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Metabolic efficiency and energy expenditure during short-term overfeeding

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Abstract

Objective: To investigate whether efficiency of weight gain during a short period of overfeeding is related to adaptive differences in basal metabolic rate (BMR) and physical activity.
Subjects: Fourteen healthy females (age 25 ± 4 years, BMI 22.1 ± 2.3 kg/m^2).
Design and measurements: Subjects were overfed with a diet supplying 50% more energy than baseline energy requirements for 14 days. Overfeeding diets provided 7% of energy from protein, 40% from fat and 53% from carbohydrates. Body composition was determined using hydrodensitometry and isotope dilution, total energy expenditure (TEE) with doubly labeled water and basal metabolic rate (BMR) with indirect calorimetry. Physical activity (PA) was recorded with a tri-axial accelerometer.
Results: Body weight increased by 1.45 ± 0.86 kg (mean $\pm$ S.D.) ($P < 0.0001$), fat mass increased by 1.05 ± 0.75 kg. Energy storage was 57.0 ± 17.9 MJ, which is the difference between energy intake (207.2 MJ) and energy expenditure (150.2 MJ) during overfeeding. There was no difference between metabolically efficient and metabolically inefficient subjects in changes in BMR and PA.
Conclusion: These results indicate that the metabolic efficiency of weight gain was not related to adaptive changes in energy expenditure.
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1. Introduction

An energy intake that exceeds energy expenditure for longer periods will lead to weight gain. However, when healthy adults are overfed, most persons gain less weight than expected from the excess energy intake and show a wide inter-individual range in weight gain on the same overfeeding regime [1–6]. One possible explanation is that some persons can increase their energy expenditure when overeating to resist weight gain. Whether there are adaptive physiological changes in energy expenditure is studied intensively. While some investigators found evidence for adaptive thermogenesis [7] others did not [1,8,9] but accuracy and sophistication of methods used to measure

energy expenditure and physical activity could be improved. Three overfeeding studies, approximately comparable in amount and duration of overfeeding, measured free-living energy expenditure with doubly labeled water but reached different conclusions. Levine et al. [5] found that individual changes in non-exercise activity thermogenesis (NEAT), defined as the thermogenesis associated with fidgeting, maintenance of posture and other activities of daily life, could explain differences in fat gain in subjects overfed with 4.2 MJ/day for 56 days. Diaz et al. [3] found no evidence for any adaptive energy-dissipating mechanism when overfeeding subjects with 50% more energy than baseline requirements (mean 6.2 MJ/day) for 42 days. Also, Roberts et al. [4] did not find a significant increase in energy expenditure in young and older men overfed with 4.2 MJ/day for 21 days.

Diet composition is known to influence energy expenditure, as different substrates will increase dietary induced

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thermogenesis (DIT) to various degrees. DIT is greater on a high protein and carbohydrate diet than on a fat diet [10]. In several studies the metabolic response to overfeeding diets of different composition (low-protein, high-carbohydrate, high-fat) has been investigated [6,7,11,12]. These experiments show considerable inter-individual differences in energy cost of weight gain within and between experiments. Stock [13] and Dulloo and Jacquet [14] showed that differences were most noticeable when diets were unbalanced with respect to protein and therefore suggested that overfeeding low-protein diets could serve as a tool to exaggerate individual differences in energetic efficiency by maximizing DIT. We overfed 14 healthy females with a low-protein diet to investigate whether efficiency of weight gain is related to adaptive differences in BMR and physical activity.

2. Subjects and methods

2.1. Subjects

Fourteen healthy female subjects, aged 19–36 years, participated in the study. Characteristics of the subjects are shown in Table 1. Before participating in the study subjects were medically screened by a detailed health questionnaire. Subjects had had a stable body weight (body weight changes ≤ 2 kg) for at least a year at the start of the study. Three were light smokers, they maintained their habitual smoking pattern during the study. All subjects received verbal and written information and signed a written consent form. The study was approved by the Ethics Committee of Maastricht University.

2.2. Experimental design

Baseline energy requirements were defined over a 7-day period (days 1–8). During the 14-day overfeeding period (days 8–22) subjects were overfed with a diet supplying 50% more energy than the baseline energy requirements. All foods and drinks were provided daily in weighed food packages while subjects consumed the main course (dinner) at the university. Alcohol consumption was not allowed during the study. Body weight was measured on days 1, 8 and 22. Body composition and basal metabolic rate were measured at baseline and after overfeeding (days 8 and 22). Total energy expenditure was measured with doubly

Table 1
Initial characteristics of the 14 female subjects

	Mean	SD
Age (years)	25	4
Height (m)	1.72	0.06
Body weight (kg)	64.8	7.0
Body mass index (kg/m^2)	22.1	2.3
Body fat (%)	27.5	4.4

labeled water during the 2 weeks preceding overfeeding ($n=7$, because of limited availability of doubly labeled water) and during the 2 weeks of overfeeding ($n=14$). For the entire study period subjects wore an accelerometer to measure physical activity. Subjects maintained their normal lifestyles (i.e. work, education, sports participation) throughout the study.

2.3. Dietary intake

During the baseline period subjects chose their diets from a variety of food items provided daily in weighed food packages, bringing back the left-overs the next day, for calculation of habitual energy intake. When subjects had not been in energy balance (i.e. body weight changed from day 1 to day 8), baseline energy requirements were calculated from basal metabolic rate measured with indirect calorimetry and physical activity level measured with accelerometry. Subjects were overfed with a diet containing 50% more energy than the baseline energy requirements. The excess energy intake during the overfeeding period was introduced gradually to allow the bowels to adjust to the increased amount of food. Overfeeding diets were calculated to be relatively low in protein, providing 7% of energy from protein as derived from the analysis of overfeeding experiments by Stock [13], 40% from fat and 53% from carbohydrates. Food composition of the diets was largely the same for each subject, but some adjustments were made according to the subject's preferences to make the overfeeding diets more palatable. All foods and drinks were weighed to the nearest gram. Macronutrient composition of baseline and overfeeding diets was assessed with a computerized version of the Dutch food composition table (Komeet, version 2.0d, 1996, B·ware Nutrition Software).

2.4. Procedures

Anthropometry and body composition. Measurements were carried out in the morning after voiding and before breakfast. Body weight and height were measured to the nearest 0.01 kg and 0.1 cm, respectively. Body mass index (BMI, kg/m^2) was calculated as body weight (kg) divided by height (m) squared. Body composition was estimated by using hydrodensitometry and isotope dilution. Body density was determined by underwater weighing with simultaneous measurement of residual lung volume with the helium dilution technique. Total body water (TBW) was determined with deuterium dilution following the Maastricht protocol [15]. Body composition was calculated from body density and TBW using the three-compartment model of Siri [16].

Total energy expenditure. Total energy expenditure (TEE) was measured with the doubly labeled water (DLW) technique following the Maastricht protocol [15]. Briefly, isotopes were administered as a mixture of 5 at% ^2H_2O and 10 at% $H_2^{18}O$ resulting in an initial excess body

water enrichment of 150 ppm for deuterium and 300 ppm for oxygen-18, leaving a sufficient excess enrichment at the end of the observation period. The volume was 80–160 ml. Subjects collected a background urine sample immediately before isotope consumption to correct for isotopic backgrounds, subsequent urine samples were collected from the second and the last voiding on the first, mid and last day of the 14-day observation period. Isotope enrichments of the urine samples were analyzed with isotope ratio mass spectrometry (Optima, VG, UK). Theoretical considerations and calculations of energy expenditure by the DLW method as described in detail elsewhere by Westerterp et al. [15] were checked for validity during overfeeding.

Basal metabolic rate. Basal metabolic rate (BMR) was measured by indirect calorimetry using an open-circuit, ventilated-hood system [17] in the morning after an overnight fast with subjects lying in a supine position for 30 min. BMR was calculated from O_2 consumption and CO_2 production using the formula of Weir [18].

Physical activity. Physical activity was registered with a tri-axial accelerometer for movement registration (Tracmor, Philips Research, Eindhoven, The Netherlands), which measures frequencies covering the frequency content of activities of daily living [19]. The tri-axial accelerometer has been validated against DLW [20] and has been used before in our department [21,22]. Subjects wore the accelerometer on a belt at the lower back during waking hours.

2.5. Statistical analysis

All results are presented as mean±S.D. Student's paired *t*-test (two-sided) was used to compare parameters before and after overfeeding. A simple regression analysis between weight gain and energy storage (which is the difference between energy intake and energy expenditure during overfeeding) was used to distinguish between metabolically efficient (positive residuals) and metabolically inefficient (negative residuals) subjects. Metabolically efficient and inefficient subjects were compared regarding changes in BMR and physical activity using a one-way ANOVA. $P < 0.05$ was considered as statistically significant. SPSS 11 for Macintosh (2002, SPSS Inc.) was used for the analysis.

3. Results

3.1. Dietary intake

Table 2 summarizes the changes in energy balance parameters induced by overfeeding. Self-selected baseline diets provided mean percentages energy of 14±2% from protein, 30±3% from fat and 57±4% from carbohydrates. The macronutrient composition of the overfeeding diets was as intended: 7% of energy from protein, 40% from fat and 53% from carbohydrates, which was low in protein on a

Table 2
Energy balance parameters at baseline and after 14 days overfeeding*

	Baseline	Overfeeding	$P^{\dagger}$
Body weight (kg)	64.8±7.0	66.3±6.7	<0.0001
Fat mass (kg)	18.0±4.5	19.0±4.3	<0.001
Energy intake (MJ/day)	9.2±1.2	14.8±1.6	<0.0001
TEE (MJ/day) (*n*=7)	10.18±0.68	10.58±1.00	0.10
(*n*=14)	–	10.73±1.06	–
BMR (MJ/day)	5.74±0.37	6.13±0.56	<0.01
Physical activity (Mcounts/day)	6666±1286	7177±1645	0.21
Energy storage (=EI − TEE) (MJ)	–	57.0±17.9	–

*mean±S.D., †Student's paired *t*-test (two-sided), TEE = total energy expenditure, BMR = basal metabolic rate, EI = energy intake.

relative basis (%) and on an absolute basis (61±6.1 g/day). The mean energy intake during baseline was 9.2±1.2 MJ/day. During overfeeding mean energy intake was 14.8±1.6 MJ/day or a total of 207.2±21.6 MJ (Table 2).

3.2. Body weight and body composition

Body weight increased by 1.45±0.86 kg ($P < 0.0001$) with a range from 0.19 to 3.00 kg. Fat mass increased by 1.05±0.75 kg ($P < 0.001$) ranging from 0.12 to 2.65 kg (Table 2). There was no significant effect of menstrual cycle (defined as the change from pre- to post-ovulation (*n*=6) or from post-to pre-ovulation (*n*=8) during the overfeeding period) on weight gain, neither alone nor after correction for energy storage (data not shown).

3.3. Metabolic efficiency and energy expenditure

There were no indications for malabsorption, therefore energy storage was calculated as the difference between energy intake (207.2 MJ) and energy expenditure (150.2 MJ) during overfeeding. Mean energy storage was 57.0±17.9 MJ (Table 2).

Fig. 1 shows the individual changes in body weight plotted against energy storage. Subjects with a positive residual from the regression line were considered metabolically efficient (relatively high weight gain for the amount of energy stored), subjects with a negative residual from the regression line were considered metabolically inefficient (relatively low weight gain for the amount of energy stored). For the whole group mean BMR increased significantly with 0.38±0.47 MJ/day ($P < 0.01$), with a large interindividual variation. When comparing metabolically efficient and inefficient subjects we did not observe a significant difference in BMR change ($P = 0.09$). The progress of energy expenditure during overfeeding was examined by comparing mean TEE during the first and the second week of overfeeding. TEE increased by 0.38±0.68 MJ/day from the first to the second week, but this increase was not statistically significant. Although not statistically significant, there was a tendency towards a relation between this increase in TEE and the increase in BMR, which was measured before and after overfeeding.
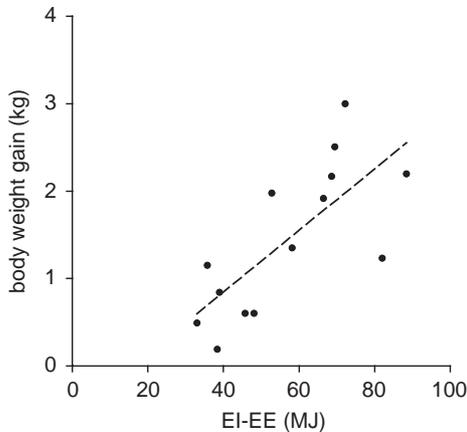
Fig. 1. Individual changes in body weight plotted against energy storage (EI − EE (MJ)). EI = energy intake, EE = energy expenditure.

Physical activity as measured with accelerometry did not change significantly (511 ± 1450 Mcounts/day). There was no difference in change in physical activity between metabolically efficient and inefficient subjects ($P = 0.43$). When we compared the subjects outside the 95% confidence interval of the mean, there was still no difference in BMR change ($P = 0.12$) or physical activity change ($P = 0.50$).

4. Discussion

The relevance of adaptive changes in thermogenesis in the etiology of obesity is controversial as such changes are believed to be no more than a few percent [23,24]. With prolonged overfeeding changes in energy expenditure are of the order of 5–15%, which depends on the type and amount of overfeeding (DIT) [25,26]. The unexplained large inter-individual variation in efficiency of weight gain with overfeeding [1–6] shows that the matter of adaptive thermogenesis is still an issue. The aim of the present study was to investigate whether efficiency of weight gain is related to adaptive differences in BMR and physical activity by overfeeding healthy females for 14 days with a diet supplying 50% more energy than baseline requirements. If energy expenditure does not follow excess energy intake to the same extent, absolute energy storage will be greater in a subject with a baseline energy intake of for instance 12 MJ/day ($252 - 168 = 84$ MJ) compared to a subject with a baseline energy intake of 8 MJ/day ($168 - 112 = 56$ MJ). This absolute difference in excess energy intake will also influence absolute weight gain. The absolute differences allowed us to distinguish between subjects with a relatively high weight gain for the amount of energy stored (metabolically efficient) and a relatively low weight gain for the amount of energy stored (metabolically inefficient).

If any adaptive thermogenesis is present, this will show up in the BMR. Mean BMR did increase, however, when we compared those subjects that gained body weight efficiently with those that did not, we did not see any difference in BMR change. The changes in BMR were equivalent to the expected rise in DIT due to the increased amount of food eaten. The 9–10 h interval between the last food consumption in the evening and measurement of BMR in the morning did not eliminate influences of DIT on metabolic rate. Goldberg et al. [27] showed that after overfeeding the DIT from a large evening meal caused a higher sleeping metabolic rate compared to normal conditions. BMR measured directly at waking was still increased, despite a 13-h interval between the last meal and the measurement. This suggests that the increase in DIT due to the increased amount of food eaten persists for 24 h a day and is therefore observed in our BMR changes.

The most variable component of energy expenditure is AEE, which can be divided in exercise activity thermogenesis (EAT) and non-exercise activity thermogenesis (NEAT). EAT is the thermogenesis accompanied with sports participation, NEAT is defined as the thermogenesis that accompanies fidgeting, maintenance of posture, and other physical activities of daily life. The concept of NEAT seems important in energy balance regulation as in the study of Levine et al. [5] who overfed 16 non-obese subjects with 4.2 MJ/day for 56 days, changes in NEAT directly predicted resistance to fat gain with overfeeding. In this study physical activity was registered with a tri-axial accelerometer, which is sensitive to small human body accelerations and very low frequencies of accelerations and can therefore detect fidgeting [28]. Subjects maintained their normal lifestyles throughout the study period (i.e. work, education, sports participation). Mean accelerometer output did not change significantly, therefore both exercise and non-exercise activity remained constant.

When comparing TEE during the first and the second week of overfeeding there seemed to be a gradual increase in TEE, but this was not statistically significant. This increase in TEE tended towards a relation with the increase in BMR and although this relation was not statistically significant, we believe that the rise in TEE on overfeeding is largely due to an increase in BMR, and thus DIT.

However, we were not able to answer the question why some subjects can store a certain amount of energy with hardly any weight gain. We have no indications for non-compliance to the diet or measurement errors for the whole group and these subjects in particular. We can only speculate on how the excess energy was stored, by either hypertrophy or hyperplasia of the fat cells.

In short, we did not find differences in BMR and physical activity between metabolically efficient and metabolically inefficient subjects during overfeeding, indicating that the metabolic efficiency of weight gain is not related to adaptive changes in energy expenditure.

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