Deleterious effects of omitting breakfast on insulin sensitivity and fasting lipid profiles in healthy lean women[1–3]

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ABSTRACT

Background: Breakfast consumption is recommended, despite inconclusive evidence of health benefits.

Objective: The study's aim was to ascertain whether eating breakfast (EB) or omitting breakfast (OB) affects energy intake, energy expenditure, and circulating insulin, glucose, and lipid concentrations in healthy women.

Design: In a randomized crossover trial, 10 women [$\bar{x} \pm$ SD body mass index (BMI; in kg/m^2): 23.2 $\pm$ 1.4] underwent two 14-d EB or OB interventions separated by a 2-wk interval. In the EB period, subjects consumed breakfast cereal with 2%-fat milk before 0800 and a chocolate-covered cookie between 1030 and 1100. In the OB period, subjects consumed the cookie between 1030 and 1100 and the cereal and milk between 1200 and 1330. Subjects then consumed 4 additional meals with content similar to usual at predetermined times later in the day and recorded food intake on 3 d during each period. Fasting and posttest meal glucose, lipid, and insulin concentrations and resting energy expenditure were measured before and after each period.

Results: Reported energy intake was significantly lower in the EB period ($P = 0.001$), and resting energy expenditure did not differ significantly between the 2 periods. OB was associated with significantly higher fasting total and LDL cholesterol than was EB (3.14 and 3.43 mmol/L and 1.55 and 1.82 mmol/L, respectively; $P = 0.001$). The area under the curve of insulin response to the test meal was significantly lower after EB than after OB ($P < 0.01$).

Conclusion: OB impairs fasting lipids and postprandial insulin sensitivity and could lead to weight gain if the observed higher energy intake was sustained.   *Am J Clin Nutr* 2005;81:388–96.

INTRODUCTION

Breakfast consumption by adults appears to have declined in recent decades (1, 2). It also was reported that eating breakfast cereal was associated with a lower body mass index (BMI; in kg/m^2) than was not eating breakfast cereal (3). Further investigations in children (4), adolescents (5), and adults (6) confirmed the negative relation between breakfast consumption and the risk of obesity. In contrast, one cross-sectional study (7) did not find any relation between obesity and breakfast consumption in adults. In a clinical weight-loss trial (8), 52 obese women were stratified according to their breakfast habits as eating or omitting breakfast (EB and OB, respectively), and they were then randomly assigned to eat breakfast or to skip it. The results were

somewhat contradictory, because baseline breakfast skippers had more weight loss when they ate breakfast, whereas the breakfast eaters lost more weight when they skipped breakfast.

Daily energy intakes (EIs) appeared to be unaffected by EB in adults (2, 9). However, a lower EI was reported (3, 5, 10) in those who omitted breakfast than in those who ate breakfast, despite higher BMI in the OB group (3, 5).

Morgan et al (2) showed that adults who consumed ready-to-eat cereals had significantly lower daily fat and cholesterol intakes than did those who ate other foods at breakfast or omitted breakfast. This result was confirmed by another study using data from the second National Health and Nutrition Examination Survey (11). A further intervention study (12) also indicated that daily total and saturated fat intakes were reduced only when breakfast contained cereals.

Altered circulating triacylglycerol (13–15), insulin (16), uric acid (17), and total, LDL-, and HDL-cholesterol, concentrations are recognized as risk factors for cardiovascular disease. A limited number of studies have investigated the effect of OB on serum lipid concentrations. Previous epidemiologic studies indicate that EB, especially the consumption of ready-to-eat cereals, tends to be associated with lower serum cholesterol concentrations than is OB (11, 18). Further studies showed that the consumption of whole-grain but not of refined-grain cereal is associated with lower BMI and serum total cholesterol, LDL-cholesterol, and insulin concentrations (19, 20). It was also reported that the intake of whole-grain breakfast cereal may tend to reduce the mortality rate, especially cardiovascular mortality, more than does the intake of refined breakfast cereal (21). The only intervention study (12) of which we are aware in free-living healthy subjects also confirmed that regular breakfast cereal consumption reduces total and saturated fatty acid intakes, which leads to reductions in serum cholesterol concentrations. No intervention study has evaluated the effect of EB on various aspects

of energy metabolism. The purpose of this study was to investigate the effect of OB on EI, resting energy expenditure (REE), and circulating glucose, lipid, and insulin concentrations in lean healthy women.

SUBJECTS AND METHODS

Subjects

Ten healthy, lean women aged 19–38 y ($\bar{x} \pm$ SD age: 25.5 ± 5.7 y) who were menstruating regularly or were taking the oral contraceptive pill, who were neither pregnant nor lactating, and who had no self-reported history of hypercholesterolemia, hyperglycemia, or any serious medical conditions were recruited from the students and staff of the Queen's Medical Centre, Nottingham, United Kingdom, via a poster advertisement. All subjects reported consuming breakfast regularly, but only 4 of the 10 ate cereal for breakfast, and even those subjects ate cereal only occasionally. Subjects were excluded if they reported that they were dieting (a score of > 30 on The Eating Inventory; 22) or experiencing depression [a score of > 10 on the Beck Depression Inventory (BDI); 23]. Mean BMI was 23.2 ± 1.6).

Ethical permission for the study was obtained from The University of Nottingham Medical School Research Ethics Committee. Written informed consent was obtained from all subjects.

Design

Each subject participated in a randomized crossover trial consisting of two 14-d periods over a total of 42 d: one intervention was EB, and the other was OB. In the EB period, subjects were asked to consume a pack (45 g) of whole-grain cereal (Bran Flakes; Kellogg's, Manchester, United Kingdom) with 200 mL low-fat (2%-fat) milk between 0700 and 0800 and to eat a 48-g chocolate-covered cookie (Kit Kat; Nestlé) between 1030 and 1100. Then they consumed 2 additional meals and 2 snacks of content similar to usual at predetermined times every day. In the OB period, subjects consumed the chocolate-covered cookie between 1030 and 1100 and then had the cereal and 2%-fat milk between 1200 and 1230. They then consumed 2 additional meals and 2 snacks of content similar to usual by the same procedure as was used in the EB period. The timetable for the 4 additional eating occasions during both the EB and the OB periods was 1330–1400, 1530–1600, 1800–1830, and 2030–2100. Subjects were asked to consume their main evening meal (dinner) between 1800 and 1830. Between the 2 intervention periods, subjects were asked to consume their normal diet and to follow their normal eating pattern for 14 d as a washout period. Subjects were provided with the cereal, milk, and chocolate-covered cookies before the start of each intervention. Five subjects started with the EB intervention, and the other 5 started with the OB intervention. The participants remained free-living during the study, and the diet content was self-selected. Food intake records were kept by using household measures on 2 weekdays and 1 weekend day before the start of the interventions. The subjects also recorded their food intake on the 3rd, 11th, and 14th days of the EB and the OB periods to assess their adherence to the diet. Each volunteer came to the laboratory on the first and the last days of each intervention, for a total of 4 visits. Each visit lasted ≤4 h.

Free-living procedures

Food intake measurement

The participants were given training in keeping a food intake record by using a semiquantitative method based on household measurements. An instruction booklet with an example of a 1-d food intake record was also given to each subject before each recording. Food diary records for the subjects' habitual EB and OB periods were analyzed by using MICRODIET software (version 1.2; Downlee Systems Limited, Salford, United Kingdom).

Protocol for laboratory visits

Subjects were asked to fast overnight (for ≥10 h) and to take no exercise other than the walking required for the activities of daily living for 48 h before the laboratory visit. On arrival, weight, height, and waist and hip circumferences were measured. Then, a 20-gauge cannula was inserted retrogradely into a dorsal hand vein for collection of arterialized venous blood. Two baseline blood samples were taken in the fasting state, a milkshake test meal was consumed within 10 min (at 0900), and then blood samples were taken at 15-min intervals for 3 h. REE was measured in the fasting state and then for two 15-min periods every hour for 3 h after the test meal. Subjects also completed visual analogue scales (VAS) for hunger-related values before and for 3 h after consuming the test meal. All visits were undertaken in the morning.

Laboratory procedures

Anthropometric measurements

Weight was measured to the nearest 0.1 kg on an electronic scale (model no. 882; Vogel and Halke, Hamburg, Germany) when subjects were fasting, had an empty bladder, were wearing light clothing with empty pockets, and were not wearing shoes. Height was measured to the nearest 0.1 cm by using a stadiometer (Seca) during the screening visit. Waist circumference was measured to the nearest 0.1 cm in a horizontal plane at the level of the midpoint between the lower margin of the last rib and the crest of the ileum by using a flexible, nonstretchable nylon tape while the subject stood with her feet 25–30 cm apart (24). Hip circumference was also measured to the nearest 0.1 cm in a horizontal plane at the maximum point over the buttock at the level of the femoral greater trochanter (24). Body composition was estimated from measured bioelectrical impedance (QuadScan 4000; Bodystat Ltd, Douglas, United Kingdom) while the subject lay on a nonconductive couch and had her arms and legs abducted.

Blood sampling

On arrival at the laboratory, the subject's hand was warmed in a heated ventilated perspex box (50–55 °C) for 15–20 min to open the arteriovenous anastomoses (25). A 20-gauge cannula was inserted retrogradely into a dorsal hand vein, and a slow-running infusion of saline (154 mmol sodium chloride/L) was started to keep the cannula patent. Blood samples were withdrawn via a 3-way tap; the first 2 mL was discarded to avoid contamination with saline. Two baseline blood samples were tested for fasting blood glucose, serum insulin, and plasma cholesterol (total, HDL, and LDL) and triacylglycerol concentrations.

After the test meal, blood samples were taken every 15 min for 3 h. These blood samples were analyzed for blood glucose and serum insulin concentrations.

Test meal consumption

The milkshake test meal was given as a breakfast. The volume of test meal that subjects were given was based on their weight at the start of the experiment [10 kcal (41.8 kJ)/kg body wt]. The percentages of total energy from the macronutrients were 50% as carbohydrate, 35% as fat, and 15% as protein. The test meal contained 2%-fat milk (Build-up; Nestle SA, Lausanne, Switzerland), double cream (Sainsbury's, London), and Polycal (Nutricia Clinical Care, Trowbridge, United Kingdom) in either strawberry or vanilla flavor. The meal was served at a temperature of 18–20 °C in an open glass. Subjects were asked to consume the drink within 10 min.

Visual analogue scales

Each subject completed VAS questionnaires to assess subjective hunger, satiety, fullness, and desire to eat. Ratings were made on 100-mm VAS questionnaires with words at each end that expressed the most extreme rating (26).

Energy expenditure and substrate oxidation

REE was measured after a 10-h fast by using an open-circuit indirect calorimeter (GEM system; Nutren Technology Ltd, Burnley, United Kingdom). After a 30-min warm-up period, a reference gas (5% CO_2 and 95% O_2) was used to calibrate the oxygen and carbon dioxide analyzers. Ingoing and outgoing air was analyzed for oxygen and carbon dioxide every minute during each period of measurement. Readings from the metabolic monitor were collected every minute with a personal computer.

Subjects rested for ≈20 min on a bed in a room maintained at 20–22 °C. Fasting REE was then measured for 30 min while the subject lay in the supine position. A light-transparent ventilated hood was positioned over the subject's head, Collins tubing was used to connect the hood to the monitor, and expired gases were continuously collected. Starting immediately after consumption of the test meal, postprandial metabolic rate (PPMR) was measured for periods of 15 min twice an hour for 3 h. Subjects rested on the bed but were not allowed to sleep during the EE measurements. In the intervals between the measurements, subjects also rested on the bed, but they were permitted to read. The thermic effect of food (TEF) was measured by using the trapezoidal method to measure the area under the curve (AUC) of PPMR above the baseline REE for all of the visits.

Processing of blood samples

Blood glucose was measured immediately by using a B-Glucose Analyser (Hemocue AB, Angelholm, Sweden). Blood samples for insulin were left to clot for ≥30 min after collection before being centrifuged for 10 min at 3000 RPM (Minifuge RF; Heraeus Equipment Ltd, Brentwood, United Kingdom). The serum samples were then sealed and stored at −80 °C for future analysis. Blood samples for measurement of cholesterol and triacylglycerol concentrations were taken into tubes containing lithium heparin. The lipid samples were then kept in an icebox until the end of each visit, and then they were centrifuged for 10 min at 3000 RPM (Minifuge RF; Heraeus Equipment Ltd). The plasma was transferred into a fresh tube

containing 25 μL EGTA for subsequent measurement of lipids and uric acid. The tube was then sealed and stored at −80 °C for later analysis.

Insulin measurements were performed by using a solid-phase ^{125}I radioimmunoassay (RIA) method using coated-tube technology (Count-A-Count; Diagnostic Products Corp, Los Angeles). The intraassay CVs were 2.8% and 3.3% for blood glucose and serum insulin, respectively.

Plasma total cholesterol and triacylglycerol concentrations were measured enzymatically by using kits and standards supplied by VITROS (Ortho-Clinical Diagnostics, Rochester, NY). HDL cholesterol was measured after precipitation of apolipoprotein B–containing lipoproteins with heparin and manganese chloride (27) by using an EZ HDL Cholesterol Kit (Sigma Diagnostics, St Louis). LDL cholesterol was calculated by using the formula of Friedewald et al (28). Plasma uric acid concentration was measured enzymatically (29, 30) by using kits supplied by VITROS. The intraassay CVs were 2.2%, 2.6%, 1.7%, and 1.6% for total cholesterol, HDL cholesterol, triacylglycerol, and uric acid, respectively.

Homeostasis model assessment for insulin resistance (HOMA-IR) was used when the subjects were in the fasting state. The values for the subjects were calculated by using the following formula (31):

$$HOMA\text{-}IR = \text{fasting serum insulin } (\mu IU/mL) \times$$
$$\text{fasting blood glucose (mmol/L)}/22.5 \quad (1)$$

The AUC above the baseline for blood glucose and serum insulin concentrations was measured during the posttest meal period by using the trapezoidal method.

Statistical analysis

SPSS software (version 10; SPSS, Chicago) was used for data entry and analysis. All data are reported as means ± SDs unless otherwise indicated. Data were tested for normality (Kolmogorov-Smirnov statistic with Lillefors correction). Comparisons of the preintervention data were performed by using Student's paired *t* test (two-tailed) to investigate possible differences before the intervention periods. Repeated-measures analysis of variance (ANOVA) was used for the comparison of glucose, insulin, and REE profiles after the test meal. To investigate the interactions between the factors, we carried out either two-factor [ie, visit (before and after the intervention period) and intervention (EB or OB)] or three-factor [ie, 3 within-subject factors: intervention (EB or OB), visit (before and after the intervention period), and time after the test meal] repeated-measures ANOVA as appropriate. When ANOVA indicated a significant effect, a paired *t* test with Bonferroni's correction was undertaken to compare the postintervention results in both periods and the difference between preintervention and postintervention measurements in both periods. Significance was set at $P < 0.05$ for all statistical tests, except when Bonferroni's correction was applied.

RESULTS

Body weight did not differ significantly between the preintervention and postintervention periods. There were also no significant differences in anthropometric measurements or body composition before and after either intervention period (**Table 1**).

TABLE 1
Physical characteristics of the 10 subjects over the course of the experiment[1]

	Eating breakfast period		Omitting breakfast period	
	Before intervention	After intervention	Before intervention	After intervention
Body weight (kg)	55.7 ± 6.0	55.6 ± 6.1	55.5 ± 5.8	55.9 ± 5.9
BMI (kg/m^2)	23.2 ± 1.6	23.1 ± 1.7	23.1 ± 1.6	23.2 ± 1.6
Waist (cm)	75.5 ± 5.8	76.0 ± 5.3	78.5 ± 6.5	77.0 ± 5.4
Waist-hip ratio	0.78 ± 0.05	0.77 ± 0.05	0.79 ± 0.05	0.78 ± 0.04
Body fat (%)	25.2 ± 2.6	25.9 ± 2.8	24.8 ± 2.4	26.1 ± 2.7

[1] All values are $\bar{x}$ ± SD. No significant differences were observed in body weight and anthropometric measurements over the course of the experiment (ANOVA).

Energy intake

The preintervention food records did not show any significant difference in EI between the mean of the 2 weekdays (6.97 ± 0.80 MJ/d) and the one weekend day (7.12 ± 0.82 MJ/d). Furthermore, there were no significant differences in the food macronutrient composition between weekdays and weekends.

All subjects reported having adhered to the appropriate meal patterns during the 2 interventions. Mean energy intake recorded over 3 d was significantly lower during the EB period (6.97 ± 0.59 MJ/d) than during the OB period (7.35 ± 0.65 MJ/d; P = 0.001, paired t test) (**Table 2**). The macronutrient composition (percentage of energy from protein, fat, and carbohydrate) did not differ significantly between the 2 interventions (Table 2).

Appetite measurement

The response curves for the 4 hunger-related measures [ie, hunger, satiety, fullness, and prospective food consumption (desire to eat)] are shown in **Figure 1**. Fasting values for each variable and the profiles after the test meal did not differ significantly over the course of the experiment.

Energy expenditure, postprandial metabolic rate, and the thermic effect of food

The fasting REE values did not differ significantly between the pre-EB and pre-OB period visits, and there was no significant effect of either intervention on fasting REE (**Figure 2**). Metabolic rate increased significantly above fasting values after the test meal at all visits. PPMR also showed no significant difference over the experiment (Figure 2). Furthermore, TEF did not differ significantly between the pre-EB and pre-OB period visits. No significant effect of either intervention on TEF was observed (**Figure 3**).

Blood glucose and serum insulin

Fasting blood glucose did not differ significantly between the pre-EB and pre-OB period visits, and there was no effect of either intervention on fasting blood glucose (**Table 3**). Blood glucose concentrations rose significantly after the test meal at all 4 visits (**Figure 4**). The peak of blood glucose concentrations before each intervention showed no significant difference (Table 3), and there was no effect of either intervention on peak blood glucose concentrations. The AUC of glucose profiles above the baseline did not differ significantly between the pre-EB and pre-OB period visits, and there was no effect of either intervention on AUC of glucose profiles over the course of the study.

Fasting serum insulin did not differ significantly between the pre-EB and pre-OB period visits and did not change with the 2 interventions. The HOMA-IR values did not differ significantly between the pre-EB and pre-OB period visits and did not change significantly after either intervention (Table 3).

Serum insulin concentrations rose significantly in response to the test meal at all visits. The peak insulin values after the test meal did not differ significantly between the pre-EB and pre-OB period visits. There was a trend for a significant breakfast pattern
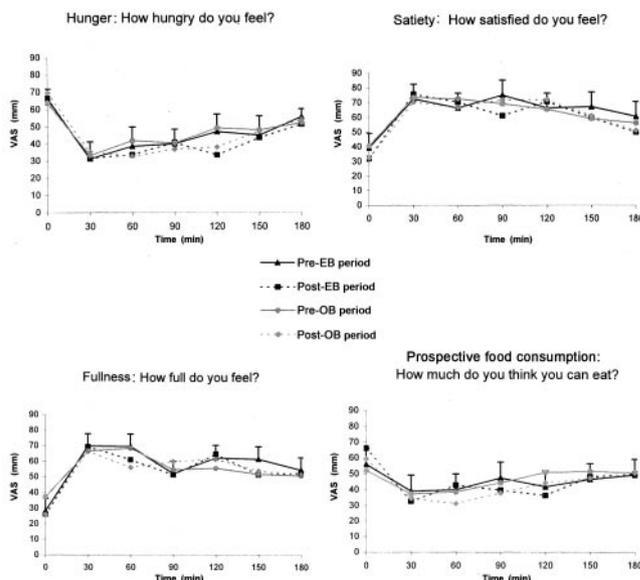
TABLE 2
Mean daily nutrient intake and macronutrient composition (as % of energy) during the intervention periods[1]

	Eating breakfast period	Omitting breakfast period
Energy (MJ)	6.97 ± 0.59	7.35 ± 0.65[2]
Protein (% of energy)	14.5 ± 2.2	15.1 ± 2.3
Fat (% of energy)	34.5 ± 4.4	34.5 ± 2.3
Carbohydrate (% of energy)	50.4 ± 5.1	48.5 ± 3.8

[1] All values are $\bar{x}$ ± SD; n = 10. There were no significant differences in macronutrient composition over the course of the experiment.

[2] Significantly different from the eating breakfast period, P = 0.001 (paired t test).

FIGURE 1. Mean (±SEM) subjective appetite scores (hunger, satiety, fullness, and prospective food consumption) in 10 healthy lean women before and after the test meal that preceded and followed the eating and omitting breakfast (EB and OB, respectively) periods. No significant differences were observed (ANOVA). VAS, visual analogue scale.
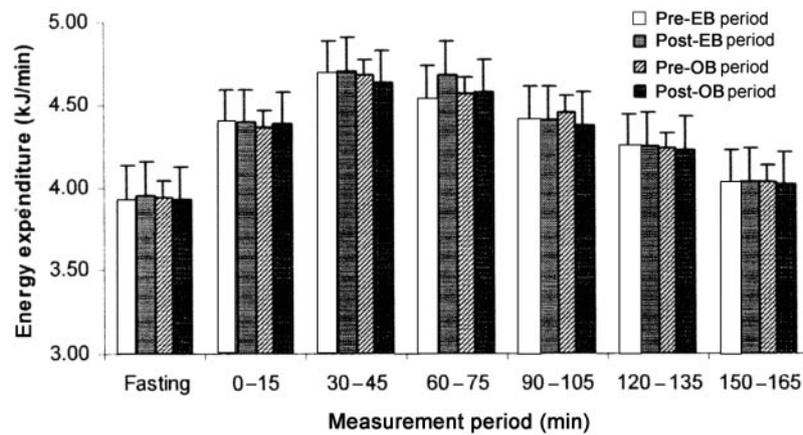
FIGURE 2. Mean (±SEM) energy expenditure in 10 healthy lean women before and after the test meal that preceded the eating and omitting breakfast (EB and OB, respectively) periods. Subjects drank the milkshake test meal within 10 min. Time zero refers to the end of the test meal consumption. Fasting energy expenditure and energy expenditure profiles did not differ significantly during the experiment (ANOVA).

(EB or OB)–by–visit (before intervention or after intervention) interaction for the peak serum insulin concentration [$P = 0.07$, two-factor ANOVA (factors are intervention and visits)]. Thus, the peak of serum insulin tended to rise after the OB period and tended to decrease after the EB period (Table 3). The AUC of postprandial serum insulin did not differ significantly between the pre-EB and pre-OB period visits, but there was a significant breakfast pattern (EB or OB)–by–visit (before intervention or after intervention) interaction for the AUC of insulin response ($P = 0.001$, two-factor ANOVA; Figure 4 and **Figure 5**). The AUC of serum insulin response fell significantly after the EB period ($P = 0.014$, paired t test) but rose significantly after the OB period ($P = 0.006$, paired t test).

Plasma lipids and plasma uric acid

Table 3 also shows the mean values of fasting plasma total, LDL, and HDL cholesterol and triacylglycerol concentrations at all visits. The lipid values did not differ significantly between the pre-EB and pre-OB period visits. There was a significant breakfast pattern (EB or OB)–by–visit (before intervention or after intervention) interaction for plasma total cholesterol concentrations ($P = 0.002$, two-factor ANOVA). Plasma total cholesterol did not change significantly after the EB period, but it increased significantly after the OB period ($P = 0.02$, paired t test). Plasma total cholesterol was also significantly higher after the OB period than after the EB period ($P = 0.001$, paired t test). There was also a significant breakfast pattern (EB or OB)–by–visit (before intervention or after intervention) interaction for plasma LDL concentration ($P = 0.009$, two-factor ANOVA): it rose significantly after the OB period ($P = 0.04$, paired t test) but did not change significantly after the EB period (paired t test). Plasma LDL cholesterol was also significantly higher after the OB period than after the EB period ($P = 0.001$, paired t test). However, no significant differences were observed in plasma HDL concentration over either period. Plasma triacylglycerol concentrations also showed no significant difference over the course of the
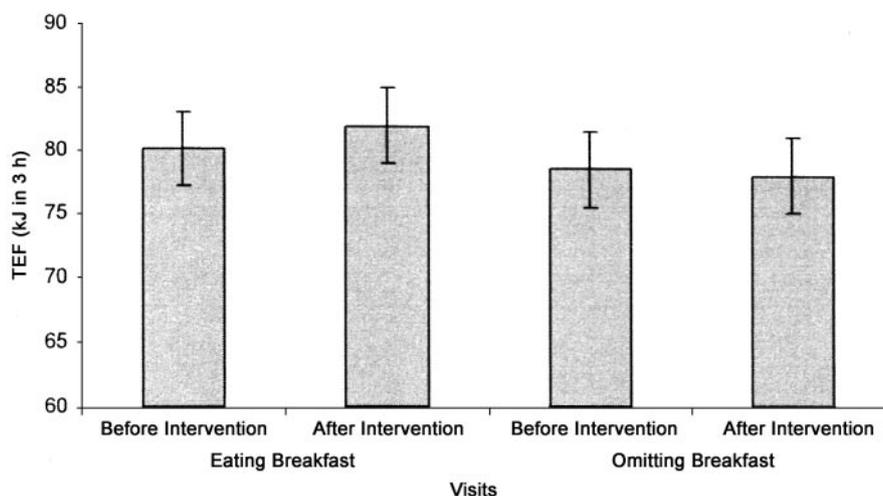
FIGURE 3. Mean (±SEM) thermic effect of food (TEF) in 10 healthy lean women before and after the eating and omitting breakfast (EB and OB, respectively) periods, measured by the trapezoidal method. There were no significant differences between the 2 interventions (ANOVA).

TABLE 3
Fasting glucose, insulin, lipid, and uric acid concentrations and postprandial glucose and insulin concentrations over the course of the experiment[1]

	Eating breakfast period		Omitting breakfast period	
	Before intervention	After intervention	Before intervention	After intervention
Blood glucose (mmol/L)	4.59 ± 0.25	4.60 ± 0.22	4.56 ± 0.32	4.65 ± 0.28
Serum insulin (pmol/L)	41 ± 12	40 ± 10	40 ± 9	41 ± 9
HOMA-IR	1.38 ± 0.44	1.38 ± 0.34	1.35 ± 0.33	1.36 ± 0.27
Plasma cholesterol (mmol/L)[2]				
Total	3.25 ± 0.42	3.14 ± 0.41	3.23 ± 0.47	3.43 ± 0.44[3]
HDL	1.48 ± 0.30	1.50 ± 0.31	1.48 ± 0.32	1.46 ± 0.31
LDL[4]	1.63 ± 0.41	1.55 ± 0.28	1.61 ± 0.35	1.82 ± 0.30[5]
Plasma triacylglycerol (mmol/L)	0.69 ± 0.21	0.67 ± 0.18	0.70 ± 0.18	0.76 ± 0.18
Plasma uric acid (mg/L)	232 ± 50	224 ± 47	241 ± 62	231 ± 52
Peak postprandial blood glucose (mmol/L)	6.67 ± 0.71	6.51 ± 0.45	6.77 ± 0.50	6.83 ± 0.51
Peak postprandial serum insulin (pmol/L)[6]	370 ± 188	362 ± 166	368 ± 179	400 ± 188

[1] All values are $\bar{x}$ ± SD; n = 10. HOMA-IR, homeostasis model assessment of insulin resistance.

[2] Significant breakfast pattern (eating breakfast or omitting breakfast)–by–visit (before intervention or after intervention) interaction was observed for plasma total cholesterol, P = 0.002 (two-factor ANOVA).

[3] Significantly different from before intervention, P = 0.02 (paired t test), and significantly different from after intervention in the eating breakfast period, P = 0.001 (paired t test).

[4] Significant breakfast pattern (eating breakfast or omitting breakfast)–by–visit (before intervention or after intervention) interaction was observed for plasma LDL concentration, P = 0.009 (two-factor ANOVA).

[5] Significantly different from before intervention, P = 0.04 (paired t test).

[6] A trend for significant breakfast pattern (eating breakfast or omitting breakfast)–by–visit (before intervention or after intervention) interaction was observed for peak postprandial serum insulin, P = 0.07 (two-factor ANOVA). The peak of serum insulin tended to rise after the omitting breakfast period and tended to decrease after the eating breakfast period.

experiment. In addition, there were no significant changes in plasma uric acid over the course of the experiment (Table 3).

DISCUSSION

The aim of this study was to compare the effects of OB and EB on EI, REE, and indexes of carbohydrate and lipid metabolism and plasma uric acid concentrations. We found that, in healthy lean women, OB led to a higher plasma total and LDL-cholesterol concentrations and lower postprandial insulin sensitivity than did EB. Mean reported total EI was significantly lower during the EB period than during the OB period.

The incidence of OB has increased in recent years, perhaps due in part to a belief that skipping breakfast can help to reduce total EI and control weight (10). It was also reported that genetic and environmental factors could affect breakfast eating habits (32), and this indicates that, in the future, advice about potential benefits of breakfast consumption should be tailored to the individual. The poor description in that report of breakfast composition and of the time at which breakfast was eaten and the lack of consideration of confounding factors in previous studies weaken any comparison that can be made with the results in the current study. We clearly defined breakfast as a prescribed amount of milk and cereal consumed between 0700 and 0800. Because some of the previous studies reported beneficial effects of cereal consumption only in the context of EB, we gave subjects whole-grain cereal to eat (before 0800 in the EB period and between 1230 and 1300 in the OB period) so that we could investigate the effect of the time of eating the same breakfast food. Cyclic fluctuations have been reported in women's food intake (33) and REE (34) throughout the menstrual cycle. To overcome this possible factor, each intervention period started at the same stage of the menstrual cycle. To reduce potential variability between subjects (7), only subjects who reported that they usually ate breakfast were recruited for the present study. Our previous studies found that an irregular meal frequency disturbs energy metabolism (35) and creates a degree of insulin resistance and higher fasting lipid profiles (36). Thus, in the current study, subjects were asked to eat 6 times/d at predetermined times during the EB and OB periods.

The mean reported EI was significantly lower in the EB period than in the OB period. This is at variance with previous studies that reported either no difference (2, 3, 9, 10) or even lower EIs (3, 10) in persons who omitted breakfast than in those who ate breakfast, despite a lower BMI in the latter group (3, 10). We did not find any differences in macronutrient composition between the EB and OB groups, which was inconsistent with the previous studies (11, 12). However, this inconsistency is likely to reflect the fact that we ensured breakfast cereal was consumed in both intervention periods; the difference was the time of its consumption. Underreporting of EIs, especially for snacks (37), might lead to errors in data interpretation and also to inconsistent results. We also had underreporting in this study, but the similar degree of underreporting between the habitual diet and the EB period, as well as the crossover design, suggests that the higher total intake in the OB period is a reliable observation even if the absolute intake is not.

The current study did not find any difference in fasting REE and TEF between the EB and OB periods. It is suggested that, if OB has any effect on EE, a longer intervention is needed for that effect to emerge. There also were no significant differences in body weight over the course of the experiment, but that was to be expected because of the short-term nature of the intervention.
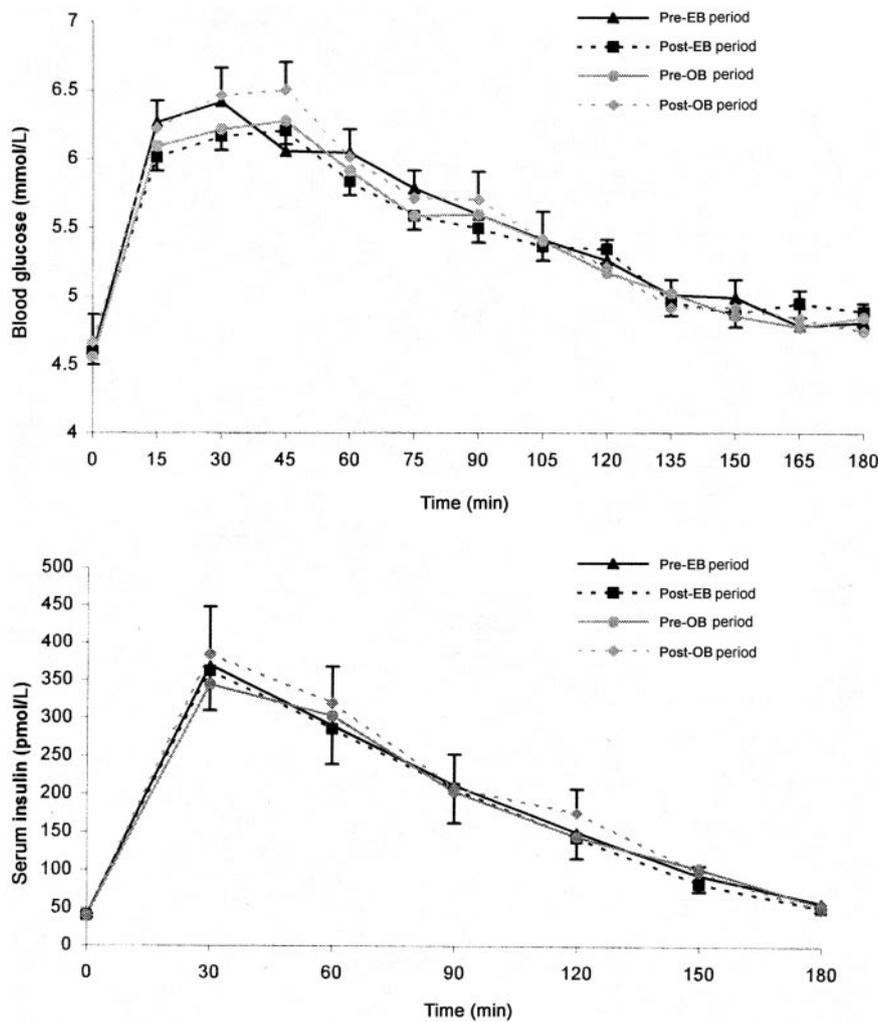
FIGURE 4. Mean (±SEM) blood glucose and serum insulin concentrations in 10 healthy lean women in the fasting state and after the test meal that preceded and followed the eating and omitting breakfast (EB and OB, respectively) periods. No significant differences were observed in blood glucose and serum insulin profiles over the course of the experiment (ANOVA).

Previous reports showed that EB is associated with lower BMI (3–6), although that is not a universal finding (7). Further long-term studies are required to explore the effect of breakfast consumption on EI, EE, and, finally, body weight.

Elevated circulating concentrations of total and LDL cholesterol, triacylglycerol, insulin, and uric acid and reduced HDL-cholesterol concentrations have been identified as risk factors for cardiovascular disease. The effect of breakfast consumption on these risk factors has been of interest to many researchers (11, 12, 18–20). However, no previous studies evaluated the effect of EB on all those variables, and the studies that were performed did not have conclusive results.

The current study reports no significant difference in fasting blood glucose and glucose profile after the test meal. These results were expected because, during short-term interventions in healthy subjects, blood glucose is likely to remain constant, and any compensation would occur via changes in insulin secretion. Furthermore, no significant differences appeared in baseline insulin concentrations or HOMA-IR values over the course of the experiment. The peak postprandial insulin response tended to be lower after the EB period than after the OB period, and the AUC of insulin profile after the test meal showed a significantly higher

response after the OB period than after the EB period. Overall, we suggest that OB may reduce postprandial but not fasting insulin sensitivity in lean people. Previous studies showed that impaired thermogenesis is associated with insulin resistance in obesity (38, 39). However, it seems that the degree of insulin insensitivity in the present study was not enough to impair TEF.

It is not clear why 14 d of OB led to reduced postprandial insulin sensitivity after the postintervention test meal. Variations in insulin sensitivity occur between breakfast and the evening meal of the same day (40, 41), but there are no reports of effects of altering the timing of the first meal of the day. It would be of interest in future studies to examine insulin sensitivity at different times of the day in subjects who eat or omit breakfast. This could be combined with studies of insulin receptor and postreceptor events and counterregulatory hormone concentrations (eg, cortisol and glucagon) in response to a test meal.

Regarding the changes in plasma lipids, the present study indicates that plasma total and LDL-cholesterol concentrations increased after the OB period more than they did after the EB period. Fasting plasma HDL-cholesterol and triacylglycerol concentrations, however, showed no significant differences between the EB and OB periods. The effect of EB in reducing lipid
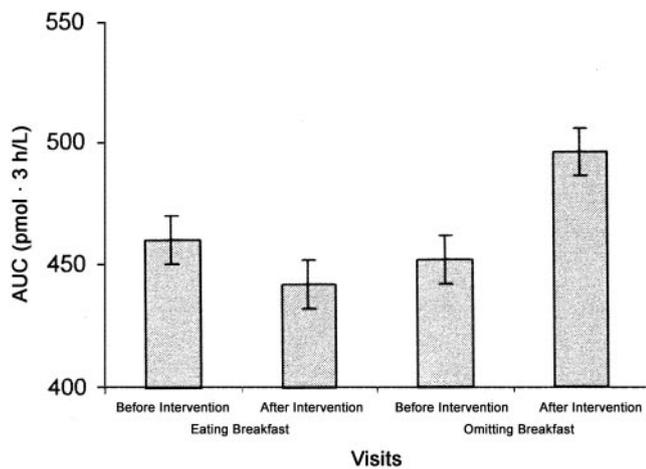
FIGURE 5. Mean (±SEM) area under the curve (AUC; above the baseline) for the serum insulin profiles in 10 healthy lean women responding to the test meal that preceded and followed the eating and omitting breakfast (EB and OB, respectively) periods. There was a significant breakfast pattern (EB or OB)–by–visit (before intervention or after intervention) interaction for serum insulin profile ($P = 0.001$, ANOVA) and a significant reduction after the EB period ($P = 0.01$, paired t test), whereas there was a nonsignificant increase in serum insulin after the OB period ($P = 0.006$, paired t test).

concentration was in agreement with the findings of previous studies (11, 12, 18). However, the mechanism proposed in the previous studies, in which a lower fat intake was associated with EB, cannot explain our results, because we did not find any significant difference in total fat intake.

Insulin stimulates hydroxy methyl glutaryl-Co-A reductase, one of the rate-limiting enzymes in cholesterol synthesis. Lower total and LDL-cholesterol concentrations after the EB period might be due to a lower insulin stimulation of hydroxyl methyl glutaryl-Co-A reductase.

The prevalence of obesity has increased in industrial countries in recent decades. At the same time, OB has become more common, possibly because of efforts to lose weight. The results of this study have showed the potential importance of breakfast consumption to insulin sensitivity and plasma cholesterol concentrations, which are known risk factors for cardiovascular disease. The current study also reports higher EIs with OB than with EB. This indicates a potential mechanism by which breakfast omission could lead to weight gain in the longer term. Further long-term studies are required to ascertain the potential magnitude of such effects and whether they interact with any genetic characteristics (32).

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