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ORIGINAL CONTRIBUTION

Short-term isocaloric manipulation of carbohydrate intake: effect on subsequent ad libitum energy intake

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Abstract
Background Isocaloric manipulation of carbohydrate or fat intake could alter subsequent *ad libitum* food intake.
Methods In a controlled inpatient study, we investigated whether isocaloric manipulation of carbohydrate or fat would alter subsequent *ad libitum* energy intake. Eighteen non-diabetic subjects (age range 19–53 years.; 15 M/3F; % body fat 38.5 ± 9.1 (mean ± SD)) were fed for 3 days an isocaloric high-carbohydrate diet (HC; 60% carbohydrate, 20% fat, 20% protein) and a high-fat diet (HF; 50% fat, 30% carbohydrate, 20% protein) in random order each followed by 3 days of *ad libitum* food intake.
Results There were no differences in mean daily energy intake (EI) following each diet (HC vs. HF: 4,811 ± 1,190 vs. 4,823 ± 1,238 kcal/d; $P = 0.7$) or in the percent of weight maintenance energy needs (%EN-WM; 173 ± 41 vs. 173 ± 46%, $P = 0.5$). However, the individual difference in EI between the HF versus HC diet (ΔEI) both on day one and over the 3 days of each *ad libitum* period was negatively associated with % body fat (%BF) and waist circumference (day 1: ΔEI vs. %BF, $r = -0.49$, $P = 0.04$; mean day 1–3 kcal ΔEI vs. %BF, $r = -0.66$, $P = 0.003$, and ΔEI vs. waist, $r = -0.65$, $P = 0.004$).
Conclusions A short-term isocaloric HC diet did not result in overall lower EI compared with a HF diet in the same individuals. However, we did find that increasing body fat was associated with less decline in EI following the HC versus HF diet indicating that increasing adiposity is associated with altered regulation of EI in response to macronutrient changes.

Keywords Carbohydrates · Adiposity · Energy intake · High-fat diet · Clinical nutrition

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Introduction

Obesity is a result of a chronic energy imbalance (i.e. energy intake exceeding energy expenditure) [1]. Twenty-four-hour energy expenditure (EE) appears unlikely to be the primary cause of this energy imbalance [2, 3]. Therefore, energy intake (EI) appears to be the more important component of this balance equation and elucidating the mechanisms that control food intake is crucial. For instance, dietary macronutrients can influence both the satiation signals (meal duration) and satiety signals (inter-meal interval) [4]. There is evidence for both higher proportions of fat or carbohydrate influencing subsequent energy intake. Fat in the intestine appears to generate potent satiety signals [5] but this does not translate to decreased energy intake in those given a high-fat diet. In fact, the propensity of fat-rich diets to induce overeating has been shown in short- and long-term studies [6–9]. In addition, consumption of a higher fat to carbohydrate ratio leads to higher calorie intake compared to consuming a lower fat to carbohydrate ratio [10].

It has been hypothesized that carbohydrate balance regulates subsequent energy intake. Flatt [11] reported a

negative association between carbohydrate balance on one day and food intake on a subsequent day in mice. He proposed the glycogenostatic model suggesting that the body's storage capacity for carbohydrate is limited and approximately equal to the amount that is both ingested and oxidized per day, whereas the storage capacity for body fat greatly exceeds the daily flux. Thus, it might be possible that preloading with carbohydrate (thereby increasing glycogen stores) would change subsequent EI. However, studies investigating this in humans have been mixed. Stubbs et al. [12] did not find any difference in ad libitum food intake after one day of an isocaloric carbohydrate depletion compared to a control diet. Snitker et al. found that carbohydrate balance on day 1 explained only 9% (although this was significant) of the variance of the subsequent day's EI [13]. In support of the glycogenostatic theory, higher carbohydrate oxidation and lower carbohydrate balance measured during energy balance in a respiratory chamber predicted subsequent ad libitum food intake [14]. Carbohydrate balance during a high-carbohydrate diet predicted weight and fat mass gain over 4 years [15].

The aim of the present study was to test the effect of carbohydrate intake on subsequent food intake. In a crossover study, we investigated whether short-term (3 days) isocaloric manipulation of dietary macronutrient content (selectively increasing fat or carbohydrate) would alter subsequent ad libitum EI.

Research design and methods

Subjects

Twenty subjects participated in this study; two were excluded from data analysis because of non-adherence to the required diets. Before participation, volunteers were fully informed of the nature and purpose of the study, and written informed consent was obtained. The experimental protocol was approved by the Institutional Review Board of the National Institute of Diabetes and Digestive and Kidney Diseases (ClinicalTrials.gov Identifier: NCT00342732). All subjects were found to be free of disease according to physical examination, medical history, and laboratory testing.

Study protocol

Subjects were admitted for 21–25 days to the Clinical Research Unit of the National Institute of Diabetes and Digestive and Kidney Diseases in Phoenix, Arizona. On admission, volunteers were provided a standard weight-maintaining (WM) diet containing 50% of calories as carbohydrate, 30% as fat, and 20% as protein. The WM diet on the metabolic ward was calculated for each subject on the basis of weight and sex: for men, energy intake (EI) on WM diet = 9.5 × weight (in kg) + 1,973 kcal/d; for women, WM = 9.5 × weight (in kg) + 1,745 kcal/d [16]. The subjects were weighed daily, and food intake was adjusted to maintain body weight ±1%. During their stay, volunteers are asked not to exercise and to restrict their activities to those available on the research unit. After at least 3 days, volunteers underwent a 2-h 75-g oral glucose tolerance test (after a 12-h overnight fast). Only non-diabetic subjects, according to the World Health Organization diagnostic criteria [17], participated in the present study. Body composition was measured by dual-energy X-ray absorptiometry (DXA) using a total body scanner (DPX-L; Lunar Corp, Madison, WI). Percentage of body fat (%BF), fat mass (FM), and fat-free mass (FFM) were calculated as previously described [18].

During day 5 of the study on WM diet, subjects spent 24 h in the respiratory chamber (detailed below) and then, in a randomized crossover fashion, subjects completed 3 days of isocaloric high-carbohydrate (HC; 60% of calories as carbohydrate, 20% as fat, and 20% as protein) or high-fat feeding (HF; 50% of calories as fat, 30% as carbohydrate, and 20% as protein). On the 3rd day of the experimental diet, half of the volunteers spent 24 h in the respiratory chamber. After each of the intervention diets, all subjects were asked to self-select all their food from a computer-operated vending machine system for 3 days (detailed below). After the vending period, subjects had 3 more days on the weight-maintaining diet (wash-out) and then completed the other intervention diet (high carbohydrate/fat) followed by 3 days of self-selection of food from the vending machine (Fig. 1).

Ad libitum food intake

The measurement of ad libitum food intake by an automated food-selection system has been previously described, validated, and tested for reproducibility [14, 19, 20]. Briefly, the automated food-selection system is made up of a refrigerated vending machine (model 3,007; U-Select-It, Des Moines, IA). Forty food items were made available to the subjects on each of the 3 days consisting of foods to which the subject had assigned an intermediate high hedonic rating on a food-preference questionnaire. In addition, a core group of condiments and foods was provided to each subject on each day. The same selection was offered each day and accommodated the appropriateness of certain foods for breakfast, lunch, dinner, and evening snacks. The subjects had unrestricted access to the vending machine for 23.5 h/d and were asked to follow their typical eating pattern as closely as possible. Daily energy intake (EI; expressed as kcal/d) and protein, fat, and carbohydrate

intakes were calculated from the actual weights of the food and condiments consumed by using the Food Processor Diet Analyzer Program (Food Processor SQL Edition, Version 9.8.0, ESHA Research, Salem, Oregon). The database was modified to reflect the nutrient content of specific food items as indicated by the manufacturer.

Respiratory chamber

Measurement of energy expenditure (EE) and substrate oxidation were performed in a respiratory chamber [21]. In brief, volunteers entered the chamber at 08:00 AM after having fasted overnight and eating breakfast and remained therein for 23.25 h. Further meals were provided at 11:00, 16:00, and 19:00 h (evening snack). For the WM chambers, only 80% of EN-WM (but at the correct macronutrient composition) on the metabolic ward were provided in the respiratory chamber, as previously described [21]. For the HF and HC chambers, energy intake as calculated for the WM diet was provided. Oxygen and carbon dioxide concentrations were measured using a Siemens analyzer (OXYMAT 6; Siemens GmbH, Karlsruhe, Germany) and ABB analyzer (AO 2020; ABB Automation, GmbH, Frankfurt am Main, Germany); O_2 and CO_2 concentrations from the last 8 s of each minute were used to calculate the amount of VO_2 consumed and VCO_2 produced as previously described [21]. Spontaneous physical activity (SPA) was detected by radar sensors and expressed as the percentage of time over the 24-h period in which activity was detected. Twenty-four-hour energy expenditure (24-h EE) was calculated from previously derived equations [22]. Propane burn tests to determine the accuracy of the energy expenditure measurement demonstrated mean recoveries of $\pm 1\%$ for O_2 and CO_2. The 24-h respiratory quotient (RQ) was calculated as the ratio of 24-h carbon dioxide production and 24-h oxygen consumption. The substrate balances were calculated from the 24-h energy intake, 24-h EE, and 24-h RQ. Carbohydrate and fat oxidation rates were calculated from the 24-h RQ, accounting for protein oxidation (calculated from the measurement of 24-h urinary nitrogen excretion) [23].

Analytic measurements

Plasma glucose concentrations were measured by the glucose oxidize method (Beckman Instruments, Fullerton, CA).

Statistical analysis

Power calculations for this study were based on previous studies of food intake using this vending machine model [14]. Assuming a mean ad libitum energy intake of 4,498 ± 1,368 kcal/d and a standard mean of the difference of 611 kcal, our crossover design with $n = 20$ had a power of 0.88, at an alpha of 0.05 to detect a 10% reduction in EI following the HC diet. With $n = 18$, the power dropped only slightly to 0.84 to detect a 10% reduction.

Statistical analyses were performed by using the procedures of the SAS statistical package (version 8.2; SAS Institute Inc, Cary, NC). Unless otherwise specified, all data are expressed as means ± SDs. The general, anthropometric, and metabolic characteristics in Tables 1 and 2 were evaluated using Student's t test or chi-square analyses for continuous and categorical variables, respectively. All subjects served as their own controls. Comparison between EI following each diet was compared by using a paired t test. Pearson correlations were used to examine associations between variables. Using general linear models, 24-h EE was adjusted for age, sex, FFM, FM, and spontaneous physical activity [22], whereas the 24-h RQ was adjusted for age, sex, energy balance, and %BF [24]. Similarly, general linear models were used to adjust 24-h carbohydrate (24-h Carbox) and fat oxidation rates (24-h Lipox) and 24-h carbohydrate balance for age, sex, %BF, and energy balance [24].

Results

Baseline variables

General, anthropometric, and metabolic characteristics of the study population are shown in Table 1. Age, body weight, fasting or 2-h plasma glucose did not differ by sex, but, as previously reported [20, 25], women had greater %BF, and higher BMI and waist circumference than did men. Thirteen subjects started with the HC diet and five subjects had the HF diet first (more subjects who started with the HF diet failed to complete the study).

In general and as previously described in this model [13], volunteers overate during the ad libitum feeding from the vending machines regardless of prior dietary intervention (percent of standard weight maintenance energy needs (%EN-WM): 173 ± 41% after HC diet and 173 ± 46% of EN-WM after HF diet, $P = 0.5$).

Effect of high-carbohydrate versus high-fat diet on energy intake

There were no differences in day 1, 2, 3, or in the mean daily energy intake (EI) during the ad libitum period after 3-d HC versus HF diet calculated as kcal/d (Table 2) or as weight of food (Fig. 2). There was also no significant difference in the mean daily protein, carbohydrate, and fat intake during the ad libitum period (Fig. 2). Despite more people receiving the HC diet first, there was no effect of diet

Table 1 General anthropometric and body composition parameters of study subjects. Data are expressed as mean ± SD (with ranges)

	All ($n = 18$)	Men ($n = 15$)	Women ($n = 3$)
Ethnicity (C/N/A)	10/7/1	9/5/1	1/2/0
Age (years)	38.5 ± 9.1	38.9 ± 10.4 (19–53)	34.5 ± 2.2 (32–37)
Body weight (kg)	97.5 ± 17.9	89.9 ± 19.5 (65–131)	95 ± 12 (91–107)
Body mass index (kg/m^2)	31.1 ± 6.8	29.7 ± 6.9 (24–43)	36.7 ± 3.0 (34–39)
Body fat (%)*	30.9 ± 10.0	27.5 ± 8.0 (13–40)	47.3 ± 3.1 (42–45)
Fat mass (kg)	28.7 ± 12.5	25.8 ± 11.7 (8–51)	43.0 ± 3.7 (39–45)
Fat-free mass (kg)	61.5 ± 10.4	63.4 ± 9.8 (53–80)	51.5 ± 8.6 (46–61)
Waist circumference (cm)	104.8 ± 16.0	100 ± 16 (80–137)	121 ± 6 (114–126)
Fasting plasma glucose (mmol/l)	5.20 ± 0.50	5.28 ± 0.5 (4.72–6.22)	4.89 ± 0.56 (4.25–5.17)
2-h Plasma glucose (mmol/l)**	6.84 ± 1.81	6.94 ± 2.0 (4.39–11.0)	6.28 ± 1.28 (4.89–7.39)

C Caucasians, *N* native Americans, *A* Afro-Americans

* Measured by DXA

** Measured during oral glucose tolerance test

Table 2 Energy metabolism data and mean daily energy intake (EI)

Energy metabolism	Diet			*P* value	
	WM ($n = 13$)	HC ($n = 9$)	HF ($n = 7$)	HC versus WM	HF versus WM
24-h Energy expenditure (kcal/d)[a]	2,275 (2,198, 2,353)	2,335 (2,239, 2,431)	2,296 (2,186, 2,405)	NS	NS
24-h respiratory quotient[a]	0.846 (0.82, 0.873)	0.880 (0.852, 0.908)	0.788 (0.759, 0.818)	0.06	0.006
Carbohydrate oxidation (kcal/d)[a]	945 (709, 1,180)	1,277 (1,027, 1,526)	510 (213, 806)	0.04	0.03
Lipid oxidation (kcal/d)[a]	826 (616, 1,036)	611 (388, 833)	1,356 (1,092, 1,621)	0.1	0.003
Protein oxidation (kcal/d)[a]	341 (271, 410)	391 (316, 464)	420 (332, 508)	NS	NS
Carbohydrate balance (kcal/d)[a]	381 (116, 646)	186 (−95, 467)	126 (−207, 461)	NS	NS
Fat balance (kcal/d)[a]	−173 (−428, 80.4)	−12 (−282, 257)	−66 (−387, 254)	NS	NS
Protein balance (kcal/d)[a]	107 (24, 161)	93 (24,163)	74 (−8,156)	NS	NS
Energy intake in chamber					
Total (kcal/d)	2,279 ± 174	2,620 ± 196	2,690 ± 338		
Carbohydrate (kcal/d)	1,139 ± 89	1,563 ± 190	792 ± 109		
Fat (kcal/d)	681 ± 51	571 ± 89	1,353 ± 145		
Protein (kcal/d)	455 ± 34	523 ± 46	548 ± 86		

Energy intake on floor	WM	HC	HF	Ad libitum EI after HC	Ad libitum EI after HF
Total (kcal/d)*	2,806 ± 201	2,848 ± 196	2,792 ± 210	4,811 ± 1,190	4,823 ± 1,238
Carbohydrate (kcal/d)*	1,403 ± 101	1,678 ± 130	829 ± 70	2,429 ± 591	2,417 ± 614
Fat (kcal/d)*	842 ± 60	612 ± 104	1,387 ± 96	1,847 ± 580	1,877 ± 575
Protein (kcal/d)*	561 ± 40	558 ± 46	576 ± 49	657 ± 262	609 ± 159

* EI data are expressed as mean ± SD. Effect of the diet on ad libitum EI was evaluated by paired *t* test; *NS* not significant, *WM* weight-maintaining, *HC* high carbohydrate, *HF* high fat

[a] Twenty-four-h energy expenditure adjusted for age, sex, fat mass, and fat-free mass, and physical activity; 24-h RQ, carbohydrate and lipid oxidation, and carbohydrate balance adjusted for age, sex, %BF and energy balance in linear regression models and are presented as least-squares means (95% CI). Carbohydrate, fat, and protein balances were based on $n = 13$, 8, and 7 individuals for the WM, HC, and HF diets, respectively

order on ad libitum food intake. In addition, adjustment for sex also did not change our results (data not shown).

Consistent with the similar calorie intake, we found a significant ($P < 0.001$) increase in body weight during 3 days of ad libitum EI and the increase was similar after each diet (1.6 ± 1.2 kg after HC diet and 1.3 ± 1.2 kg after HF diet, $P = 0.1$).

As the effect of carbohydrate stores might be short lived, we investigated the first-meal initiation, first-meal energy intake, and cumulative energy intake on day one of each vending machine period in particular. The time of the initiation of the first meal on day 1 of the vending period was comparable after both HF and HC diets (at 08:00 ± 0.8 h after HC and 08:00 ± 0.7 h after HF diet). Furthermore, there was no significant difference in energy intake of the first meal consumed (1,263 ± 572 kcal after HC diet and 1,434 ± 940 kcal after HF diet). Cumulative energy and macronutrient intake over the first day of the ad libitum

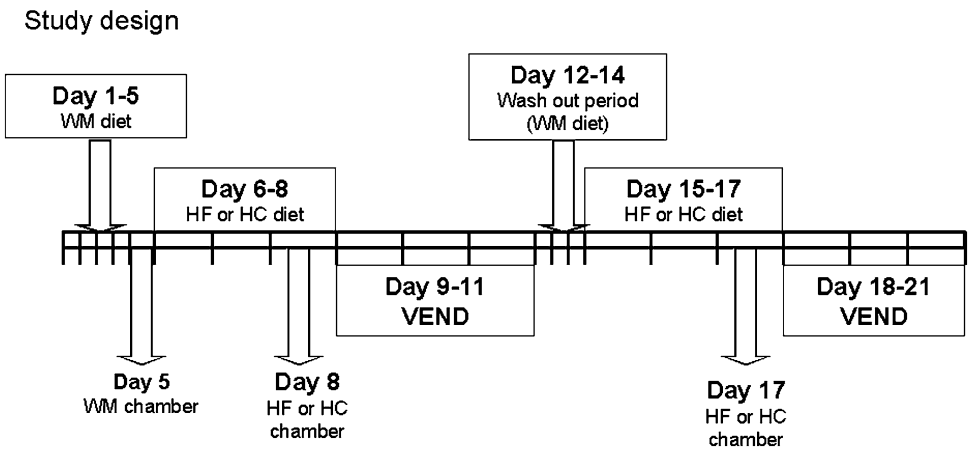

Fig. 1 Study design. *WM* weight-maintaining, *HF* high fat, *HC* high carbohydrate, *VEND* ad libitum food intake from the automated vending machine

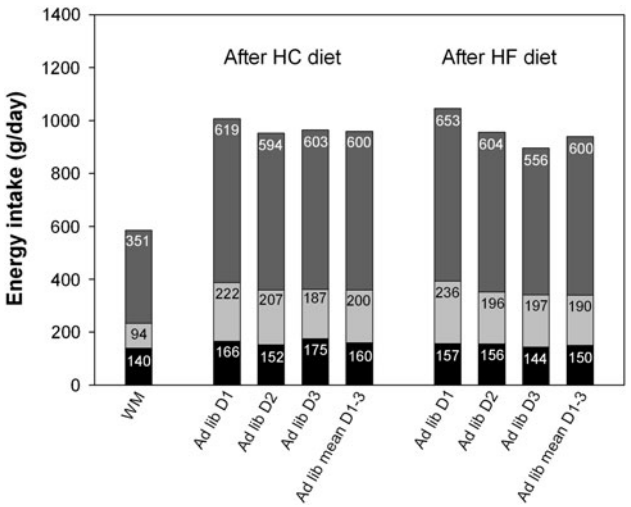

Fig. 2 Daily energy and macronutrient intakes in g/day. *WM* weight-maintaining diet, Day 1, 2, 3, and mean day 1–3 of ad libitum energy intake after high-carbohydrate (HC) and high-fat (HF) diet. The differences in ad libitum EI were evaluated by paired Student *t* test. Protein ■, fat □, carbohydrate ▩

feeding did not differ after either HC vs. HF feeding (Fig. 3).

Association of difference in energy intake after high-fat versus high-carbohydrate diet with adiposity

Although the mean of the individual differences in EI after each diet was not significantly different from zero, we did find a negative association between the difference in ad libitum EI after HF vs. HC (calculated as HF kcals-HC kcals) on day 1 and %BF ($r = -0.490$, $P = 0.04$; Fig. 4). Similarly, there was a strong negative association between the difference in ad libitum mean day 1–3 EI (HF-HC diet) and %BF ($r = -0.660$, $P = 0.003$) and also with waist circumference ($r = -0.653$, $P = 0.004$, respectively; Fig. 4). Age was not associated with the difference in ad libitum EI (data not shown).

Energy metabolism

Data from the respiratory chamber were available only in 13 subjects on the WM diet and in fewer subjects on the intervention diets (HC, $n = 8$ and HF, $n = 7$) (Table 2). Twenty-four-hour EE adjusted for age, sex, fat mass, fat-free mass, and SPA on the 3rd day of each intervention diet was not affected by diet. As expected, the 24-h RQ adjusted for age, sex, %BF, and energy balance was higher on the HC than HF diet, consistent with changes in 24-h carbohydrate oxidation and fat oxidation. Carbohydrate oxidation over 24 h adjusted for age, sex, %BF, and energy balance increased during the HC diet in comparison with the WM diet and was lower on the HF diet versus the WM diet. Lipid oxidation over 24 h adjusted for age, sex, %BF, and energy balance was lower on the HF vs. WM diet. There was no difference in 24-h carbohydrate, fat, or protein balance adjusted for age, sex, %BF, and energy balance between the different diets. Neither adjusted 24-h RQ, 24-h carbohydrate and lipid oxidation nor carbohydrate balance was associated with subsequent food intake in this small sample.

Discussion

The present study tested if short-term (3 days) isocaloric macronutrient manipulation would affect subsequent ad libitum energy intake. In the 18 subjects who completed the study, despite a substantial difference in carbohydrate intake during each diet, there was no difference in day 1 or in the mean 3 days total daily ad libitum energy, carbohydrate, and fat intake or in the time of the first meal after each diet. However, we did find that the individual difference in day 1 and also the mean day 1–3 ad libitum EI in the HF versus HC diet was strongly correlated with adiposity.

The main objective of the study was to investigate whether isocaloric macronutrient manipulation had any

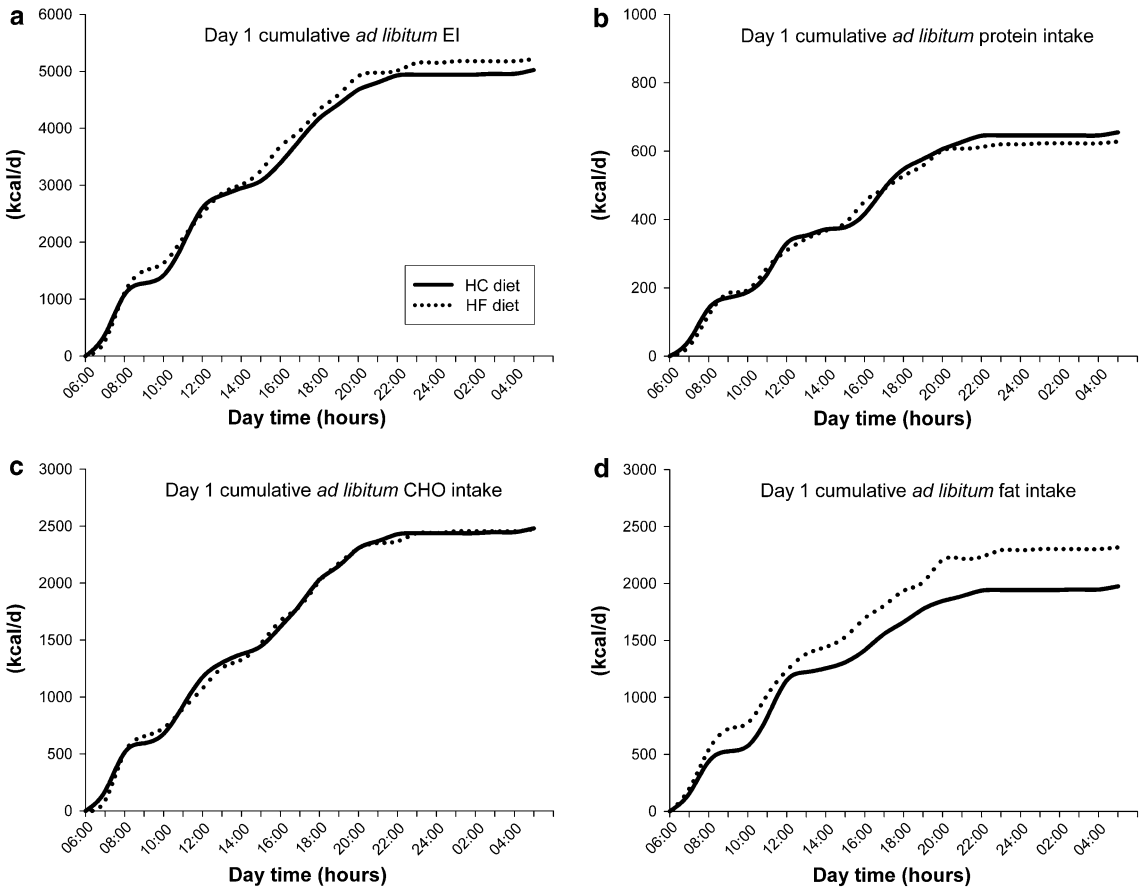

Fig. 3 Cumulative day 1 ad libitum total (**a**), protein (**b**), carbohydrate (**c**), and fat (**d**) EI after isocaloric high-carbohydrate (HC; *solid line*) and high-fat (HF; *dash line*) diet (the ad libitum EI start at 0600 AM and ended the next day at 0500 AM)

effect on subsequent energy intake. If Flatt's [11] glycogenostatic model is correct, higher EI (at least in the short term) would be expected after a high-fat diet, because of the need to replete glycogen stores. Previous attempts to investigate this hypothesis have yielded mixed results. Sparti et al. [26] reported higher EI following a high-fat diet compared to a high-carbohydrate or low-carbohydrate energy deficit diet. However, Stubbs et al. found that ad libitum energy intake did not differ after 1 day of isocaloric low-carbohydrate versus a control diet, although carbohydrate balance was a small but significant determinant of the next day's EI accounting for 5.5% of the variance [12]. Snitker et al. reported that short-term (3 day) high-carbohydrate treatment (diet: 75% of energy intake as carbohydrate plus 150 g of glucose in intravenous infusion during first two nights) or low-carbohydrate treatment (diet: 10% of energy intake as carbohydrate plus isocaloric isoosmolar intravenous infusion of fat emulsion during first two nights) did not result in differences in ad libitum energy intake despite a significant difference in muscle glycogen content [13]. They did not measure the liver glycogen content directly but it is very likely that the two treatments created drastic differences in whole body (in particular hepatic) glycogen content between the two treatments. Covert manipulation of the ratio of dietary fat to carbohydrate also did not alter subsequent energy consumption [13, 14]. The results of our study are consistent with those demonstrating a lack of difference in EI or weight of the food during ad libitum food intake after either diet.

Subjects with higher carbohydrate oxidation would tend to have a lower carbohydrate balance (thus theoretically depleting their glycogen stores) and therefore would be expected to eat more total calories. Pannacciulli et al. [14] found that higher 24-h carbohydrate oxidation and lower carbohydrate balance on a regular weight-maintaining diet predicted subsequent ad libitum food intake. On the other hand, Snitker et al. [13] found significant increases in 24-h RQ after high-carbohydrate treatment, but no effect on subsequent EI, indicating that short-term imbalances in glycogen stores are reestablished not by adjustment of energy intake, but by adjustment of macronutrient oxidation rates (by increasing carbohydrate oxidation on the HC diet). We assumed that the average difference in

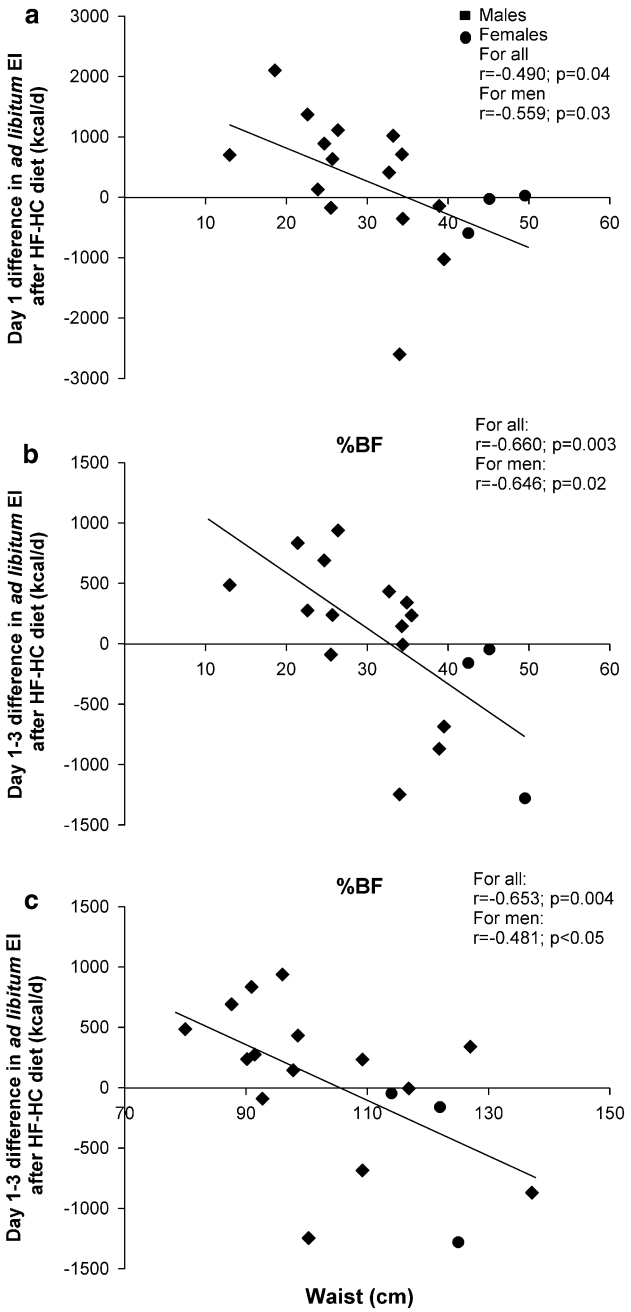

Fig. 4 Relationship between the difference in ad libitum energy intake (EI) after high fat (HF) vs. high-carbohydrate (HC) diet and % of body fat (%BF) on a day 1 (**a**), the relationship between the difference in mean day 1–3 ad libitum (EI) after HF vs. HC diet and %BF (**b**), and waist circumference (**c**). The Pearson *r* value was calculated and a negative correlation was statistically significant when $P < 0.05$

carbohydrate intake created in our current study ($\sim 140 \pm 20$ g) would have had an impact on hepatic glycogen content, but we found that this did not impact subsequent EI. We must acknowledge that carbohydrate balance as measured in the metabolic chambers in a limited number of volunteers was not significantly different on the HC compared to the HF diet. This is due to a more rapid increase in carbohydrate oxidation compared to intake and certainly could explain why energy intake is not as responsive to these macronutrient changes. While our results may raise some questions about Flatt's hypothesis, they also broach issues about how best to test his glycogenostatic model. In addition, the relatively short diet periods may not have been long enough for lipid or carbohydrate oxidation to fully adapt to the changes. Longer periods on each diet may have produced differing results. However, shorter periods also may reflect more "real world" changes in diet from day to day.

Of great interest is that although we found no difference in ad libitum energy intake following each diet, we did find a negative association between the difference in total energy intake after the HF vs. HC diets both at day 1 and over the 3 days of the ad libitum period and % body fat and waist circumference. These novel results indicate that the ability to respond to dietary macronutrient changes and adjust subsequent energy intake is affected by (or possibly precedes) adiposity. The regulation of food intake involves complex neuronal circuitry (involving hypothalamus, brainstem, and cortex) that integrates sensory signals between the gut and circulating metabolites. Hormones such as insulin and leptin secreted in proportion to adipose tissue mass and acting via the hypothalamus may affect the amount/composition of food over one or several days [27]. Vice versa, the food macronutrient content influences insulin and leptin levels [28]. A previous study showed that high-fat meals lowered 24-h circulating leptin concentrations [28]. Therefore, decreases in 24-h circulating leptin (as induced by the high-fat diets) could contribute to higher EI. If decreases in leptin concentrations induced in the setting of a high-fat diet were associated with increased adiposity, this might also explain our results. It is worth noting that relatively lower leptin levels were also predictive of later weight gain in Pima Indians [29]. Additional studies are needed to investigate lean-obese differences in hormonal responses (involved in food intake regulation) to dietary macronutrient changes.

Another explanation for our results may be due to differences in fat-induced satiety signals. It has been suggested that fat produces a strong post-absorptive satiety signal when it is being oxidized [30] and that conditions which favor fat storage only produce a weak satiety signal. On a mixed diet (which was also our experimental diets), the ingestion of fat in excess of energy requirements does not increase fat oxidation in the short term (carbohydrate oxidation will dominate), and thus will promote fat storage [31]. Fat oxidation did increase in the high-fat diet, but neither this nor the change in fat oxidation from the WM or HC diet was associated with energy intake. Since the vending machines offer energy dense high-fat food,

individuals who regularly consume this diet may have tended to consume more of these foods. However, this does not explain why relatively greater EI following a high-fat diet was associated with greater adiposity.

On average, the ad libitum energy intake in our current study was 70% above the weight-maintaining energy needs. This has also been observed in our previous studies [13, 14, 32, 33], when volunteers are given ad libitum access to a wide variety of high palatable food items using the same model. Despite this, previous studies have shown that this model can detect important differences in EI. For instance, orally administered glucocorticoids clearly lead to increase in ad libitum EI compared to placebo [33]. The number of volunteers who completed this study was small, but because of its crossover design, the power was high to detect a small (10%) difference in EI. Another limitation of our study was the small number of women ($n = 3$); however, as shown in Fig. 3, their response was as expected based on their degree of adiposity.

In conclusion, the results of the present analyses indicate that a short-term 3-day isocaloric HC diet did not result in alteration of ad libitum EI compared to that following an isocaloric HF diet in the same individuals. However, the novel finding of our study was that increasing body fat was associated with less decline in food intake following the HC compared to the HF diet. If differences in macronutrient intake play a role in regulating EI, our results indicate that increasing adiposity is associated with altered ability to regulate EI in response to these macronutrient changes.

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Conflict of interest The authors declared no conflict of interest.

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