023$ (SE = 0.068)], whereas in the HF condition EB over time did not significantly change [mean slope = $-0.081$ MJ/day; $t = -0.720; P = 0.495$ (SE = 0.112)]. The difference between the conditions was not statistically significant ($P = 0.093$).

**Pleasantness of food and motivation to eat.** Subjects rated both diets as being equally pleasant, with mean scores of 83 and 82 (SED = 0.93) on the HF and LF diets, respectively [$F(1,21) = 1.96; P = 0.179$]. Similarly they rated both diets as being equally satisfying, with mean scores of 82 and 80 (SED = 1.43) on the HF and LF diets, respectively [$F(1,21) = 1.86; P = 0.190$].

Subjects reported feeling significantly more hungry, a stronger desire to eat, greater prospective consumption, and stronger thoughts of food on the LF condition compared with the HF condition ($P < 0.05$). Additionally, exercise condition produced a significant effect on hunger, desire to eat, thirst, thoughts of food, and tiredness on the Hex condition compared with the Nex condition ($P < 0.05$). There were no significant differences between ratings in diet $\times$ exercise interactions.

**DISCUSSION**

**Validation of the use of HR to predict EE.** There are considerable limitations in predicting EE from HR and aerobic power from submaximal fitness tests. In the present study, subjects spent significant amounts of time above FLEX, engaged in the same types of physical activities (i.e., cycling) that were used to calibrate the HRM. The study also employed a within-subject, repeated-measures design. Spurr et al. (28) showed that under these conditions there is a good relationship between total daily EE (measured by indirect calorimetry) and HR, even in groups of four to six subjects. A potential problem with the present study is that a reduction in HR both at rest and during submaximal exercise is associated with exercise training. Thus the actual protocol used in the present study may have influenced the relationship between HR and EE. This raised the further possibility that the trends observed over time may be an artifact of a change in the relationship between HR and EE. Clearly before discussing these trends it was important to verify that they were real and not artifactual. A number of issues arise in this consideration. Was there a change in the relationship between HR and $\dot{V}O_2$ at the calibration before and after each run? If so, did this systematically differ between the exercise and nonexercise treatments? Did any of these changes significantly influence estimates of daily EE? These issues were addressed in the validation of the relationship between HR and $\dot{V}O_2$ (and hence EE), in **RESULTS**. The data suggest that resting HR and FLEX HR did significantly change between the pre- and posttreatment calibrations, but on the Nex treatment only. The direction of change is consistent with a decrease in activity over this time. However, this did not significantly change estimates of daily EE when comparing values taken from the calibrations before and after each treatment. It therefore follows that the reduction in daily EE as a consequence of the Hex treatment alone does not appear to be an artifact of the change in the HR:$\dot{V}O_2$ relationship, as consequence of either exercise or lack of exercise. Parenthetically, because HR significantly rose on the Nex treatment, and nonsignificantly dropped on the Hex regimen, it is reasonable to estimate that their habitual activity lay closest to the midway point between the zero and Hex treatment. This would equate to the medium exercise treatment (1.5 MJ/day) in our previous studies (15, 34). In the present study, this would equate the midway between the zero and Hex treatment, or the energy expended on the zero treatment plus 1.5 MJ/day.

**Effect of the dietary and exercise interventions on total daily EE and intake.** We interpreted the greater fluid intake in response to exercise as a need to defend water balance in
preference to EB. It has been suggested that exercise may stimulate preferential selection of carbohydrates (37, 44). This may be so. It may also be that subjects were adopting behavioral strategies that prioritize the defense of water balance over EB and that carbohydrate intake rose as a consequence of this. Alternatively, it may be that subjects were selecting fluids that contain energy to defend fluid and EB with no real selective drive to defend carbohydrate balance. It is not possible to distinguish from these three alternatives using the current database and this remains an important area for future research.

_Trends in EI, EE, and EB over time._ When EI, EE, and EB were regressed against study day some interesting patterns emerged that shed light on the rate and nature of compensation for induced energy imbalances. As regards EI, there was some weak evidence that subjects decreased EI by \(-0.22\) MJ/day as a response to the higher EI on the HF condition (Fig. 3). No such compensatory response was seen on the LF condition. Although weak, this suggests that subjects would have compensated by \(1.5\) MJ/wk. It would take \(\sim 4\) wk for the difference in EB to be reduced to zero if this compensatory trend continued at a linear rate. A similar trend occurred on the N treatment, compared with the Hex treatment, but due to the variability in the data this effect was not significant (Fig. 3). There was no compensation of EI over time on the Hex condition. We interpret this as being due to the tendency for subjects to defend fluid balance over EB. In addition, it may well be that a large part of the reduction in EE was due to a fatigue effect. It may be they were too tired over the course of the study to compensate EI more.

Interestingly, compensatory trends were more marked for changes in EE than in EI in response to the exercise conditions (Fig. 2). Goran and Poehlman (11) also found a marked average decrease in nonexercise activity EE, by \(0.97\) MJ/day, in response to endurance training, in 11 healthy, elderly men. In the present study, the daily decrease in EE of 0.32 MJ/day (or \(2.2\) MJ/wk) on the Hex condition was largely due to a progressive decrease in nonexercise EE as the week progressed. A period of 2.4 wk would be required at this rate for the difference in EB between the two conditions (5.3 MJ/day) to decrease to zero. It is notable that subjects also decreased daily EE over time on the LF compared with the HF condition (Fig. 2). It is on the LF condition that intakes were far below those required to meet EB. This suggests that the low level of EB limited the capacity for these subjects to expend energy through exercise. It is known that at far lower levels of EI (e.g., semistarvation and starvation) physical activity decreases significantly, and this has a sparing effect on total EB (9, 14, 18). In the present study, each dietary treatment was of a fixed composition and energy density. This means that to achieve EB on the LFHex treatment, subjects would have had to eat \(\sim 5–7\) kg of food per day. This would clearly create a conflict between the demands of the mandatory exercise regimen and the need to eat to EB.

Thus the conditions that produced a marked negative EB at the outset of the study (Hex, LF) led to a significant trend of more positive EB as the study progressed (Fig. 4). The effect of no exercise and of an HF diet (which would both tend to elevate EB) was far less apparent but in the opposite direction. Together these data suggest that subjects compensate EB more readily in response to energy deficits than surfeits (Fig. 4). The compensatory changes are due to changes in both EE (at this level of activity) and changes in EI (Figs. 2–4).

As far as we are aware this is one of the first data sets that has assessed the rate of change of restoration of EB in response to manipulations of both diet and exercise. The rate estimates, although imperfect, are of particular importance because they suggest a time window of compensation of \(2–4\) wk. The majority of studies examining the effects of diet on exercise make inferences about compensation over periods at or below 2 wk or in excess of \(4\) wk (including cross-sectional studies; 8, 36, 38, 39, 42). It is important to note that the rate of compensatory change in EB will most likely be a function of the initial rate of change of EB (9). Thus our estimate of rate of EB restoration primarily pertains to the current experimental conditions and may well not apply to other subjects or other conditions. Furthermore, we presumed that compensation would progress at a linear rate. There is no reason to assume this is necessarily so. These observations may help explain the apparent paradox whereby the majority of studies lasting \(1\) wk or less show virtually no compensation for changes in dietary energy density or exercise-induced changes in EE, and why the majority of studies conducted over several months and cross-sectional studies show far greater compensation of EI in relation to habitual EE (for discussion, see Ref. 19). There are far fewer dietary manipulations conducted over several months, but they too show greater compensation (30).

It is also interesting that motivation to eat was elevated in response to the LF and the Hex conditions. This is not surprising when considering the degree of energy imbalance attained, particularly on the HFHex treatment. Indeed, it would be rather disconcerting if this level of energy imbalance did not alter motivation to eat. These effects were more detectable in this study than our previous studies, where only some of these effects were apparent (15, 34). This probably relates to the power of the \(2 \times 2\) design over the nonfactorial design (using 3 treatments).

**Changes in body weight and EB.** Estimated daily energy imbalance was \(-3.8, 0.8, -8.2,\) and \(-2.0\) MJ/day by the end of the 7 days on the HFFHex, HFNex, LFHex, and LFNex treatments, respectively. Body weight changes were \(-0.31, 0.19, -0.33,\) and \(-0.68\) kg, respectively, over the 7 days of each treatment period. Assuming an energy cost of weight gain of \(31\) MJ/kg and of weight loss of \(26\) MJ/kg, these weight changes translate into cumulative energy imbalances of \(-1.2, 0.8, -1.2,\) and \(-2.5\) MJ/day. Although in the same direction, the greatest discrepancies between EB estimated from body weight and from EI–EE occurred on the Hex treatments. Indeed analysis confirmed that although diet condition significantly influenced body weight, exercise condition did not. Under conditions of relatively intense exercise and at weight changes below \(1.5\) kg, a subject’s fat and fat free mass can change by \(-0.7\) kg, which does not translate into changes in body weight. For instance, fat mass may decrease whereas fat free mass slightly increases (8). It is in these situations that estimates of EB from weight change alone become precarious.

**Advantages and limitations of the present study.** Specific advantages of the present study were that we recorded EI by weighing subjects’ consumption of covertly manipulated diets. This overcomes some of the problems inherent in misreporting of dietary intakes. EI, EE, and body weight were independently assessed (albeit approximately). The energy cost of exercise...
was also quantified, as were subjective indexes of motivation to eat and mood. The present study assessed day-to-day changes in EI, EE, and EB over 7 days.

There are a number of limitations inherent in any experimental design and the present work was no exception. The estimates for rate of compensation over longer periods should be treated with far greater caution as they assume that compensation of EI and EE would continue 1 at a linear rate and 2) until the difference between treatments was reduced to zero. Neither of these assumptions may be correct. The sample size was limited to eight lean men and the duration of the study was limited to 7 days per treatment. The small sample size may be a particular issue in relation to the generalizability of the data. It should also be noted that this study used lean, relatively young men whose habitual activity patterns were likely to have been at the high end of the sedentary range (~1.8 × BMR). Other subjects may behave differently. The energy imbalances induced by the dietary and exercise conditions were quite considerable and smaller manipulations may not induce detectable compensatory changes in EI, EE, and EB over this time period.

There are limitations in the use of HR to estimate EE (see above). There are also a number of assumptions inherent in using the relationship between HR and VO2 to predict total aerobic power (VO2max; 25–27). These tests assume consistent mechanical efficiency of exercise (26). Mechanical efficiency on a cycle ergometer can show a 4–5% variation (26). The tests also assume linearity in the relationship between HR and VO2 at incremental workloads. Some deviation from linearity can occur, especially at the high and low end of the range. Subjects are likely to have become more efficient using the cycle ergometer as they became accustomed to using it. It may take several days for subjects to become maximally efficient on the ergometer, and apparent, small rises in predicted VO2max may well reflect a combination of increased fitness and increased mechanical efficiency on the ergometer.

It should be noted that as discussed above, caution should be exercised when inferring changes in EB from body weight alone, particularly on the Hex condition. The precision of estimating change in EB from body weight would have been far lower than from estimates of EI—EE.

Habitual day-to-day variability in EI and EE are not clear. However, it is often assumed that a within-subject coefficient of variation (CV) for EI of 23% and for daily EE of 12.5% is a reasonable estimate (1, 2). Given the average levels of EI and EE in the present study it is clear the variability in habitual day-to-day EI and EE is considerable relative to the size of the effects detected in this study. These effects were detected because of the size and constancy of the manipulation we used and the rigor with which daily estimates of EI and EE were made. Such changes may be much harder to detect under free-living conditions. These observations emphasize the importance of measuring EB and its components in studies such as these.

In conclusion, as in previous studies, the present study showed that changes in EE through exercise and changes in EI due to alterations of dietary energy density and fat content led to marked alterations of EB amounting to ~5–6 MJ/day. This induced significant compensatory changes in EB over time of ~0.3–0.4 MJ/day. These were due to changes in both EI and EE in the opposite direction to the initial perturbation in EB.

Although these changes were significant, they were relatively small but persistent, amounting to ~0.2 and ~0.35 MJ/day for EI and EE, respectively. Thus we estimate that under these experimental conditions, compensation for a perturbation of EB of ~5 MJ/day will take 2–4 wk. Compensation tended to be more marked in relation to induced energy deficits that surfeited. The estimated time course for the restoration of EB through compensatory mechanisms corresponds to the time window, which the majority of studies miss.

**GRANTS**

This work was supported by the Scottish Executive Rural Affairs Department and Biotechnology and Biological Science Research Council Grant F02501.

**REFERENCES**


