

Higher Eating Frequency Does Not Decrease Appetite in Healthy Adults^{1,2}

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Abstract

Background: Consumption of small, frequent meals is suggested as an effective approach to control appetite and food intake and might be a strategy for weight loss or healthy weight maintenance. Despite much speculation on the topic, scientific evidence is limited to support such a relation in the absence of changes to diet composition.

Objective: We examined the effects of high compared with low eating frequency (EF) on self-reported appetite as a secondary outcome in a controlled trial.

Methods: We conducted a randomized, crossover intervention trial in 12 participants (4 men, 8 women) who completed 2 isocaloric 3-wk intervention phases of low EF (3 eating occasions/d) compared with high EF (8 eating occasions/d). On the last morning of each study phase, participants completed a 4-h appetite testing session. During the appetite testing session, participants completing the low EF phase consumed a meal at 0800. Participants completing the high EF intervention consumed the same meal spread evenly over 2 eating occasions at 0800 and 1030. Standardized ratings of hunger, desire to eat, fullness, thirst, and nausea were completed every 30 min with the use of paper-and-pencil semianchored 100-mm visual analog scales. A composite appetite score was calculated as the mean of hunger, desire to eat, and the inverse of fullness (calculated as 100-fullness rating). Linear regression analysis compared ratings between low EF and high EF conditions.

Results: The mean composite appetite score was higher in the high EF condition for the total testing period (baseline through 1200) ($P < 0.05$) and for the time period from baseline through 1030 ($P < 0.001$).

Conclusion: The results from this study in 12 healthy adults do not support the popularized notion that small, frequent meals help to decrease overall appetite. This trial was registered at clinicaltrials.gov as NCT02548026. *J Nutr* doi: 10.3945/jn.115.216978.

Keywords: eating frequency, meal frequency, appetite, satiety, postprandial, hunger

Introduction

Cardiovascular disease, type 2 diabetes, and cancer are among the leading causes of death in the United States and worldwide (1). The burden of these diseases can be partly attributed to overweight and obesity due to excess energy intake and poor diet quality (2). One strategy to improve control of food intake and body weight could involve better regulation of appetite.

The consumption of several small, frequent meals may contribute to feelings of greater fullness and satiety than less frequent, larger meals. Eating frequency (EF)⁶ is proposed to influence appetite via effects on several physiologic (3) and

cognitive pathways (4), and the effects of EF may be largely determined by diet composition. However, few studies have investigated this topic with the use of repeated-measures assessment of self-reported appetite especially in the context of a diet that is not manipulated in terms of energy or macronutrient content (3). In 1 study with obese males, researchers found that increased frequency of eating was associated with reduction in self-reported appetite ratings directly before a consumed lunch and with lower energy consumption at lunch (5). Conversely, another trial showed that increased frequency of eating was associated with lower satiety in healthy males over the morning but with a delay in gastric emptying with more frequent feeding (6). Other studies have collected satiety data at only 1 time point per day, either directly before 1 large meal or in the form of 1 question that asked about hunger throughout an entire day (7, 8). On the basis of the current research available on EF and appetite, it is unclear what the impact of alterations in EF is on appetite or subsequent food and caloric intake. The role of EF in human appetite regulation thus remains unclear.

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⁶ Abbreviations used: EF, eating frequency; FHCRC, Fred Hutchinson Cancer Research Center; GEE, generalized estimating equation; MAGS, Meals and Grazing Study; VAS, visual analog scale.

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The goal of the present study was to investigate the relation between EF and self-reported appetite in the absence of alterations to the caloric or macronutrient content of the diet. Specifically, in a randomized crossover trial, we tested whether the consumption of food consumed as 1 eating occasion would result in higher or lower self-reported appetite ratings compared with the same amount of food consumed as 2 equal servings over the same time period in 2 separate appetite testing sessions. We hypothesized that increased EF would be associated with decreased appetite in a sample of men and women. The variables analyzed comprise secondary outcomes of a larger parent study, called the Meals and Grazing Study (MAGS) whose primary outcome was changes in biomarkers related to disease risk and appetite.

Methods

Participants. All study participants were enrolled in the MAGS, a randomized, crossover controlled clinical trial that investigated the impact of EF on health-related outcomes. Recruitment was completed with the use of posters and online advertisements at the Fred Hutchinson Cancer Research Center (FHCRC) and the University of Washington campus in Seattle, Washington. Briefly, participants were told that researchers were interested in learning more about whether it was more beneficial to eat more often throughout the day or fewer times throughout the day. Participants were healthy 18- to 50-y-old men and women with a BMI (in kg/m^2) ≥ 18 (normal to obese). Exclusion criteria included diabetes, smoking, following a diet to gain or lose weight, athletes in training, nonnormal blood cholesterol or blood pressure, taking prescribed medication other than oral contraceptives, and pregnancy or nursing (women) because these conditions would not be compatible with the protocol or could have confounded results. All experimental protocols were approved by the Institutional Review Office at the FHCRC, and all participants provided written informed consent. Participants were paid \$100 for completion of the parent study plus the optional appetite testing sessions to compensate for their time and travel expenses.

Study design. Participants were recruited with the use of flyers on the FHCRC campus in Seattle, Washington, and online advertisements. Interested individuals were invited via e-mail or telephone for an initial orientation session at FHCRC in which eligibility criteria were verified and study procedures were explained in detail. Participants were free-living and consumed their own food throughout the study with the use of an individually tailored meal plan, which was designed with the use of the following procedures. Eligible participants who enrolled in the study were provided detailed written and verbal instructions on keeping a 7-d food record. Participants then recorded details (type and quantity) for all food and drink except water consumed for 7 consecutive days and returned food records to study staff via hand delivery or US Postal Service. On receipt, the study dietitian analyzed the 7-d food record for energy and macronutrient content with the use of The Food Processor software (ESHA Research). Keeping food items, energy, and macronutrient content of the diet constant, a low EF meals meal plan (providing all energy as 3 evenly spaced eating occasions per day) and a high EF grazing meal plan (providing all energy as 8 evenly spaced eating occasions per day) were individually designed for each participant. Initial and final eating occasions for each participant were set to match approximately their usual schedule, and equal time was allotted between each daily eating occasion. Weight-maintaining meal plans were designed to rotate every 7 d, and participants were instructed to eat only the foods on their individual eating plan at the specified hours. All meal and snack consumption (including time of intake) was reported daily with the use of an electronic meal plan checklist to monitor compliance during the 21-d intervention phases.

This study was a crossover trial, with each participant serving as his or her own control. Participants in the MAGS completed two 21-d study phases in random order with a 14-d washout period during which time

they were instructed to consume their habitual diet. Participants attended 4 clinic visits at the FHCRC Prevention Center at 0800 on day 1 and day 21 of both phases. All other study activities were completed at home. Appointments were scheduled on the same day of the week whenever possible. Participants were asked to consume nothing other than noncarbonated water for 12 h before their clinic appointments and to refrain from drinking alcohol or eating or exercising outside of their normal routine. During all 4 clinic visits, body weight, height, waist, hip, pulse, and systolic and diastolic blood pressures were measured by trained staff with the use of a highly standardized protocol, and blood samples were taken. During the first appointment, DXA GE Lunar DPX Pro (GE Healthcare Lunar) was used to measure body fat percentage.

Appetite testing sessions. All participants were invited to participate in the appetite testing on the last day of each study phase. The appetite testing sessions were conducted from ~0800 through 1200 on the last day of each study period. On arrival at the clinic, participants were seated in private clinic rooms where they would remain for the duration of the test. At baseline and every 30 min through 1200, participants rated feelings of appetite with the use of 100-mm visual analog scales (VASs). Immediately after the baseline assessment, participants in both conditions were provided a serving of food, which they were required to consume in entirety within 30 min. In the low EF condition there was 1 eating occasion (directly after baseline measurements), and in the high EF condition there were 2 eating occasions (directly after baseline and at 1030). Throughout the testing session, participants remained in clinic rooms and were allowed to engage in quiet activities, such as reading, listening to music with headphones, or using a personal computer, and to leave briefly to use the restroom.

We measured the impact of EF on self-reported appetite at the end of each 3-wk phase. Order of conditions followed the crossover design used for the parent MAGS, so that each participant in the present analysis completed a low EF appetite testing session and a high EF appetite testing session. During appetite testing sessions, participants consumed either 1 large portion of food at 1 occasion (low EF) or 2 smaller portions of food at 2 occasions (high EF) and rated appetite for the duration of the testing session. Foods provided during the appetite testing session were selected from the FHCRC cafeteria and were closely matched to the foods normally eaten by the participant at that time and weekday. In the low EF condition, participants consumed roughly 33% of their usual daily caloric intake in 1 serving. In the high EF condition, 33% of the participant's estimated daily caloric intake was consumed in 2 equally divided servings. For example, if a participant usually ate 250 mL oatmeal with 84 g blueberries and 2 hard-boiled eggs for breakfast, they would receive the same foods during their appetite testing session. In the low EF condition, they would consume all foods at 1 occasion, and in the high EF condition they would consume 125 mL oatmeal, 42 g blueberries, and 1 hard-boiled egg at each of 2 separate occasions, so total energy intake between the 2 conditions would be equal. Participants were to consume all of the food and drink provided during the appetite testing session and were not allowed outside food or drink.

VASs to assess appetite. Participants rated their hunger, desire to eat, fullness, thirst, and nausea on a semianchored 100-mm VAS every 30 min throughout the study. VASs were presented as a booklet with 1 scale per page with questions such as "How hungry do you feel right now?" and were labeled with anchors such as "not at all" at 0 mm and "extremely" at 100 mm. Participants used a pen to place a single mark on the horizontal bar at the point which best described their feeling at the time of each rating. Ratings were manually scored with the use of a ruler, measured to the nearest millimeter. A composite appetite score was calculated as the mean of hunger, desire to eat, and fullness, following previous investigations (9–11).

Statistical analysis. The primary analytic goal was to assess differences in self-reported appetite ratings between the low EF condition and the high EF condition. We conducted additional analyses restricted to time points from baseline through 1030 (~2 h) and restricted to time points from 1100 through 1200 (1 h) to examine whether self-reported appetite scores differed at the point in time where the total energy and total food

consumed would have been equivalent across the 2 conditions. The generalized estimating equation (GEE) modification of linear regression with a working unstructured correlation was used for the analysis. This method accounts for the correlation within individuals over time and covariate adjustment. Models were adjusted for order of conditions, sex, and body fat percentage only if they altered parameter estimates by >10%. This did not occur in any of the models tested. Differences in AUC (calculated with the use of the trapezoidal rule) between the 2 conditions were examined with the use of paired *t* tests. We tested differences over the entire testing period from baseline through 1200 (~4 h), from baseline through 1030 (~2 h), and from 1100 through 1200 (1 h). Total energy (in kcal); percentage of energy from carbohydrate, protein, and fat; fiber (in g) consumed during testing sessions; weight; and waist-to-hip ratio were also analyzed for between-conditions differences with the use of the GEE modification of linear regression. Statistical analyses were performed with Stata version 12.0 (StataCorp LP). All tests were 2-sided, and statistical significance was set at $P < 0.05$. Values are presented as means \pm SDs.

Results

Thirty-four participants attended the initial screening session, of which 32 were eligible to participate and enrolled. Of those, 15 completed the MAGS. Twelve participants completed the optional appetite testing sessions for this analysis (Table 1). No difference was found in the energy content ($P > 0.05$) or macronutrient composition ($P > 0.05$) of the diets assigned to participants during the 3-wk low EF and high EF intervention phases. As measured by the 7-d food record, participants habitually consumed an average of 2227 kcal/d (47% carbohydrate, 18% protein, 35% fat). Linear regression models showed no significant differences between conditions in total energy, percentage of carbohydrate, percentage of protein, percentage of fat, and grams of fiber provided during appetite testing sessions. Summary characteristics of the foods consumed during appetite testing sessions are provided in Table 2. Linear regression models revealed no significant difference between conditions in weight ($P = 0.84$), waist-to-hip ratio ($P = 0.99$), systolic blood pressure ($P = 0.09$), or diastolic blood pressure ($P = 0.81$).

Self-reported appetite rating for hunger. Hunger ratings were highest at baseline in both the low EF and high EF conditions (Figure 1A). In the low EF and high EF conditions, hunger ratings decreased after the first eating occasion, and in the high EF condition, ratings continued to increase through the final rating at 1200. High mid-morning hunger in the high EF condition was suppressed after the second eating occasion, after which time ratings also increased until 1200. Analysis with the use of GEE showed that mean hunger was significantly lower over the entire testing period in the low EF condition than in the high EF condition ($P < 0.001$). In the analysis restricted to baseline through 1030, hunger was significantly lower in the low compared with high EF condition ($P < 0.001$). The 1100 through

TABLE 1 Characteristics of participants in a randomized, crossover trial of eating frequency¹

Characteristic	Men ($n = 4$)	Women ($n = 8$)	Overall ($n = 12$)
Age, y	25.0 \pm 4.7	28.1 \pm 8.4	27.1 \pm 7.3
BMI, kg/m ²	22.4 \pm 1.2	24.3 \pm 4.2	23.7 \pm 3.5
Total body fat, %	25.5 \pm 2.8	35.2 \pm 6.2	31.9 \pm 7.0
Waist-to-hip ratio	0.84 \pm 0.1	0.80 \pm 0.1	0.82 \pm 0.1

¹ Values are means \pm SDs.

TABLE 2 Nutritional composition of meals/snacks consumed during satiety testing sessions¹

Nutritional composition	Low eating frequency	High eating frequency
Total energy, kcal	547 \pm 221	540 \pm 229
Carbohydrate, % energy	58.4 \pm 11.7	58.1 \pm 11.4
Protein, % energy	14.6 \pm 2.7	14.6 \pm 2.9
Fat, % energy	30.0 \pm 12.5	30.3 \pm 12.0
Fiber, g/eating occasion	8.0 \pm 4.0	7.8 \pm 3.9

¹ Values are means \pm SDs, $n = 12$.

1200 testing periods were not significantly different between the 2 conditions ($P = 0.23$). In paired *t* tests, AUC for hunger for 0800 through 1030 was greater in the high EF condition than in the low EF condition ($P < 0.05$), but it did not remain significantly different for the entire testing period ($P = 0.26$) nor for the final hour ($P = 0.69$).

Self-reported appetite rating for desire to eat. In the low EF condition, desire to eat was suppressed by the first eating occasion with a nadir at 1000 and then increased steadily until completion of the test at 1200. In the high EF condition, desire to eat was suppressed to a lesser degree in response to the first eating occasion. Ratings then increased more dramatically until the second eating occasion at 1030, after which time they decreased to levels lesser than those seen in the low EF condition (Figure 1B). In regression analyses, mean desire to eat was significantly lower in the low EF condition than in the high EF condition over the entire testing period and in the analysis restricted to baseline through 1030 ($P < 0.001$ for both). No significant differences were observed in regression analyses that compared conditions of low EF and high EF in desire to eat from 1100 through 1200 ($P = 0.59$). AUC for desire to eat was greater in the high EF condition for the entire testing session ($P = 0.02$) and for the restricted time 0800 through 1030 ($P = 0.07$). No significant difference was observed in AUC for desire to eat between the low and high EF conditions during times 1100 through 1200 ($P = 0.65$).

Self-reported appetite rating for fullness. Fullness was initially low and increased after the first eating occasion in both conditions, reaching a peak at 1000. Fullness then decreased in the low EF condition through 1200; in the high EF condition fullness increased again after the second eating occasion at 1030 (Figure 1C). In regression analyses, comparison of mean fullness ratings over the total testing period and for the restricted times baseline through 1030 showed lower fullness ratings in the high EF condition than in the low EF condition ($P = 0.05$ and $P < 0.05$, respectively). Mean fullness ratings were significantly higher in the high EF condition in regression analyses that compared times 1100 through 1200 ($P < 0.05$). Paired *t* tests showed no significant difference between conditions in the AUC for fullness over the total testing period ($P = 0.13$). AUC for fullness was significantly lower in the high EF condition when the paired *t* test was comparing ratings restricted to times baseline through 1030 ($P = 0.04$). A paired *t* test found no difference in AUC for fullness for the restricted time period 1100 through 1200 ($P = 0.65$).

Composite appetite score. Temporal profiles for the composite appetite score are shown in Figure 1D. Mean composite

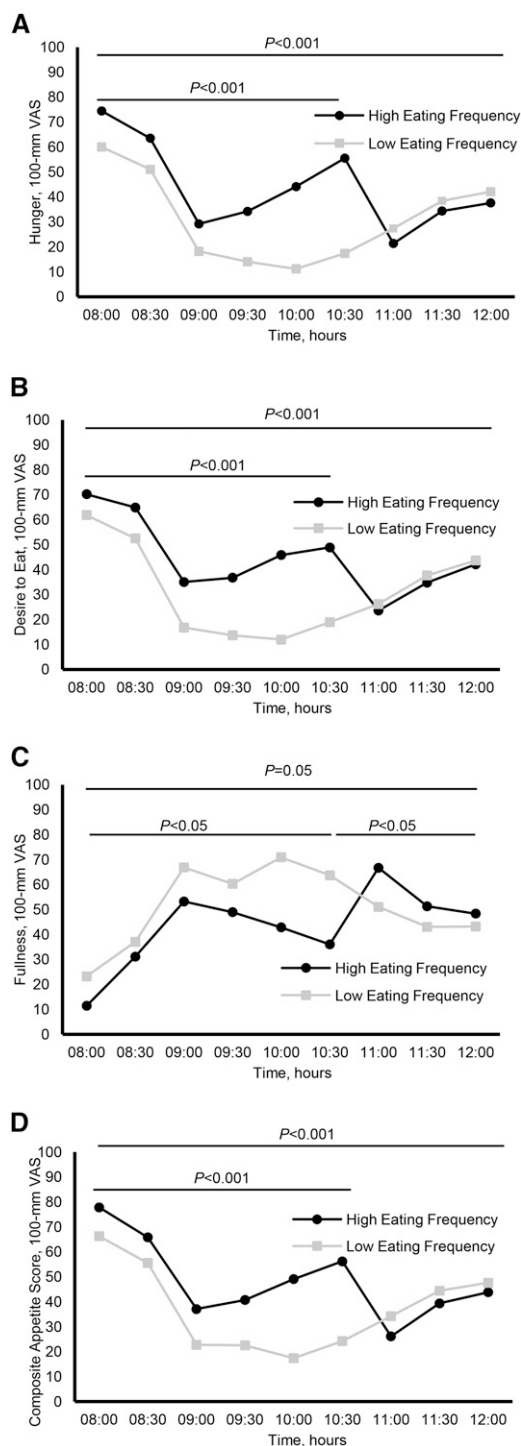


FIGURE 1 Self-reported hunger (A), desire to eat (B), fullness (C), and composite appetite score (D) in high and low eating frequency conditions by healthy adults. Values are means, $n = 12$. Significant differences over the entire testing period, from baseline through 1030 and from 1100 to 1200 are shown. VAS, visual analog scale.

appetite was higher in the high EF condition for the total testing period ($P < 0.05$) and for the time period baseline through 1030 ($P < 0.001$) in regression analyses. No significant difference was detected between conditions in mean composite appetite for the final hour of testing ($P = 0.12$). In paired t tests, the AUC for composite appetite over the entire testing period was greater in the high EF condition ($P < 0.05$) and for the time period 0800 through 1030 ($P < 0.05$). No significant difference was found

between conditions for the time period 1100 through 1200 ($P = 0.55$).

Discussion

In this randomized crossover trial that tested the impact of EF on self-reported appetite, we found that participants experienced significantly stronger hunger and desire to eat and they tended toward feeling less full when they consumed equal amounts of food as 2 eating occasions compared with 1 eating occasion over a 4-h period. In analyses restricted to baseline through 1030, participants in the high EF condition had completed only 1 eating occasion after baseline that provided on average 273 kcal and reported higher hunger and desire to eat and lower fullness than they did in the low EF condition after having 1 eating occasion that provided on average of 547 kcal. When analyses were restricted to the final hour of testing, participants had consumed equivalent amounts of food in both conditions. Ratings of hunger and desire to eat were indistinguishable between conditions, but fullness was significantly higher in the high EF condition. Taken together, these preliminary findings suggest that the consumption of fewer, smaller meals may not decrease appetite. However, the observations collected during the final hour of appetite testing (1100 through 1200) suggest that, when total food and macronutrient consumption is equal, EF may not affect satiety. Further research is necessary to definitively test whether total calories consumed or frequency of consumption has the greatest influence on satiety.

In our study, the higher satiating effect of equal total food consumption in the low EF condition suggests that consumption of fewer, larger meals may suppress appetite to a greater degree over a given period of time. As observed in analyses restricted to the times baseline through 1030, and over the total testing period, higher satiety may be achieved by consumption of higher volume, higher energy eating occasions. These findings may be because of differences between conditions in rate of stomach emptying on the basis of volume, energy, or nutrients consumed; different rates of nutrient metabolism; or may reflect an inadequacy in the length of time of our appetite testing session. Further studies conducted over the course of an entire day may help to elucidate other mechanisms by which equal total energy consumption may lead to similar appetite between conditions of high and low EF.

The notion that increased EF can help suppress appetite and curb food and caloric intake is supported by limited experimental evidence. In 1 crossover study by Stote et al. (7), participants consumed total daily calories as 3 meals per day or as 1 large evening meal for two 8-wk phases. Appetite ratings were collected once per day before the evening meal in both conditions. Participants reported significantly higher hunger when consuming 1 meal per day than when consuming 3 meals per day (7). In that study, it is possible that the higher hunger ratings observed in the lower EF condition were a reflection of the lower overall total energy and volume consumption at the time appetite was measured. In a short-term crossover study with obese males, Speechly et al (5) provided participants with isoenergetic preloads served at 1 eating occasion after baseline or as 5 hourly eating occasions before a consumed test lunch. No significant differences in overall ratings of hunger, prospective food consumption, or urge to eat were detected between conditions for the time period before the test lunch. Directly before the test lunch, when energy intake was equal in both conditions, hunger ratings were higher in the lower EF condition. Test lunch

energy consumption was also higher in the lower EF condition. Comparison of satiety ratings before and after lunch showed that participants rated hunger, prospective food consumption, and urge to eat significantly lower in the lower EF condition after the test lunch, whereas no difference was observed in the higher EF condition (5). The findings of Speechly et al (5) suggest that higher EF may suppress hunger and subsequent intake. In another crossover study, healthy male subjects consumed isoenergetic meals as either 2 eating occasions spaced 3 h apart or 6 hourly eating occasions on 2 different testing occasions. No significant difference was observed between conditions in terms of appetite ratings (6). Given these varying study designs in which the eating frequencies, food provided, and appetite testing intervals varied, including our own, it is no surprise that results and inferences are not consistent across studies. Taken together, the published studies to date suggest that the relation between EF and appetite is complex and will require further study before definitive recommendations can be offered to the public.

Although few controlled trials have addressed the issue, findings from observational studies suggest some link between EF and health-related outcomes. Most epidemiologic studies show evidence of an inverse relation between EF and body weight, body fatness, and other markers for disease risk (12–26). Some studies have detected a positive relation (27–29), and still others have reported mixed results on the basis of participants' demographic characteristics, including age and sex (30, 31). However, major shortcomings exist in the available research, including underreporting of intake, unclear definition of terms such as meals and snacks, and inconsistencies across studies, leaving this issue largely unresolved. Moreover, none of these observational studies directly measured appetite, so a relation between EF, satiety, and health outcomes could not be determined.

This study had several notable strengths. First, we used a reliable tool to assess appetite, which was used in numerous other studies, and the measurement properties of the tool are thought to be valid and reproducible (32). Second, the total energy and volume of food were identical for the high and low EF test meals; the total food provided was simply divided into 1 or 2 eating occasions. This ensured that the appetite ratings did not differ between conditions on the basis of any possible differences in palatability, macronutrient distribution, or total energy consumed. Participants were compliant with the protocol, and there were no dropouts. There are also limitations. This study assessed the short-term (~4 h) effects of alterations in EF on self-reported appetite ratings in a laboratory environment. Manipulations in EF in a free-living population may not have similar effects on appetite over a longer period of time. Other researchers have measured satiety either on a daily basis in a long-term crossover (7) or have incorporated measurement of energy intake at a test meal in the study design (5). Future investigations will benefit from a combination of longer-term intervention periods, daily satiety ratings, and appetite testing sessions with measurement of consumed test meal energy intake. Further, findings from studies on EF and appetite will ultimately be translated into recommendations for optimal EF. More frequent measures of appetite in a naturalistic setting and measurement of outcomes such as quality of life should be used to determine whether altering EF is a realistic behavioral change. Finally, most of our study participants were women with normal BMI. Results may therefore not be generalizable to the overweight and obese population, who may benefit most from this research.

In conclusion, results from this investigation indicate that increased EF is not associated with decreased appetite over a short time period. Thus, although it is often recommended as a means by which to control intake, the grazing, nibbling, or snacking meal pattern may not result in decreased appetite.

Acknowledgments

MMP conceived of the study, performed study design and coordination, and drafted the manuscript; AD provided guidance for study design and manuscript preparation; C-YW provided oversight for data analysis; and MLN oversaw all aspects of study design, coordination, data analysis, drafted the manuscript, and secured study funding. All authors read and approved the final manuscript.

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