Corrective responses in human food intake identified from an analysis of 7-d food-intake records\(^1\)–\(^3\)

George A Bray, Jean-Pierre Flatt, Julia Volaufova, James P DeLany, and Catherine M Champagne

**ABSTRACT**

**Background:** We tested the hypothesis that ad libitum food intake shows corrective responses over periods of 1–5 d.

**Design:** This was a prospective study of food intake in women.

**Methods:** Two methods, a weighed food intake and a measured food intake, were used to determine daily nutrient intake during 2 wk in 20 women. Energy expenditure with the use of doubly labeled water was done contemporaneously with the weighed food-intake record. The daily deviations in macronutrient and energy intake from the average 7-d values were compared with the deviations observed 1, 2, 3, 4, and 5 d later to estimate the corrective responses.

**Results:** Both methods of recording food intake gave similar patterns of macronutrient and total energy intakes and for deviations from average intakes. The intradividual CVs for energy intake ranged from ±12% to ±47% with an average of ±25%. Reported energy intake was 85.5–95.0% of total energy expenditure determined by doubly labeled water. Significant corrective responses were observed in food intakes with a 3- to 4-d lag that disappeared when data were randomized within each subject.

**Conclusions:** Human beings show corrective responses to deviations from average energy and macronutrient intakes with a lag time of 3–4 d, but not 1–2 d. This suggests that short-term studies may fail to recognize important signals of food-intake regulation that operate over several days. These corrective responses probably play a crucial role in bringing about weight stability. *Am J Clin Nutr* 2008;88:1504–10.

**INTRODUCTION**

Food intake and energy balance are regulated in both the short and long term. The satiety cascade described by Blundell and Stubbs (1) provides one approach to integrating the single meals and the postabsorptive period. Time of day, food availability and diversity, absence of environmental deterrents, and social settings provide external signals that modify eating. A dip in circulating glucose provides one internal signal for beginning food intake (2). Inhibition of glucose oxidation with 2-deoxyglucose or of lipid oxidation with mercapto-acetate (3) suggests important short-term metabolic signals that may be mediated through AMP kinase and the changing intracellular ratio of ATP to AMP (4). Other internal signals related to the termination of food intake include the palatability and mass of the food eaten, the general state of health of the person as reflected in the level of hunger, gastric distension, intestinal distension, gastrointestinal peptides that inhibit (cholecystokinin, polypeptide YY\(^1\)–\(^3\)) or stimulate (ghrelin (5)) food intake, and absorption of nutrients (6, 7). Leptin release from adipose tissue is highly correlated with body fat and can reduce food intake (8).

Despite these short-term signals in terminating single meals, food intake varies greatly from day to day. Thus, regulation of food intake over the longer term is essential if body weight and body fat stores are to remain stable. Signals related to energy depletion may be stronger than those from excess energy stores. With the use of diets with different energy density, Stubbs et al (9–11) found that a covert increase of energy density, produced by adding either carbohydrate (maltodextrin) or fat, produced weight gain. Surprisingly, covert reduction in energy density did not produce weight loss.

Signals for feeding may also operate over a period of several days. In a study on military recruits by Edholm et al (12), food intake and energy expenditure were measured over a 2-wk period. Considerable variation was observed in daily food intake and energy expenditure and poor regulation of energy balance from day to day. However, over an interval of 7 d the correlation of intake and expenditure improved considerably, suggesting the existence of corrective regulatory systems operating over >1 d. Saris (13) noted a similar multiday lag between intake and expenditure in cyclists participating in the Tour de France.

In mice fed ad libitum, Flatt (14, 15) identified day-to-day corrective responses in food intake that were negatively correlated with the preceding day’s carbohydrate balance and proposed that carbohydrate stores as glycogen might provide a signal for regulation of food intake. In a 7-d clinical study that used continuous indirect calorimetry to determine substrate balances in 6 men eating ad libitum, Stubbs et al (11) found a negative correlation between food intake and prior carbohydrate balance, which accounted for 5–10% of the variance in food intake. The present study was a post hoc test of the hypothesis that corrective signals influence food intake over a 1- to 5-d interval (16).

**SUBJECTS AND METHODS**

**Subjects**

The subjects in this study were 20 women, half of whom were dietitians and half were not dietitians (16). The women were...
TABLE 1
Macronutrient and energy intake determined by the weighed and measured methods of obtaining food-intake records

<table>
<thead>
<tr>
<th>Variable</th>
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<th>Measured food intake</th>
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<tbody>
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<td>MJ/d kcal/d g/d</td>
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<td>Energy</td>
<td>8.27 ± 2.46 1980 ± 589</td>
<td>7.93 ± 2.67 1898 ± 640</td>
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<tr>
<td>Fat</td>
<td>2.55 ± 1.30 610 ± 312</td>
<td>2.44 ± 1.27 585 ± 303</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>4.22 ± 1.17 1009 ± 281</td>
<td>3.96 ± 1.23 948 ± 295</td>
</tr>
<tr>
<td>Protein</td>
<td>1.27 ± 0.46 304 ± 110</td>
<td>1.26 ± 0.47 302 ± 113</td>
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<tr>
<td>Alcohol</td>
<td>0.24 ± 0.72 58 ± 173</td>
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1 Values are $x \pm SD$ (n = 280); there are no statistically significant differences.

recruited from the local dietetic association and from the institutional database. After the nature of the study was described, subjects signed an informed consent form, approved by the Pennington Institutional Review Board. The Pennington Institutional Review Board also approved the protocol.

Food intake
Energy and macronutrient intake were estimated by 2 different methods in both groups of women. The women were provided with a food diary along with forms and instructions for keeping food records. The instructions given to all women who used written material and a video included guidelines for keeping food records, descriptive information for identifying foods eaten, and guidelines for calculating portion size for various foods. For the measured food record, the participant was told to report portions with the use of household measures such as measuring cups and measuring spoons where appropriate. When the weighed food record was kept, the participant was provided a food scale and asked to weigh as many of the foods consumed as possible for greater accuracy. The 7-d weighed food record was completed during the time when energy expenditure was determined by doubly labeled water (16). Energy intake was computed with the use of coefficients for carbohydrate (16.7 kJ/g; 4.0 kcal/g), fat (38.9 kJ/g; 9.3 kcal/g), protein (18.0 kJ/g; 4.3 kcal/g), and alcohol (29.7 kJ/g; 7.1 kcal/g).

Doubly labeled water determination
The details for determining energy expenditure from doubly labeled water were described previously (17). Briefly, subjects drank a dose of heavy water, and saliva samples were taken 3 and 4 h later for total body water measurements. Subjects provided morning urine samples on days 1, 2, 7, and 8. The mean daily CO₂ production was calculated with the use of revised dilution space constants (18, 19). Energy expenditure was calculated by multiplying rCO₂ by the energy equivalent of CO₂ for an estimated respiratory quotient of 0.86.

Statistical analysis
The primary response variables analyzed in this study were total energy intake (EI; in MJ) and fat, carbohydrate, and protein intake (in g). For each of the 20 subjects, the average over 7 d for total EI and for each of the macronutrients was calculated from each of the recording methods. Regression analysis was used for comparison of the 2 methods. Additional analysis with the use of the Altman and Bland approach (20) was done to examine the weighed and measured methods of obtaining food intake.

For the prediction models, the deviation of EI for each subject was calculated for each day and each method by subtracting the total weekly intake divided by 7 from each subject’s actual daily intake. These deviations were then used in the predictive model by comparing the deviation on a certain day against the deviation $\geq 1$ d later. All analyses were performed with simple procedures such as PROC MEANS, PROG REG, and the STATVIEW (v5.0.1; SAS Institute, Cary, NC) software.

RESULTS
Subjects
The 20 women who participated in this study were healthy with an average age ($x \pm SD$) of 34.9 ± 10.8 y. They were of normal weight (62.3 ± 9.4 kg) with an average body mass index (in kg/m²) of 23.0 ± 3.7. Some women consumed alcohol, but the quantities were small and variable. We have thus analyzed the data without and with alcohol.

Comparison of measured and weighed food-intake records
The weighed and measured food-intake records provided similar estimates of energy and macronutrient intake, although the mean value for EI was $\approx 340$ kJ/d (82 kcal/d) higher during the week with the weighed diet (Table 1). No differences were observed in results obtained by dietitians or nondietitians. Highly significant correlations were observed between total energy and carbohydrate, fat, and carbohydrate + fat intakes, but not with total energy and protein intakes. The deviations from average intakes are essentially the same during both weeks of recording. Although the mean EIs during the 2 wk of observation are correlated ($r = 0.66; R^2 = 0.44$), it appears that the subjects with relatively low intakes during the first week (measured intake) increased their intake slightly during the second week, whereas the subjects with relatively high intakes during the first week tended to decrease their intake during the second week (weighed intake). The intakes during the 2 wk were not influenced by body mass index or weight, whereas the energy expenditure (in kcal/d) as measured by doubly labeled water was related to body weight (energy expenditure $= 897.7 + 21.46 \times weight R^2 = 0.42$). With the use of equations predicting basal energy expenditure for men and women described in the dietary reference intake report (21), the physical activity level was 1.65 ± 0.18, indicating that the subjects were moderately active (21).

A wide range of variation was observed in daily EI. As shown in Figure 1, the range for the smallest difference between the 25th and 75th percentiles of intake was from 6500 to 6900 kJ/d (1550–1650 kcal/d; subject 16) and the range for the highest was from 5040 to 12 600 kJ/d (1200–3000 kcal/d; subject 9) (16).

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These records were reviewed with the dietitians before entry and, to the extent possible, verified. The intraindividual CVs in EI ranged from 12% to 47% with an average of 25%.

To illustrate this variability, a histogram describing the frequency distribution is shown in Figure 2. It shows that on 58% of the days, these deviations were 200 kcal/d or 200 kcal/d, with deviations from average intake exceeding 600 kcal on 1 of 7 d.

Effect of macronutrient consumption on EI

The overall EI was correlated with the fat content of the foods consumed: EI (kcal/d) = 1327 + 20.6 × percentage of dietary fat; $R^2 = 0.11; P < 0.0001$ (Figure 3) when all 280 d of observation are considered. The effect of dietary fat clearly manifests itself as well intraindividually, as seen when daily deviations from average EI ($\Delta EI$) are considered: $\Delta EI$ (kcal/d) = -265 + 8.9 × percentage of dietary fat; $R^2 = 0.04; P = 0.0012$ (Figure 3).

Protein intake as a percentage of calories was similar to protein intakes that have been reported over the past 100 y (22). The variance for protein intake was smaller than for the other 2 major macronutrients, carbohydrates and fat. The fraction of energy consumed as protein tended to decline slightly when larger amounts of food were consumed, but it was not influenced by the percentage of fat in the diet.

Alcohol accounted for 3% of overall $\Delta$EIs. On 65 of the 280 d, alcohol intake exceeded 104 kJ/d (25 kcal/d), averaging 1095 ± 1082 kJ/d (262 ± 259 kcal/d) and contributing 12% ± 10% of daily intakes on these days. Including alcohol, EIs estimated from the weighed food-intake record averaged 95.0% ± 6.2% of the energy expenditure assessed by doubly labeled water among dietitians and 85.5% ± 6.0% among nondietitians. These differences were not statistically different.

Corrective responses affecting EI

The data on EI were examined to detect possible correlations between deviations in a subject’s daily intakes from her average intake on days separated by intervals of 1, 2, 3, 4, and 5 d. This was also done independently for carbohydrate, fat, and protein. A total of 280 observations were available from the 20 women over the 14 d of record collection, allowing us to make 240 comparisons of intake 1 d apart, 200 comparisons 2 d apart, 160 comparisons 3 d apart, 120 comparisons 4 d apart, and 80 comparisons of intake 5 d apart.

FIGURE 1. Box and whisker plots of energy intake for 20 subjects determined from weighed food-intake records. Each subject provided a 7-d weighed record (n = 140). The line in the middle of the box is the mean, the box is the 25th to 75th percentile of intake, and the vertical line is the range.

FIGURE 2. Frequency distribution for individual deviations from average energy intakes (n = 280).

FIGURE 3. Relations of total daily energy intakes (A) and of deviations from average ($\Delta$) energy intakes (B) to the percentage of fat in the diet (n = 280). The regression lines for these figures are (A) energy intake = 1327 + 20.6 × percentage of dietary fat; $R^2 = 0.11; P < 0.0001$ and (B) $\Delta$ energy intake = -265 + 8.9 × percentage of dietary fat; $R^2 = 0.04; P = 0.0012$. 
The relation between individual daily deviations from their \( \Delta EI \) on a given day with the deviations from \( \Delta EI \) 1, 2, or 5 d apart, whereas marked negative correlations with the deviations observed 3 and 4 d apart became apparent. The relations between deviations from average daily carbohydrate, fat, and protein and their respective deviations 1, 2, 3, 4, and 5 d apart were similarly examined, as well as the deviations from \( \Delta EI \) in relation to the deviations in carbohydrate, fat, and protein intakes for these intervals. In all cases, statistically significant negative correlations were observed for intervals of 3 and 4 d, but no statistically significant effects were observed for intervals of 1, 2, and 5 d, except for deviations from average protein intakes, which also showed a statistically significant negative correlation for 2-d intervals. It was not possible to determine whether or which one particular macronutrient played a more determining role in eliciting the observed corrective responses. Because these individual macronutrient-related evaluations provided no additional information over that of total energy, they are not shown.

Negative correlations are indicative of corrective trends; thus, they reflect the actions of potentially important regulatory factors. To evaluate the statistical significance of this phenomenon, the correlations between deviations from average intakes with intervals of 1, 2, 3, 4, and 5 d were calculated for each subject. The means (±SE) of the slopes of these correlations are shown in Figure 5. The means are significantly different from 0 for deviations from average intakes 3 d apart (\( -0.23 \pm 0.06; P = 0.0016 \)) and 4 d apart (\( -0.28 \pm 0.10; P = 0.0083 \)) (Table 2).

To ascertain that these effects represent a real biological phenomenon, the sequence of each subject’s food-intake observations was randomized for each subject within each week of the study. After randomization the negative correlations between \( \Delta EI \) separated by 3 and 4 d disappeared, whereas an apparently negative correlation between \( \Delta EI \) separated by 1 and 2 d can be noticed (Table 2). This can be attributed to a regression to the mean effect, because unusually high or low values in a series of random numbers will appear to be negatively correlated with neighboring values that are closer to the average.

**DISCUSSION**

This study shows that corrective responses in food intake in human beings occur after a lag of 3 and 4 d. The magnitude of these deviations is of some 100 kJ per 400 kJ (25 kcal per 100
kcal) from the deviations incurred 3 and 4 d earlier. These corrective responses were present in each of the 2 different dietary records used to obtain daily estimates of macronutrient and EI in 20 women for two 7-d periods. Considerable day-to-day variation of food intake was observed, with intraindividual CVs \(\frac{SD}{x} \times 100\), ranging from ±12% to ±47% with an average of ±25%. These data are thus in harmony with those reported by Black et al (23) and are similar to the average CV of ±23% reported by Bingham et al (24). A wide variability of food intake was also reported by others (25–34).

Fat content of the diet is generally believed to promote higher EIs (35). Our data support the view that dietary fat content promotes higher EIs, be it by its effect in enhancing the palatability of foods or by raising their energy density. Challenges to this view are generally based on observations made while food intake is voluntarily reduced in an effort to lose weight or affected by deliberately restricting carbohydrates or fat (36). However, in affluent societies, ad libitum food consumption is the prevailing situation. Our data are therefore noteworthy by showing that, under normal living conditions, dietary fat content is a factor promoting higher EIs (35).

Alcohol contributed to overall EI by an average of 3% of calories in this study. Alcohol consumption appeared to promote higher EI and thus may contribute to the development of obesity (37). When included in the calculated EI, it brought the 2 groups to within 6% and 11% of the EI estimated to be needed for weight maintenance with the use of doubly labeled water. This provides a fairly good indication that the food-intake data are reasonably accurate.

We are only able to identify 2 previous reports in human beings with evidence for corrective responses with a delay of 2–5 d (12, 13). The first of these was a study of 57 military trainees during basic training (12). No relation was observed between EI and expenditure on a day-to-day basis, but in some recruits significant adjustment in food intake occurred after an interval as short as 2 d, whereas for others a longer period was needed. The second study was conducted in 4 male cyclists who participated in the Tour de France (13). The investigators compared the moving average for energy expenditure and EI over 2–5 d. From days 3 to 5, the correlation between energy expenditure and food intake was considerably higher (0.91–0.97) than for days 1 and 2 (0.75–0.91). These 2 studies were in highly active men, whereas our study was in young to middle-aged, relatively sedentary or moderately active women. The correspondence of the data suggests that there is an important regulatory system operating over a period of 3–4 d.

Because carbohydrate and fat intakes are closely related, it is not possible to establish, from our data, whether the corrective responses are generated primarily by energy, carbohydrate, or fat imbalances. In studies on mice, EIs were negatively related with the carbohydrate balances on the preceding days, whereas changes in food intake were not as consistently seen in response to fat imbalances (19, 20). In a study in which food intakes and macronutrient balances were established in 6 human subjects...
CORRECTIVE RESPONSES IN FOOD INTAKE

The authors’ responsibilities were as follows—GAB, CMC, and JPD: designed the experiments; CMC and staff: collected and coded the dietary data; JPD: analyzed the doubly labeled water; 1-PF and JV: analyzed data; GAB and J-PF: wrote the manuscript; CMD, JPD, and JV: revised the manuscript. The nutrient database on which the data were analyzed is Moore’s Extended Nutrient Database (MENu), which is owned by the Pennington Center. None of the authors had a personal or financial conflict of interest.


during 7 consecutive days, Stubbs et al (10) found that food intakes were negatively correlated with previous carbohydrate balances but positively correlated with previous fat balances. Thus, only the carbohydrate balance-related responses were consistent with a negative feedback effect, which could serve to elicit a regulatory effect. The corrective responses created by this negative feedback effect serve to compensate for the large energy imbalances created by the large variability in daily EIs seen in most persons. The remarkable aspect of this regulation is that it occurs with a delay of 3–4 d. In a recent study, Pannaccio et al (38) have observed corrective responses related to carbohydrate oxidation when 24-h oxidation of carbohydrate was measured in a human respiration calorimeter.

The corrective response between energy and macronutrient intakes occurring with a delay of 3–4 d suggests that biological phenomena are involved in the adjustment of energy and macronutrient intake over a period of a few days. Signals originating from the digestive system may be one source of influence modifying food consumption, although they generally decay considerably during the night, and it is not clear whether they are likely to act several days later (39). Gains or losses of glycogen or fat or both may also provide cues in eliciting these responses. However, the nature of the mechanisms involved is yet to be identified (40). Another possibility is leptin. It is known to have an oscillatory release from fat, to be regulated by insulin-mediated uptake of glucose, and to be influenced by meal patterns. Other potential effectors of these responses could include cortisol, or growth hormone, although a number of other possible mechanisms may also be involved, including regression toward the mean.

A few potential limitations need to be considered. Differential recording bias may have occurred over time, although the congruence of the 2 different methods of measuring food intake reduces this possibility. Recording diligence may also have changed over time, and the nondietitian group did underestimate more (although not statistically significant) than did the dietitians.

We conclude from these studies that corrective responses are operating to adjust energy and macronutrient intake over periods of 3–4 d, which remain undetected when food-intake regulation is studied over periods of 1–2 d. Yet these corrective responses can be presumed to play an important role in compensating for the large variations in energy and macronutrient intake and balances that occur under free-living conditions. Such compensations are essential in bringing about weight stability, although the nature of the mechanisms involved is yet to be identified. The corrective responses created by this negative feedback effect, which could serve to elicit a regulatory effect, are essential in bringing about weight stability, although the nature of the mechanisms involved is yet to be identified. The corrective responses created by this negative feedback effect, which could serve to elicit a regulatory effect, are essential in bringing about weight stability, although the nature of the mechanisms involved is yet to be identified.

We thank the volunteers for their participation in this study. The authors’ responsibilities were as follows—GAB, CMC, and JPD: designed the experiments; CMC and staff: collected and coded the dietary data; JPD: analyzed the doubly labeled water; 1-PF and JV: analyzed data; GAB and J-PF: wrote the manuscript; CMD, JPD, and JV: revised the manuscript. The nutrient database on which the data were analyzed is Moore’s Extended Nutrient Database (MENu), which is owned by the Pennington Center. None of the authors had a personal or financial conflict of interest.

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