Meal size and frequency: effect on the thermic effect of food[1,2]

Mary M Tai, Peter Castillo, and F Xavier Pi-Sunyer

ABSTRACT The effects of meal size and frequency on thermic effect of food (TEF) were examined in seven healthy normal-weight young women. Each volunteer consumed in random order one of two identical meals [3138 kJ (750 kcal), 54.5% carbohydrate, 14.0% protein, 31.5% fat]. One meal was taken over 10 min [large meal (LM)] whereas the other was taken in six equal portions of 523 kJ (125 kcal) at 30-min intervals over a 3-h period [small meals (SM)]. Metabolic rate was measured for 1 h before and every 30 min after the meal started for 5 h. When expressed as either kJ/min (kcal/min) or kJ/5h (kcal/5h), TEF was significantly higher in the LM day than in the SM day ($P < 0.05$). We conclude that the temporal pattern in which a mixed caloric load is eaten affects the thermogenic response and may be an important determinant of energy balance after a meal. *Am J Clin Nutr* 1991;54:783–7.

KEY WORDS Meal size, meal frequency, thermic effect of food

Introduction

Meal frequency has been suggested as a possible factor in the regulation of energy balance in experimental animals and in humans (1). Few studies have focused on how the frequency with which meals are eaten will affect energy expenditure, independent of the total caloric content of the meal. Among the components of energy expenditure, the one most likely to be affected by meal frequency is the thermic effect of food (TEF), or postprandial thermogenesis, which is defined as the increase in heat production 0–8 h after the ingestion of a meal. TEF primarily represents the energy required for the transformation of dietary substrates into usable metabolites and for storage of excess fuel (2). Hill et al (3) studied the meal size and thermic response to food in male subjects and found that TEF increases with meal size and that the increase is not linear. They suggested that other factors such as meal frequency might be important determinants influencing energy expenditure. Interestingly, their later study on the thermic response to dietary fuels in humans indicated that continuous enteral administration of a diet at very low rates produced little or no TEF (4).

Nacht et al (5), comparing the TEF of an enterally administered liquid mixed meal [2.3 × each subject's resting metabolic rate (RMR)] in healthy volunteers given either as a single-bolus dose or during 3 h of nasogastric feeding, found that nutrient-induced thermogenesis was greater with the single bolus than with continuous administration. However, others obtained different results. For instance, Belko and Barbieri (6) compared the thermic effect of two large meals (each 50% of 24-h energy intake) with the thermic effect of four small meals (each 25% of 24-h energy intake) and found that the total 10-h TEF did not differ between the two meal patterns. Thus the effect of meal size and frequency on TEF remains uncertain.

The objective of the present study was to determine how the temporal pattern in which a mixed caloric load is eaten affects the TEF by comparing the thermic response during a 5-h period after two relatively extreme patterns: a bolus of 3138 kJ (750 kcal) taken in 10 min [large meal (LM)] vs six small meals of 523 kJ (125 kcal) each [small meal (SM)] taken 30-min apart for 150 min.

Methods

Subjects

Seven healthy women aged 23–30 y were recruited for the study. Women were selected who had a body weight within ±5% of desirable body weight calculated from the midpoint of the Metropolitan Life Insurance Height and Weight Table of 1983 (7), were free of known illness, had not been dieting and had maintained a stable body weight during the previous 6 mo, were not smokers, and had not been participating in any physical-training program for the past 6 mo and were not engaging in regular exercise during the experimental period. Each patient was requested to continue her regular weight-maintaining diet and activity pattern during the study and the week before the study began.

The study was carried out in accordance with the Declaration of Helsinki II and with approval of the ethical review committee (IRB) of St Luke's—Roosevelt Hospital.

Experimental design

The study was conducted on outpatients at the Metabolic Unit of the Obesity Research Center of St Luke's–Roosevelt

[1] From the Obesity Research Center, St Luke's–Roosevelt Hospital Center, Columbia University, and the Department of Nutrition, Food, and Hotel Management, New York University, New York.

[2] Address reprint requests to Tai, Department of Nutrition, Food, and Hotel Management, New York University, 1221 Education Building, 35 West 4th Street, New York, NY 10012.

Received November 29, 1990.

Accepted for publication May 16, 1991.

TABLE 1
Physical characteristics of lean women*

Age (y)	26.7 ± 2.9
Height (cm)	166.6 ± 7.4
Weight (kg)	57.9 ± 4.3
BMI†	20.8 ± 2.1
LBM (kg)	40.8 ± 5.5
Fat (kg)	10.0 ± 1.3
Fat (%)	17.1 ± 5.4

* $\bar{x}$ ± SD; n = 7.
† In kg/m^2.

TABLE 2
Chemical profile on the fasting blood of lean women*

Glucose (mmol/L)	4.6 ± 0.2
Insulin (pmol/L)	64 ± 17
Triglyceride (mmol/L)	0.59 ± 0.13
Total cholesterol (mmol/L)	3.97 ± 0.58
T_3 (nmol/L)	1.8 ± 0.3
T_4 (nmol/L)	95 ± 17
TSH (mU/L)	2 ± 0.8

* $\bar{x}$ ± SD; n = 7. T_3, triiodothyronine; T_4, thyroxine; TSH, thyroid-stimulating hormone.

Hospital Center in New York City. On two separate mornings, after an overnight fast, each subject consumed in random order one of two identical liquid test meals of 3138 kJ (750 kcal) (54.5% carbohydrate, 14.0% protein, 31.5% fat). One meal was taken over 10 min whereas the other was taken in six equal portions of 523 kJ (125 kcal) at 30-min intervals over 150 min. Oxygen consumption and carbon dioxide production were measured in a quiet, temperature-controlled room (23–25 °C), while the subject was resting, for 1 h before the meal and every 30 min after the beginning of the test meal for a total of 5 h after the meal.

Blood biochemistry and body-composition analysis

Fasting blood was collected for the analysis of plasma cholesterol (8), triglycerides (9), glucose (10), and insulin (11). Thyroid hormones were measured by using radioimmunoassay kits by DPC Diagnostic Products Corporation, Los Angeles [triiodothyronine (T_3): Coat-A Count Total T_3 kit; thyroxine (T_4: Coat-A Count Total T_4 kit; thyroid-stimulating hormone (TSH): Coat-A Count TSH IRMA kit]. Total body potassium (TBK) was measured by gamma spectrometry of ^{40}K. The SE of total body potassium was determined by the statistical counting error of the subject's net ^{40}K counting rate and the SE of the calibration factor. Lean body mass (LBM) and body fat were calculated after ^{42}K calibration (12). A factor of 60 mmol K/kg of LBM was used to calculate LBM (13).

Metabolic-rate determinations

For oxygen and carbon dioxide measurements the completely automated MMC system (Beckman Metabolic Measurement Cart, Fullerton, CA) was used. This system includes an infrared carbon dioxide analyzer, electronic temperature and two pressure transducers, a turbine volume meter, and automated sample handling, data collection, and computation. Energy expenditure was determined by using the nonprotein caloric equivalent for oxygen derived from the Weir equation (14):

$$\text{kcal} = [(\text{RQ} \times 1.1) + 3.9] \times \dot{V}O_2$$

where RQ is the respiratory quotient and $\dot{V}O_2$ is oxygen consumption (in L/min). Equipment was recalibrated on every testing day with standard gases of known concentration. Measurements were taken during a 15-min period of stable oxygen consumption in the morning after a 12–14 h fast and after a minimum of 30 min rest. The area within SD per RMR test/retest in our laboratory gives an error CV of 3.8%. The TEF was obtained for each subject from the difference between metabolic rate after the meal and the RMR. The total TEF of both meal treatments was calculated as the incremental area above the resting level, with zero time being the start of eating. There was no negative area to the TEF calculation. The total TEF measured in response to the six SMs was compared with that measured in response to one LM. Paired t tests were used to calculate statistical significance.

Results

Data on the physical characteristics of the lean volunteers are shown in **Table 1.** The fasting plasma values of subjects are shown in **Table 2.** All were within the normal range.

The TEF of lean women over 5 h is shown in **Figure 1.** The mean TEF for the seven women at each time period in the two groups is shown in **Table 3.** The values are expressed as kJ/min ($\bar{x}$ ± SE) and the summary of the results are shown in **Table 4.** RMR (kJ/min ± SE) was similar before both meal treatments. TEF, whether expressed as kJ/min (kcal/min) or as kJ (kcal) over 5 h, was significantly higher for the LM group than for the SM group ($P < 0.05$) (Table 4, **Figs 2 and 3**). Expressed as a percent of the energy ingested, it was 7.68% for the LM group vs 5.56% for the SM group.

The respiratory quotient (RQ) on the SM day (post-meal) averaged 0.89 ± 0.03 and on the LM day it averaged 0.86 ± 0.03 ($P < 0.02$). A more sustained rise in RQ was found in the SM group than in the LM group.

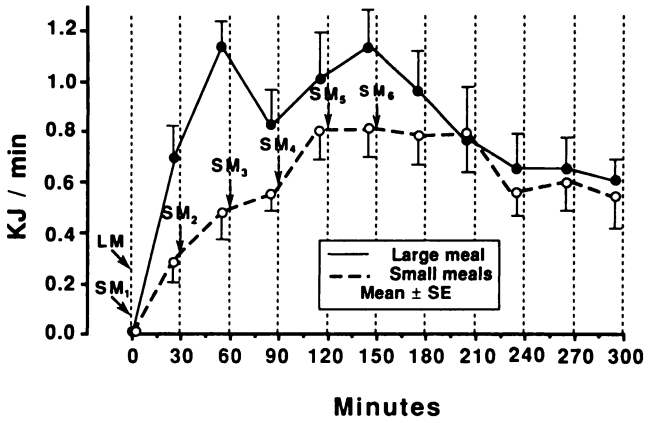

FIG 1. The thermic effect of food in lean women, one large meal vs six small meals. Metabolic rate was measured for 1-min intervals during the last 10 min of each 30-min interval. The first two determinations and the last one were discarded and the remaining 7-min readings were averaged; the average value is shown as a point on the graph. $\bar{x}$ ± SE; n = 7.

TABLE 3
Thermic effect of food (TEF) after the test meals*

Time	Large meal	Small meal
	kJ/min (kcal/min)	
T1	0.690 ± 0.134 (0.165 ± 0.032)	0.280 ± 0.075 (0.067 ± 0.018)
T2	1.138 ± 0.096 (0.272 ± 0.023)	0.477 ± 0.105 (0.114 ± 0.025)
T3	0.824 ± 0.142 (0.197 ± 0.034)	0.544 ± 0.059 (0.130 ± 0.014)
T4	1.008 ± 0.184 (0.241 ± 0.044)	0.803 ± 0.113 (0.192 ± 0.027)
T5	1.138 ± 0.146 (0.272 ± 0.035)	0.808 ± 0.113 (0.193 ± 0.027)
T6	0.962 ± 0.155 (0.230 ± 0.037)	0.778 ± 0.109 (0.186 ± 0.026)
T7	0.761 ± 0.213 (0.182 ± 0.051)	0.787 ± 0.146 (0.188 ± 0.035)
T8	0.644 ± 0.142 (0.154 ± 0.034)	0.548 ± 0.084 (0.131 ± 0.020)
T9	0.644 ± 0.130 (0.154 ± 0.031)	0.594 ± 0.105 (0.142 ± 0.025)
T10	0.598 ± 0.084 (0.143 ± 0.020)	0.536 ± 0.117 (0.128 ± 0.028)

* $\bar{x}$ ± SE; n = 7.

Discussion

Some of the factors that have been suggested to affect TEF include age, sex, previous dietary history, meal composition, meal size, meal frequency, activity level, and maximum working capacity. The present study was aimed at determining the effect of meal frequency on postprandial thermogenesis while most of the other variables mentioned above are controlled for. The results demonstrate a difference in TEF when an isocaloric load of nutrients is administered as a single-bolus dose as compared with six small doses. The difference in the pattern of response between one large dose and six small doses may be due to many physiological factors, including the rapidity of gastric emptying of nutrients and the degree of hormone responses. These factors are discussed below.

Gastric emptying

The rate of nutrient absorption depends in large part on the rate of nutrient flow into the duodenum, which is determined by the rate of gastric emptying. When a bolus dose of nutrient is given, gastric emptying quickly reaches a peak and then diminishes according to a negative exponential curve whose characteristics depend primarily on the energy content of the meal (5). The rate of gastric emptying is also influenced by factors such as pH and osmolarity of gastric contents, gastric hormones, and the lipid content of the meal (15–17).

After giving nutrients continuously, McHugh and Moran (16) found that the rate of gastric emptying was slower than when the same nutrients were given as a bolus. They ascribed this phenomenon to a lack of gastric distension during the continuous infusion. With this slowed gastric emptying they found the rate of absorption of the nutrients to be delayed. From the data of McHugh and Moran (16) we infer that the LM, creating a much greater gastric distension, emptied faster than the SM. This increased gastric emptying plus the greater initial caloric load caused a faster absorption, higher concentrations of nutrients in the blood [as was described by Jenkins et al (18)], and thereby a higher thermic response effect as the nutrients were more quickly oxidized and/or stored.

Hormonal influence

Nacht et al (5), studying the TEF of a single-bolus dose of a meal as opposed to a meal given continuously over 3 h by nasogastric tube, attributed the greater TEF when the meal was eaten as a bolus to a greater initial nutrient storage, which is mediated by the insulin response and is thermogenically more

TABLE 4
Summary of results*

	Large meal	Small meal
RMR		
(kJ/min)	3.895 ± 0.067†	3.937 ± 0.096
(kcal/min)	0.931 ± 0.016†	0.941 ± 0.023
TEF		
(kJ/min)	0.849 ± 0.096	0.611 ± 0.075‡
(kcal/min)	0.203 ± 0.023	0.146 ± 0.018‡
TEF		
(total kJ/5 h)	241.00 ± 34.56	174.47 ± 25.10‡
(total kcal/5 h)	57.60 ± 8.26	41.70 ± 6.00‡
TEF (% of energy ingested)	7.68	5.56

* n = 7.
† $\bar{x}$ ± SE; n = 7.
‡ Significantly different from large meal, $P < 0.05$ (paired t test).

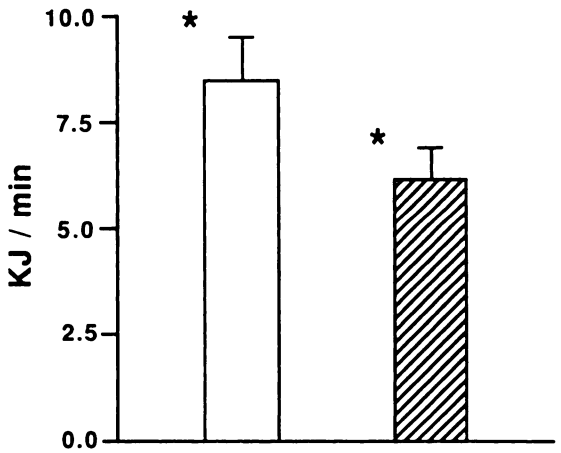

FIG 2. Thermic effect of food in lean women. One large meal LM (□) vs six small meals SM (▨). $\bar{x}$ ± SE; n = 7. *$P < 0.05$.

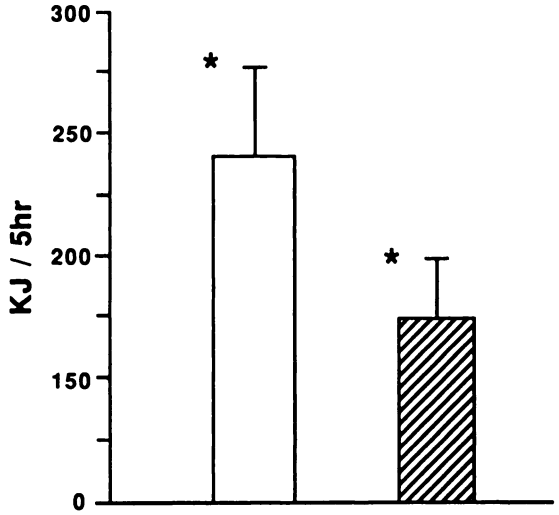

FIG 3. Thermic effect of food in lean women over 5 h. One LM (□) vs six SM (▨). $\bar{x} \pm$ SE; $n = 7$. $^*P < 0.05$.

expensive than oxidizing nutrients as they are absorbed, thereby decreasing the cost of storage. We agree with this hypothesis, which can also be applied to the present study because we also found a larger TEF in the LM group. Thus, we believe that in the LM group the thermogenic response is greater than in the SM group because of the more rapid absorption of nutrients, which induces a greater insulin response and enhances nutrient storage.

Jenkins et al (18) studied the effect of nibbling vs gorging on serum lipid concentrations and carbohydrate tolerance in normal subjects. The nibbling diet was found to maintain but not raise the concentrations of blood glucose, free fatty acids, and triglycerides and to decrease the mean postprandial insulin concentrations by 27.9% as compared with the gorging group. Jenkins' study supports our hypothesis that, when people nibble, the decreased TEF is partially due to a decreased insulin-mediated response. In fact, Jenkins et al (18) predicted in their paper that the beneficial effect of nibbling meals in reducing triglyceride synthesis through a reduction in insulin concentrations might be offset by an accompanying reduction in the postprandial thermogenesis stimulated by insulin and glucose. Our findings confirm these predictions.

Sympathetic regulation

In LeBlanc et al's study (19), which compared the TEF of gavage vs meal feeding in human subjects, a much larger TEF was found with meal feeding than with tube feeding. Norepinephrine concentrations indicated that the sympathetic nervous system was activated by meal feeding but not by tube feeding. Because in LeBlanc's study the total caloric intake of 3159 kJ (755 kcal) was similar to the caloric content of 3138 kJ (750 kcal) (LM) in the current study, it is reasonable to assume that the sympathetic nervous system was equally stimulated in the LM group in the current study. The SM group [523 kJ (125 kcal)] of the present study is more similar to tube feeding and, by LeBlanc's data, would predictably elicit lower norepinephrine concentrations. Other past findings also demonstrated that a meal appears to stimulate sympathetic nervous activity in humans (20, 21).

It is hypothesized that a larger thermic response after a large meal may be due to an increased sympathetic response. Differences in RQ values may provide support for this. In the current study higher and more sustained RQ values were found in the SM group than in the LM group. Also, DeFronzo et al (22) showed that, with beta blockade, the TEF of a glucose load can be essentially blocked. Despite this there is no general agreement on the extent to which sympathetic stimulation contributes to the acute TEF (20, 23–27). Although there are reports that TEF is not dependent on the sympathetic nervous system (28), there is much suggestive evidence that catecholamines are involved (22).

Potential caloric impact

The total difference in TEF over 5 h was 2.12%, or about a 66.9-kJ (16-kcal) difference for a total intake of 3138 kJ (750 kcal). Were this to be calculated for the hours per day, one could expect a thermogenic response from a meal (5 h postmeal × 3) and could postulate a daily difference of 200.7 kJ (48 kcal). This is a small amount of calories, but over time could be a significant factor in energy balance.

Conclusion

This study shows that an isocaloric mixed meal taken as a bolus causes a greater postprandial thermogenic response than does the same meal taken over time as six smaller portions. Though the differences in TEF are small, in this paper ~ 66.9 kJ (16 kcal), they are nevertheless significant. If such a difference were to be continued over a long time, it could add up to a significant calorie savings with nibbling, which could allow a greater deposition of reserve fat. Thus the temporal pattern in which a caloric meal is eaten can affect the thermogenic response and may have an effect on energy balance. ■

We thank S Heshka and H Kissileff for advice on statistical analysis, J Wang for body composition analysis, and Y Dam, Y Han, and P Shen for help in laboratory analyses.

References

1. Adams CE, Morgan KJ. Periodicity of eating: implications for human food consumption. Nutr Rev 1981;1:525–50.
2. Woo R, Daniels-Kush R, Horton ES. Regulation of energy balance. Annu Rev Nutr 1985;5:411–33.
3. Hill JO, Anderson JC, Ling D, Yakubu F. Effects of meal frequency on energy utilization in rats. Am J Physiol 1988;255:R616–21.
4. Hill JO, DiGirolamo M, Heymsfield SB. A new approach for studying the thermic response to dietary fuels. Am J Clin Nutr 1985;42: 1290–8.
5. Nacht CA, Schutz Y, Vernet O, Christin L, Jequier E. Continuous versus single bolus enteral nutrition: comparison of energy metabolism in humans. Am J Physiol 1986;251:E524–9.
6. Belko AZ, Barbieri TF. Effect of meal size and frequency on the thermic effect of food. Nutr Res 1987;7:237–42.
7. Metropolitan Life Insurance Company. 1983 Height and weight tables. Stat Bull Metropol Insur Co 1984;64:2–9.
8. Allain CC, Poon LS, Chan CSG, Richmond W, Fu TC. Enzymatic determination of total serum cholesterol. Clin Chem 1974;20: 470–5.
9. Bucolo C, David H. Quantitative determination of serum triglyceride by the use of enzymes. Clin Chem 1973;19:476–82.
10. Kadish AH, Little RL, Sternberg JC. A new rapid method for the determination of glucose by measurement of rate of oxygen consumption. Clin Chem 1969;14:116–9.

11. Herbert V, Lau K, Gottlieb CW, Bleicher SJ. Coated charcoal immunoassay of insulin. J Clin Endocrinol Metab 1965;25:1375–84.
12. Pierson RN Jr, Wang J, Thornton JC, Van Itallie TB, Colt EWD. Body potassium by four-pi K counting: an anthropometric correction. Am J Physiol 1984;246:E234–9.
13. Burkinsbow L, Cotes JE. Body potassium and fat free mass. Clin Sci 1973;44:621–5.
14. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol (Lond) 1949;109:1–9.
15. Hunt JN, Stubbs DF. The volume and energy content of meals as determinants of gastric emptying. J Physiol (Lond) 1975;245:209–25.
16. McHugh PR, Moran TH. Calories and gastric emptying: a regulatory capacity with implications for feeding. Am J Physiol 1979;236:R254–60.
17. Moore JG, Christin PE, Coleman RE. Gastric emptying of varying meal weight and composition in man: evaluation by dual liquid and solid-phase isotopic method. Dig Dis Sci 1981;26:16–22.
18. Jenkins D, Wolever T, Vuksan V, et al. Nibbling versus gorging: metabolic advantages of increasing meal frequency. N Engl J Med 1989;321:929–34.
19. LeBlanc J, Cabanac M, Samson P. Reduced postprandial heat production with gavage as compared with meal feeding in human subjects. Am J Physiol 1984;246:E95–101.
20. Schwartz RS, Jaeger LF, Veith RC. Effect of clonidine on the thermic effect of feeding in humans. Am J Physiol 1988;254:R90–4.
21. Wells S, Lilavivat U, Campbell RG. Thermic effect of feeding in man: increased plasma norepinephrine levels following glucose but not protein or fat consumption. Metabolism 1981;30:953–8.
22. DeFronzo RA, Thorin D, Felber JP, et al. Effect of beta and alpha adrenergic blockade on glucose-induced thermogenesis in man. J Clin Invest 1984;73:633–9.
23. Acheson KJ, Ravussin E, Wahren J, Jequier E. Thermic effect of glucose in man: obligatory and facultative thermogenesis. J Clin Invest 1984;74:1572–80.
24. Vernet O, Nacht CA, Christin L, Schutz Y, Danforth E, Jequier E. β-adrenergic blockade and intravenous nutrient-induced thermogenesis in lean and obese women. Am J Physiol 1987;253:E65–71.
25. Zwillich C, Martin B, Hofeldt F, Charles A, Subryan V, Burman K. Lack of effects of beta sympathetic blockade on the metabolic and respiratory response to carbohydrate feeding. Metabolism 1981;30:451–6.
26. Seaton T, Welle S, Alex S, Lilavivat U, Campbell R. The effect of adrenergic blockade on glucose-induced thermogenesis. Metabolism 1984;33:415–9.
27. Welle S, Campbell RG. Stimulation of thermogenesis by carbohydrate overfeeding: evidence against sympathetic nervous system mediation. J Clin Invest 1983;71:916–25.
28. Welle SL, Nair KS, Campbell RG. Failure of chronic β-adrenergic blockade to inhibit overfeeding-induced thermogenesis in humans. Am J Physiol 1989;256:R653–58.