Substrate utilization in man: effects of dietary fat and carbohydrate

Substrate Utilization in Man: Effects of Dietary Fat and Carbohydrate

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In man there is evidence that the ability to adjust fat oxidation to fat intake is less effective than the ability to adjust carbohydrate and protein oxidation to carbohydrate and protein intake. The short-term (3-day) effects of a low-fat (LF), mixed (M), and high-fat (HF) diet on human substrate balances were studied using a respiration chamber. Subjects were 14 young female students classified by means of their scores on psychometric questionnaires as "restrained" or "unrestrained" eaters. Subjects were in energy balance, ie, the mean difference between energy intake (EI) and energy expenditure (EE) was 86 ± 85 kJ/d. The fat content of the food significantly influenced the 24-hour respiratory quotient (RQ) and nonprotein respiratory quotient (NPRQ). For both the LF and M diets, the 24-hour RQ was significantly lower than the food quotient (FQ), whereas the RQ on the HF diet was not different from the FQ. Oxidation of fat and carbohydrate significantly increased with, respectively, an increasing fat and carbohydrate content of the diet for both restrained- and unrestrained-eating subjects. Restrained-eating subjects showed a decreased fat oxidation compared with unrestrained eaters in response to a HF diet, resulting in a positive fat balance for restrained-eating subjects. On a LF diet, fat balance was negative for both groups of subjects, indicating net endogenous fat oxidation. In conclusion, restrained-eating subjects have more difficulty in the handling of a HF diet, possibly explaining their higher susceptibility to becoming obese.

MAINTAINING A STABLE body weight requires that over time, energy intake (EI) equals energy expenditure (EE) and also that intakes of protein, fat, and carbohydrate equal the oxidation of each substrate.[1,2] In conditions of energy or substrate imbalance, changes occur in the body stores and hence body weight and body composition. A high-fat (HF) intake is often associated with an increasing prevalence of obesity.[3-5] There are several mechanisms for this association. First, a HF diet leads to an increase of EI,[5-7] or a decrease of EE.[8,9] Second, the body fails to adjust fat oxidation in response to excess fat intake.[1,2]

Another aspect that must be considered in the processes leading to obesity is a metabolic difference between individuals in the handling of dietary fat. Studies in post-obese subjects have suggested that decreased fat oxidation may be related to subsequent body weight gain.[9,10] Thomas et al[11] reported that lean subjects have a greater ability to increase fat oxidation in response to a HF diet than do obese subjects. This could result in a smaller increase of body fat in lean as compared with obese subjects when both consume a HF diet.

A primary purpose of the present study was to investigate the effect of an isoenergetic exchange of fat and carbohydrate on substrate metabolism, ie, oxidation and overall balance of protein, fat, and carbohydrate. A second aim was to determine metabolic responses to dietary fat and carbohydrate of subjects being more or less susceptible to becoming obese. By means of scores on psychometric questionnaires, a distinction was made in the relevant subject characteristics between a "restrained" or "unrestrained" attitude towards eating.

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SUBJECTS AND METHODS

Subjects

Fourteen healthy young female subjects participated in the study. Their physical characteristics are presented in Table 1. There were no significant differences between the restrained- and unrestrained-eating subjects with respect to age, height, weight, or percentage body fat. The procedures used in the study were carefully explained to each subject before she gave her consent to participate. The protocol was reviewed and approved by the University of Limburg Ethical Committee.

Attitude Towards Eating

Characterization of restrained- and unrestrained-eating subjects was accomplished by means of scores on psychometric questionnaires. The following two types of psychometric questionnaires were used: the Herman-Polivy (H-P) restraint scale,[12] which is designed to identify dieters and is mainly weight-concerned,[13] and the Three-Factor Eating Questionnaire (TFEQ) of Stunkard and Messick,[14] which is designed to measure successful dieting and is mainly food-concerned.[13] The TFEQ was used to discriminate between "cognitive restraint" and "unrestraint" concerning the scores on the cognitive restraint factor F_1. In the subject population we use at the Department of Human Biology of the University of Limburg in Maastricht, the median of the H-P scores was 15 and of the F_1 scores 9.[13,15,16] Subjects were classified as restrained eaters when the H-P score exceeded 15 or F_1 score exceeded 9; unrestrained-eating subjects had an H-P score no greater than 15 and an F_1 score no greater than 9. From the seven subjects in the present study classified as restrained eaters, one subject was restrained by being food-concerned, four subjects by being weight-concerned, and two subjects by being food- and weight-concerned.

Experimental Design

Subjects were fed to an estimated energy balance by consuming a low-fat (LF) and a HF diet over 3-day intervals. The order of administration of LF and HF diets was randomized. Twelve subjects additionally consumed a mixed (M) diet. The interval between two experimental periods was at least 4 days. During the first 2 days on each dietary regimen, food was provided and consumed at home, and the last day of each period was spent in a respiration chamber. In this chamber, oxygen consumption and carbon dioxide production, and hence the respiratory quotient (RQ), were the main measurements (see below). Urine samples were collected to determine nitrogen excretion and hence calculate

Table 1. Physical Characteristics of the Subjects and Order of Treatment

Subject No.	Age (yr)	Height (m)	Weight (kg)	Percentage Body Fat	Order of Treatment
Restrained					
1	20	1.75	65.5	19.8	LF-HF-M
2	20	1.73	71.1	21.1	LF-HF-M
3	21	1.71	64.5	26.5	LF-HF-M
4	21	1.60	59.5	22.7	HF-LF-M
5	21	1.73	67.2	28.6	HF-LF-M
6	21	1.75	67.7	21.7	LF-HF-M
7	19	1.61	71.3	29.6	LF-HF
Mean	20.4	1.70	66.7	24.3	
SD	0.8	0.06	4.1	3.9	
Unrestrained					
8	20	1.71	80.1	32.0	LF-HF-M
9	22	1.71	68.4	28.6	HF-LF-M
10	19	1.71	69.7	28.9	HF-LF-M
11	19	1.70	57.7	22.2	LF-HF-M
12	24	1.76	62.6	21.0	LF-HF-M
13	20	1.63	61.9	28.4	HF-LF-M
14	20	1.69	65.7	28.0	HF-LF
Mean	20.6	1.70	66.6	27.0	
SD	1.8	0.04	7.2	3.9	

EE and substrate oxidation. EI for the maintenance of energy balance was based on the calculated basal metabolic rate (BMR)[17] of the subjects multiplied by 1.76 on days 1 and 2 (Verboeket-van de Venne and Westerterp, unpublished observations); EI on day 3 while in the respiration chamber equaled 1.29 × BMR.[18]

Diets

The diets were taken as four meals daily, a breakfast at 8:00 AM (20% of daily EI), a lunch at 1:00 PM (25% of EI), a dinner at 6:00 PM (45% of EI), and an evening snack at 8:30 PM (10% of EI). Total EI was the same for the three diets. The LF diet contained 15% of EI as protein, 10% as fat, and 75% as carbohydrate; the M diet contained 15% of EI as protein, 30% as fat, and 55% as carbohydrate; and the HF diet contained 15% of EI as protein, 50% as fat, and 35% as carbohydrate. Macronutrient composition of the diets was calculated using the Dutch food composition table.[19] The food quotient (FQ), defined as the ratio of CO_2 produced to O_2 consumed during the oxidation of a representative sample of the diet,[20] was calculated using the following equations[21]: O_2 consumption (L/d) = (0.966 · protein intake) + (2.019 · fat intake) + (0.829 · carbohydrate intake), and CO_2 production (L/d) = (0.774 · protein intake) + (1.427 · fat intake) + (0.829 · carbohydrate intake), where the intake of protein, fat, and carbohydrate is expressed in grams per day.

Procedures

Subjects weighed themselves (without clothing) on the morning of days 1, 3, and 4 upon rising, after voiding, and before any food or drink consumption using a digital balance (Seca delta, model 707; Vogel & Halke, Hamburg, Germany) accurate to 0.1 kg.

Body composition was assessed once in the morning immediately after the subjects left the respiration chamber, using hydrostatic weighing with direct assessment of lung volume (Volugraph 2000, Bunnik, The Netherlands). The percentage of body fat was calculated using the equation of Siri.[22]

A twenty-four–hour urine sample was collected on day 3 of each dietary period, while subjects were staying in the respiration chamber. Samples were collected in containers with 8 mL H_2SO_4 to prevent nitrogen loss through evaporation; volume and nitrogen concentration were measured subsequently, the latter using a Heraeus analyzer (type CHN-O-Rapid).

Oxygen consumption and carbon dioxide production were measured in a respiration chamber.[23] The chamber was 14 m^3 and furnished with a bed, chair, table, television, radio, telephone, wash bowl, and toilet facilities, and was ventilated with fresh air at a rate of 50 L/min. The ventilation rate was measured with a dry gas meter (Schlumberger, type G6, Meterfabriek Schlumberger, Dordrecht, The Netherlands). The concentration of oxygen and carbon dioxide was measured using a paramagnetic O_2 analyzer (Servomex, type OA 184; Servomex, Crowborough, Sussex, UK) and an infrared CO_2 analyzer (Hartmann & Braun Aktiensgesellschaft, Frankfurt, Germany, type URAS 3G). Ingoing air was analyzed once every 15 minutes, and outgoing air once every 5 minutes. The gas sample to be measured was selected by a computer that also stored and processed the data. The RQ was calculated as the ratio of CO_2 produced to O_2 consumed; EE was calculated from O_2 consumption, CO_2 production, and urinary nitrogen excretion according to the method of Weir.[24] The physical activity of the subjects was monitored by means of a radar system based on the Doppler principle. During the daytime, subjects were allowed to move freely, sit, lie down, study, use the telephone, listen to the radio, and watch television; only sleeping and strenuous exercise were not allowed.

Analysis of Data

The 24-hour RQ and 24-hour EE were calculated from 7:30 AM to 7:30 AM. Urinary nitrogen excretion was determined for the same interval to allow calculation of the nonprotein respiratory quotient (NPRQ). Protein, fat, and carbohydrate oxidations were calculated according to the method of Jéquier et al.[21] The effects of diet composition on the RQ, NPRQ, substrate oxidation, and substrate balance (intake minus oxidation) were analyzed by repeated-measures ANOVA and Scheffé F tests or paired *t* tests. Changes between groups of restrained- and unrestrained-eating subjects on the same diet were tested using ANOVA, with "attitude towards eating" as the grouping factor. Analysis of covariance (ANCOVA) was used to detect differences between restrained- and unrestrained-eating subjects concerning the relationship between fat balance and fat intake. In the text, tables, and figures, data are presented as the mean ± standard error of the mean.

RESULTS

Body mass showed a slight increase (0.2 ± 0.1 kg) over the 2 days in free-living conditions on all three diets. During the subsequent day in the respiration chamber, body weight decreased (0.5 ± 0.1 kg). There were no significant differences in changes of body mass due to the composition of the diet. Over the 3-day intervals, body mass changes were not significantly different from zero.

No statistically significant differences in 24-hour EE between restrained- and unrestrained-eating subjects were observed on the LF, M, and HF diet (Table 2). Garrow[25] stated that an adult is in energy balance when the difference between EI and EE is less than 600 kJ/d. Energy balance was determined by subtracting EE from EI. EI − EE was near zero on all three diets, averaging +86 ± 85 kJ/d (range, −1,583 to +894 kJ/d).

There was a highly significant effect of diet composition on the RQ ($P < .001$). On a LF or M diet, the RQ was

Table 2. Average Daily (24-hour) EE, RQ, NPRQ, and FQ for Restrained- (n = 7) and Unrestrained-Eating (n = 7) Subjects on the Three Diets

	LF		M*		HF	
	Mean	SE	Mean	SE	Mean	SE
Restrained-eating subjects						
24-hour EE (kJ/d)	8,525	182	8,179	216	8,209	214
24-hour RQ	0.908	0.003	0.860	0.008	0.829†	0.004
24-hour NPRQ	0.929	0.003	0.872	0.010	0.835‡	0.005
FQ	0.936	0.000	0.879	0.000	0.820	0.000
Unrestrained-eating subjects						
24-hour EE (kJ/d)	8,698	276	8,649	135	8,604	146
24-hour RQ	0.898	0.009	0.857	0.005	0.816†	0.004
24-hour NPRQ	0.913	0.011	0.868	0.006	0.818‡	0.004
FQ	0.936	0.000	0.878	0.000	0.820	0.000

*n = 6.
†Restrained *v* unrestrained eaters, $P < .05$.
‡Restrained *v* unrestrained eaters, $P < .05$.

significantly lower than the FQ ($P < .001$), whereas the RQ was not different from the FQ on a HF diet (Fig 1). Respiratory data for restrained- and unrestrained-eating subjects are presented in Table 2. The RQ and NPRQ were significantly lower for unrestrained-eating subjects on the HF diet. No statistically significant differences in the RQ and NPRQ between restrained- and unrestrained-eating subjects were observed on the LF or M diet.

The mean intake, oxidation, and balance (ie, intake − oxidation) of protein, carbohydrate, and fat on the LF, M, and HF diet are presented in Fig 2. There was no significant effect of diet composition on protein oxidation. Protein balance was near zero for both the HF diet (−0.8 ± 1.9 g/d, NS) and the M diet (−0.5 ± 2.1 g/d, NS), and was significantly positive on the LF diet (+7.2 ± 2.7 g/d, $P < .05$). Oxidation of carbohydrate increased significantly with increasing dietary carbohydrate content ($P < .001$). Carbohydrate balance was positive on the LF diet (+44.3 ± 9.0 g/d, $P < .001$) and the M diet (+35.7 ± 6.1 g/d, $P < .001$), but not on the HF diet (+0.2 ± 4.2 g/d, NS). Fat oxidation increased significantly with increasing dietary fat ($P < .001$), presumably because the concomitant decrease in dietary carbohydrate intake led to lower insulin levels, thereby permitting more fat to be

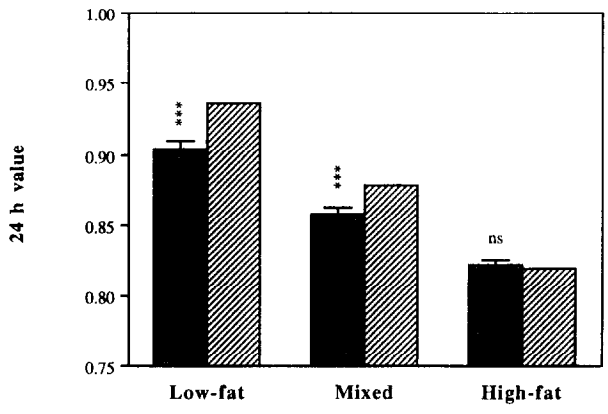

Fig 1. Mean RQ (■) and FQ (□) over 24 hours under different feeding conditions (n = 12). ***$P < .001$; ns, no significance.

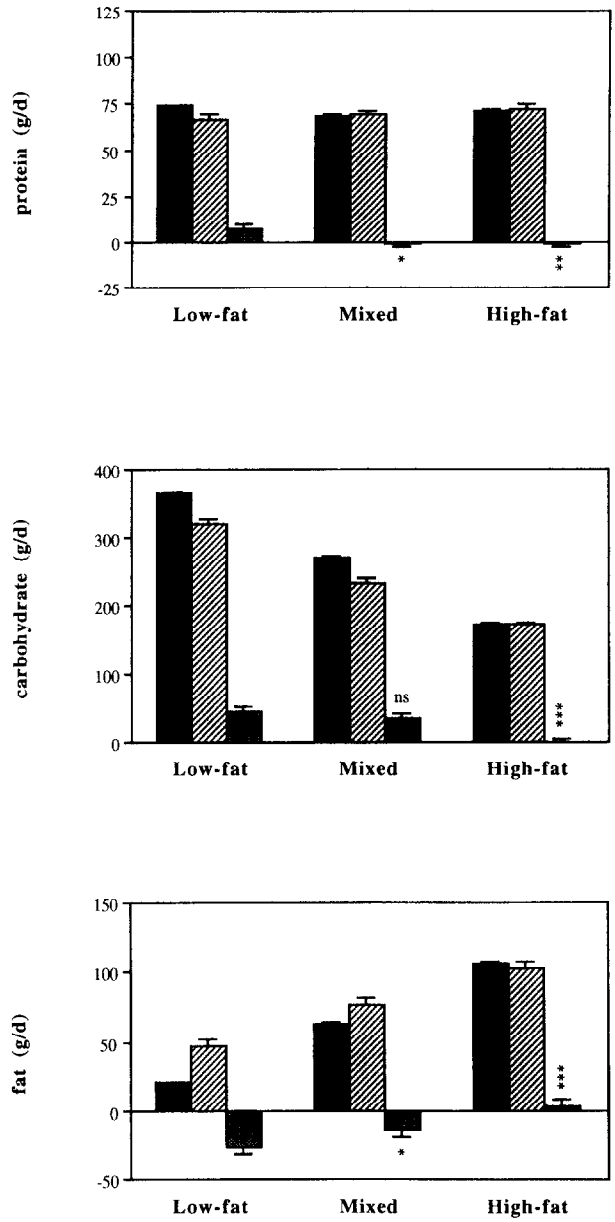

Fig 2. Mean intake (■), oxidation (□), and balance (□) of protein, carbohydrate, and fat over 24 hours under different feeding conditions (n = 12). Statistical significance comparing substrate balance on the M and HF diets with the LF diet: ***$P < .001$; **$P < .01$; *$P < .05$; ns, no significance.

oxidized. The difference between fat intake and fat oxidation was smallest on the HF diet (+3.9 ± 4.4 g/d, NS) compared with the M diet (−14.0 ± 4.6 g/d, $P < .05$) and the LF diet (−26.2 ± 4.5 g/d, $P < .001$).

Protein oxidation was significantly lower for unrestrained-eating subjects on the LF diet, resulting in a more positive protein balance compared with restrained-eating subjects (Table 3). There were no significant differences between restrained- and unrestrained-eating subjects with respect to oxidation and overall balance of carbohydrate on the LF, M, or HF diet (Table 4). Unrestrained-eating subjects had a significantly increased rate of fat oxidation while on the HF diet (Table 5). The fat balance on the HF diet was

Table 3. Protein Intake, Oxidation, and Balance (intake − oxidation) for Restrained- (n = 7) and Unrestrained-Eating (n = 7) Subjects on the Three Diets

	LF		M*		HF	
	Mean	SE	Mean	SE	Mean	SE
Restrained-eating subjects						
Protein intake	73.2	0.0	67.9	0.0	70.9	0.0
Protein oxidation	71.1†	1.7	70.8	1.6	74.2	1.6
Protein balance	2.1‡	1.7	−2.9	1.6	−3.3	1.6
Unrestrained-eating subjects						
Protein intake	74.3	1.1	69.4	1.5	71.8	0.9
Protein oxidation	61.7†	3.9	67.6	4.0	69.6	4.2
Protein balance	12.6‡	3.5	1.8	3.9	2.2	3.6

NOTE. Data are expressed as grams per day.
*n = 6.
†Restrained *v* unrestrained eaters, $P < .05$.
‡Restrained *v* unrestrained eaters, $P < .05$.

Table 5. Fat Intake, Oxidation, and Balance (intake − oxidation) for Restrained- (n = 7) and Unrestrained-Eating (n = 7) Subjects on the Three Diets

	LF		M*		HF	
	Mean	SE	Mean	SE	Mean	SE
Restrained-eating subjects						
Fat intake	20.8	0.0	62.6	0.0	106.0	0.0
Fat oxidation	41.7	2.8	73.2	6.8	94.7†	5.5
Fat balance	−20.9	2.8	−10.6	6.8	11.3‡	5.5
Unrestrained-eating subjects						
Fat intake	21.2	0.4	64.1	1.5	108.0	2.0
Fat oxidation	54.1	7.1	81.4	5.9	111.2†	3.1
Fat balance	−32.9	7.0	−17.3	6.5	−3.2‡	3.9

NOTE. Data are expressed as grams per day.
*n = 6.
†Restrained *v* unrestrained eaters, $P < .05$.
‡Restrained *v* unrestrained eaters, $P = .052$.

significantly more positive for the restrained-eating subjects than for the unrestrained-eating subjects ($P = .052$). By plotting fat balance as a function of fat intake, we showed that the lines obtained for restrained-eating subjects (fat balance = 0.38 · fat intake − 30.5; $df = 17, r = .71, P < .01$) and unrestrained-eating subjects (fat balance = 0.34 · fat intake − 39.1; $df = 17, r = .64, P < .01$) are different with respect to the intercept (ANCOVA, F value = 5.46, $P < .05$). This means that there is a statistically significant trend for increased fat retention in the restrained-eating subjects.

The effect of dietary fat and carbohydrate on substrate balance for restrained- and unrestrained-eating subjects is summarized in Table 6. For unrestrained-eating subjects, protein balance was significantly more positive on the LF diet (compared with the HF diet), whereas diet composition had no effect on protein balance in restrained-eating subjects. Carbohydrate balance was significantly (more) positive and fat balance (more) negative on the LF diet both for restrained- and unrestrained-eating subjects.

DISCUSSION

In the present study, we investigated the relationship between substrate intake and substrate oxidation under different feeding conditions by comparing the 24-hour RQ, reflecting the fuel mixture oxidized, with the mean FQ, based on the nutrient composition of the diet. In conditions of prolonged deviations from the energy balance, a subject stores or mobilizes nearly all energy in the form of body fat. Over intervals longer than 24 hours, a RQ greater than the FQ indicates that fat oxidation is less than fat intake, and a RQ less than the FQ indicates mobilization of energy from body fat stores. In the present study, we observed a highly significant effect of diet composition on the RQ, with the lowest value on the HF diet and the highest on the LF diet (Fig 1). The difference between the RQ and FQ was smallest on the HF diet (RQ − FQ = +0.003 ± 0.003 *v* −0.031 ± 0.005 on the LF diet; $P < .001$), reflecting a closer correspondence of substrate oxidation with substrate intake. Other studies investigating the relationship between dietary fat and carbohydrate and substrate utilization also report a greater difference between the RQ and FQ when a LF (high-carbohydrate) diet is consumed.[8,9,26,27] There are two possible reasons for this finding. First, the experimental HF diet appears to be the one most closely resembling the subjects' habitual diet. Note that a dietary fat content of 40% of the total EI is more or less "normal" in Western

Table 4. Carbohydrate Intake, Oxidation, and Balance (intake − oxidation) for Restrained- (n = 7) and Unrestrained-Eating (n = 7) Subjects on the Three Diets

	LF		M*		HF	
	Mean	SE	Mean	SE	Mean	SE
Restrained-eating subjects						
Carbohydrate intake	360.7	0.0	266.0	0.0	170.6	0.0
Carbohydrate oxidation	318.7	6.9	227.4	11.3	176.7	3.1
Carbohydrate balance	42.0	6.9	38.6	11.3	−6.1	3.1
Unrestrained-eating subjects						
Carbohydrate intake	366.4	5.7	271.7	5.7	174.1	3.5
Carbohydrate oxidation	310.1	15.1	238.8	4.9	166.3	6.0
Carbohydrate balance	56.3	16.5	32.9	5.6	7.8	6.2

NOTE. Data are expressed as grams per day.
*n = 6.

Table 6. Substrate Balances (intake − oxidation) and Energy Balance (EI − EE) for Restrained- (n = 7) and Unrestrained-Eating (n = 7) Subjects on the LF and HF Diet

	LF		HF	
	Mean	SE	Mean	SE
Restrained-eating subjects				
Protein balance (g/d)	2.1	1.7	−3.3	1.6
Carbohydrate balance (g/d)	42.0*	6.9	−6.1	3.1
Fat balance (g/d)	−20.9†	2.8	11.3	5.5
Energy balance (kJ/d)	−4‡	182	306	214
Unrestrained-eating subjects				
Protein balance (g/d)	12.6§	3.5	2.2	3.6
Carbohydrate balance (g/d)	56.3‖	16.5	7.8	6.2
Fat balance (g/d)	−32.9¶	7.0	−3.2	3.9
Energy balance (kJ/d)	−42	270	70	156

*LF *v* HF diet, $P < .001$.
†LF *v* HF diet, $P < .001$.
‡LF *v* HF diet, $P < .05$.
§LF *v* HF diet, $P < .05$.
‖LF *v* HF diet, $P < .01$.
¶LF *v* HF diet, $P < .01$.

societies. Furthermore, the overall energy balance can influence whether the body stores excess fuels in the form of body fat or mobilizes energy from body fat. This does not appear to be the case in the present study, where we observed a difference of less than 600 kJ/d between EI and EE, indicating that subjects were in energy balance during the third day of the study. Energy balance was not significantly different on the three diets ($EI-EE_{LF}$, -23 ± 156 kJ/d; $EI-EE_{M}$, $+95 \pm 157$ kJ/d; $EI-EE_{HF}$, $+188 \pm 131$ kJ/d).

The RQ and NPRQ were significantly higher in restrained-eating subjects on a HF diet, as compared with unrestrained-eating subjects. This suggests a relatively lower oxidation ratio of fat to carbohydrate for restrained eaters, at least on a HF diet (Tables 4 and 5). These findings are in agreement with the results of Hill,[28] where it was reported that obesity-susceptible individuals have a limited ability to rapidly adjust fat oxidation in response to a HF intake. Zurlo et al[29] associated a low oxidation ratio of fat to carbohydrate with a higher risk of subsequent body weight gain, independent of a low EE.

The results on intake, oxidation, and overall balance of protein, carbohydrate, and fat (Fig 2, Table 6) also showed that substrate oxidation is closer to substrate intake on a HF diet, as indicated by the size of the substrate balances. Alternatively, a LF diet results in a (more) negative fat balance, reflecting a greater fat oxidation than intake. This suggests that there is (more) net endogenous fat oxidation on a LF than HF diet, implicating a LF diet as a useful tool in the treatment of obesity.

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