Title

Weight Loss, but Not Dairy Composition of Diet, Moderately Affects Satiety and Postprandial Gut Hormone Patterns in Adults.

Journal

The Journal of nutrition, 151(1)

ISSN

0022-3166

Authors

Krishnan, Sridevi
Adams, Sean H
Witbracht, Megan G
et al.

Publication Date

2021

DOI

10.1093/jn/nxaa327

Peer reviewed

The Journal of Nutrition
Ingestive Behavior and Neurosciences

Weight Loss, but Not Dairy Composition of Diet, Moderately Affects Satiety and Postprandial Gut Hormone Patterns in Adults

Sridevi Krishnan,[1] Sean H Adams,[1,2] Megan G Witbracht,[1] Leslie R Woodhouse,[2] Brian D Piccolo,[1,2] Anthony P Thomas,[1] Elaine C Souza,[2] William F Horn,[2] Erik R Gertz,[2] Marta D Van Loan,[1,2] and Nancy L Keim[1,2]

[1]Department of Nutrition, University of California, Davis, Davis, CA, USA; and [2]Western Human Nutrition Research Center, USDA Agricultural Research Service, Davis, CA, USA

ABSTRACT

Background: Inclusion of dairy in diet patterns has been shown to have mixed effects on weight loss. A prevailing hypothesis is that dairy improves weight loss by influencing endocrine systems associated with satiety and food intake regulation.

Objectives: The objective of the current study was to evaluate the effect of weight loss with or without adequate dietary dairy on subjective and objective appetitive measures.

Methods: Men and women who were habitual low dairy consumers (n = 65, 20–50 y) participated in a 12-wk randomized controlled feeding weight loss trial. During the 12-wk intervention, a low-dairy (<1 serving dairy/d) was compared with an adequate-dairy (3–4 servings dairy/d) diet, both with a 500-kcal deficit/d. Test days, before and at the end of the intervention, began with 2 fasting blood draws and visual analog scale (VAS) measures, followed by a standard breakfast (25% of prescribed restricted calories), 5 postbreakfast blood draws and VASs, a standard lunch (40% of restricted energy amount), and 12 postlunch blood draws and VASs. Blood samples were used for satiety hormone measurements. On a separate day when matching standard meals were consumed, an ad libitum buffet meal was provided as dinner, at a self-selected time. Meal duration and intermeal interval were recorded.

Results: Weight loss (−6.1 kg), irrespective of dairy, resulted in reduced fasting insulin (−20%) and leptin (−25%), and increased fasting acylated ghrelin (+25%) and VAS desire to eat (+18%) ($P < 0.05$). There were no effects of dairy on objective or subjective satiety measures. Weight loss marginally reduced the intermeal interval (289 min compared with 276 min, $P = 0.059$) between lunch and the ad libitum buffet.

Conclusions: These results do not support the hypothesis that inclusion of dairy in long-term dietary patterns influences appetite during weight loss. Weight loss per se has a modest impact on select systems that regulate hunger and satiety. This trial was registered at clinicaltrials.gov as NCT00858312. *J Nutr* 2021;151:245–254.

Keywords: dairy, satiety, ad libitum buffet, ghrelin, leptin, desire to eat, weight loss, appetite

Introduction

Eating behavior in humans is closely associated with body weight regulation (1). Eating behavior is affected by a host of parameters, primary among them appetite (the drive to search for, acquire, and consume food) (2), hunger (defined as a "conscious sensation reflecting mental urge to eat") (3), satiation (which applies to intrameal processes leading to termination of food intake) (3), and satiety (which applies to postprandial satiety, reduced hunger and desire to eat, and increased fullness) (3).

The influence of weight loss on comprehensive gut hormone and satiety responses is unclear (4, 5). Whereas more is known about how satiety hormones or neuroendocrine factors affect body weight regulation, much less is known about how weight loss affects these factors (6). A recent study looking at long-term effects (2 y follow-up) of a lifestyle-induced weight loss intervention (8.4% weight loss) reported increases in fasting and postprandial hunger and reduced fullness. They also reported increased average circulating ghrelin, peptide-YY_{3-36} (PYY_{3-36}), and cholecystokinin (CCK) and reduced insulin in response to a 600-kcal breakfast meal containing 17% protein, 35% fat, and 48% carbohydrates at the end of the intervention (4). Sumithran et al. (7) reported that even 1 y after significant weight loss, ghrelin and hunger ratings were higher than at baseline, whereas insulin, leptin, PYY_{3-36}, CCK, gastric inhibitory peptide (GIP), and pancreatic polypeptide were reduced. More proximal to the weight loss intervention,

Manuscript received November 1, 2019. Initial review completed January 28, 2020. Revision accepted October 5, 2020.
First published online November 26, 2020; doi: https://doi.org/10.1093/jn/nxaa327.

a ketogenic diet (with weight loss ranging from 2% to 17%) increased self-reported hunger indexes at fasting, and increased both fasting and postprandial blood ghrelin (8). In another study, sustained weight loss (15% of body weight) increased the drive to eat in the fasting state, but this was countered with increased fullness in the postprandial state when compared with preintervention (9). Data from these studies and others suggest that weight loss likely increases hunger and circulating active ghrelin; however, its effect on CCK, PYY_{3-36}, and other satiety factors remains unclear.

Diet composition affects satiety (10), and meals high in fiber (11), fat (12), and protein (13) have been associated with increased satiety. Although dietary fat and protein may increase satiety, the specific types of these macronutrients could influence these effects differentially (14, 15). It has been posited that because dairy foods, particularly milk, are a rich source of protein (e.g., whey and casein), as well as several unique lipids (e.g., conjugated linoleic acid, dairy lipid emulsions), appetite regulation differs between people who are prescribed to a low-dairy (LD) food–rich diet as compared with an adequate dairy (AD) food–rich diet (16, 17). In a weight loss intervention, dairy was found to attenuate hunger and desire to eat when dairy was supplemented compared with a group that did not consume AD (18). This suggests that dairy consumption could aid in weight loss efforts by affecting appetite favorably.

Consuming a dairy-rich diet and increasing dietary calcium have been associated with increased weight loss (19, 20) and reduction in adiposity (21) in some studies, whereas other studies have not found similar effects (22, 23). Thus, the impact of dairy foods on weight regulation is equivocal and may be context-specific, and potential mechanisms of action remain to be explored. Jones et al. (23) reported a modest increase in circulating PYY_{3-36} summarized as a 4-h AUC after a mixed meal containing 605 kcal. In this study, subjects had increased dairy intake by 500 kcal/d in the form of nonfat or 1% milk or yogurt, and measurements were taken after a 12-wk weight loss trial. The effect of consuming a dairy-rich meal on satiety and appetite is unclear, with some studies suggesting an appetite-suppressing effect (24, 25) and others reporting no association (26, 27). A recent meta-analysis suggested that consuming >500 mL/d of dairy products increased subjective reports of fullness, reduced hunger, and reduced subsequent energy intake after a dairy preload, compared with other beverage preloads (28). A diet effect of consuming dairy foods, as opposed to an acute meal effect on appetite and satiety hormones, has not been determined, especially in the context of persons who do not consume an adequate amount of dairy foods as part of their typical diet.

Long-term effects of dairy on hunger and satiety cues, and the mechanisms involved, remain to be established. To address this gap in knowledge in the context of weight loss, we measured temporal patterns of blood active ghrelin, glucagon-like peptide-1 (GLP-1), GIP, amylin, CCK, PYY_{3-36}, and insulin, concurrently with hunger and fullness indexes, before and after a dairy-rich (AD) or reduced-dairy (LD) weight loss dietary pattern in a well-controlled metabolic laboratory setting. Adults consumed a diet with a 500-kcal deficit/d for 12 wk, and we evaluated the cumulative repeated exposure of dairy on satiety. The study design and cohort have been reported previously (29). The hypotheses were that weight loss would lead to fasting and postprandial phenotypes consistent with higher hunger cues than in pre–weight loss conditions, and that higher chronic dairy food consumption would mitigate these outcomes coincident with altered pre- and postmeal endocrine patterns (e.g., higher excursions of hormones promoting satiety).

Methods

The study (NCT00858312) was conducted in accordance with ethical standards set by the University of California, Davis Office of Research Institutional Review Board. All participants signed an oral informed consent form at the time of recruitment. Methods about the intervention are briefly mentioned in the current report. The complete details including the study intervention diets and cohort characteristics have been previously reported (29).

Subjects

A total of 71 healthy men and women, aged 20–50 y, with a BMI (in kg/m^2) between 28 and 37 and normoglycemic were recruited to participate in a 15-wk controlled feeding study. Low dairy consumers were enrolled based on a dairy and calcium screener (29) (**Supplemental Table 1**): typical dairy food consumption was ≤1 serving/d, and total calcium intake was ≤600 mg/d from all sources including dairy. Exclusion criteria included a self-reported history of heart, liver, or kidney disease, or endocrine disorders such as polycystic ovarian syndrome. Other exclusionary factors included dyslipidemia (total cholesterol >300 mg/dL and/or triglyceride value >400 mg/dL and/or LDL cholesterol >160 mg/dL) and high fasting glucose (≥110 mg/dL) (which were analyzed at the University of California Medical Center clinical laboratories), high blood pressure, use of obesity pharmacotherapeutics or over-the-counter antiobesity agents, routine participation in structured exercise for >30 min/d, recent initiation of an exercise program within the past month, use of tobacco products, pregnancy, lactation, or the recent initiation of hormonal birth control or a recent change in hormonal birth control regimen at the time of study enrollment.

General study design and weight loss intervention

The 15-wk study was divided into a 3-wk run-in baseline period followed by a 12-wk energy restriction period. During the run-in period subjects were weighed daily and their energy intake amount was prescribed on an individual basis to maintain their body weight (30). This baseline period was followed by a 12-wk intervention period with intakes reduced by 500 kcal/d from the individual baseline weight maintenance amounts. All body weight measures were

Supported by the National Dairy Council (NDC) administered by the Dairy Research Institute and the Dairy Council of California (to MDVL), USDA/Agricultural Research Service (ARS) projects 5306-51530-006-00D (to NLK) and 6026-51000-012-06S (to SHA), the Clinical and Translational Science Center of the University of California, Davis, and National Center for Research Resources (NCRR) grant UL1 RR024146. SHA and BDP are supported by USDA/ARS project 6026-51000-012-06S.
Author disclosures: the authors report no conflicts of interest.
The NDC participated in the design of this study, but had no role in the implementation of the study, the analysis and interpretation of results, or the preparation of this article. The contents of this article are the sole responsibility of the authors and do not represent the official view of the NDC, NCRR, NIH, or USDA. The USDA is an equal opportunity provider and employer.
Supplemental Tables 1–6 and Supplemental Figures 1–4 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn/.
Present address for SHA: Department of Surgery and Center for Alimentary and Metabolic Science, UC Davis School of Medicine, Sacramento, CA. Present address for BDP: Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR. Present address for MGW: Institute for Memory Impairments and Neurological Disorders, University of California Irvine, Irvine, CA. Present address for APT: Jarrow Formulas, Los Angeles, CA. Present address for ECS: Medical Center, University of California Davis, Davis, CA.
Address correspondence to NLK (e-mail: nancy.keim@usda.gov).
Abbreviations used: AD, adequate dairy; CCK, cholecystokinin; GIP, gastric inhibitory peptide; GLP-1, glucagon-like-peptide 1; LD, low dairy; PYY_{3-36}, peptide-YY_{3-36}; VAS, visual analog scale; WHNRC, Western Human Nutrition Research Center; en%, percent of total energy.

FIGURE 1 Study design overview. Participants had a 3-wk LD energy balance run-in diet, followed by 12 wk of a 500-kcal-deficit/d intervention diet randomly assigned to either an LD group or an AD group. TDEE was based on a prescribed 500-kcal-deficit diet. Relative to the lunch meal at 0 min, blood draws were done at −295 and −285 min for fasting; −240, −200, −140, −80, and −25 min for postbreakfast measures; and 5, 20, 40, 60, 90, 120, 150, 180, 210, 240, 270, and 300 min for postlunch measures. ∗The buffet meal challenge test day was on a separate test day than the endocrine measures. AD, adequate dairy; LD, low dairy; TDEE, total daily energy expenditure; VAS, visual analog scale.

performed by the study manager at the Western Human Nutrition Research Center (WHNRC). All foods and beverages were provided in portion-controlled amounts by the metabolic food laboratory in the USDA/Agricultural Research Service-WHNRC. Body composition was assessed using DXA during week 3 of the baseline period, and subjects were pair-matched based on percentage body fat, then randomly assigned to 1 of 2 treatment groups: LD (≤1 serving/d) or AD (3–4 servings/d), which included milk, yogurt, and cheese products ranging from nonfat to full fat. In general, 1 cup of milk or yogurt (137 mL milk or 245 g of yogurt), $1\frac{1}{2}$ ounces of natural cheese (32 g), or 2 ounces of processed cheese (56 g) can be considered 1 serving of dairy.

Maintenance energy intake for each participant was determined by using the DRI equations for energy intake of overweight/obese women and men and took account of height, weight, age, and physical activity level. During the 3-wk run-in period, daily body weight data were scrutinized, and energy intake was adjusted if body weight changed in a consistent direction over 3 consecutive days (excluding the initial 5-d adjustment period). The energy consumed during the last 5 d of the baseline period was assumed to represent each individual's energy intake needs for maintaining energy balance. The intervention diets for the treatment arms were constructed to provide comparable levels of macronutrients and fiber, to approximate the average consumption in the United States (fat ∼35%, carbohydrates ∼49%, and protein ∼16% of total kilocalories; fiber 8–10 g/1000 kcal), but differed in the amount of dairy foods.

Measurements of satiety, satiation, and endocrine profiles

Subjective appetite sensations and circulating gut hormone concentrations were measured separately from self-selected food intake at a buffet meal on 2 distinct, structured test days at baseline and repeated again during the last 2 wk of the intervention (**Figure 1**).

Test Day 1.

The purpose of Test Day 1 was to assess subjective appetite indexes and gut hormone concentrations before and after standardized breakfast and lunch meals. Participants arrived at the metabolic research unit in the morning after a 12-h overnight fast, first on day 14 (during the run-in weight maintenance period) and again on day 92 or 99 (during week 11 or 12 of the weight loss intervention phase) of the study. They were asked to refrain from consuming caffeinated beverages while on the intervention, and were not permitted to exercise the day before the test day. These 2 separate instances of test weeks (weeks 11 and 12) were identical, and body weight was measured at both times. Final body weight change was always calculated as the difference between week 3 and week 12. The rationale for the staggered testing regimen (week 11 or 12) was to accommodate a comparison of the acute effects of dairy in the test meal, which is not included in the current article and is beyond its scope.

On Test Day 1, immediately after arriving, the subjects were weighed, and height and blood pressure measurements were taken. They were given individual rooms with beds and asked to remain in bed for the duration of the test day (other than bathroom breaks). To ensure that clock-time-associated cues would be minimized, all rooms were devoid of clocks, and subjects were instructed to remove watches and to turn off cellular phones and laptops. An intravenous catheter was inserted into the antecubital vein and 2 baseline (fasting) blood samples were drawn. While in their rooms, subjects consumed a standardized breakfast that consisted of a bagel with butter, eggs, and water. Instructions were given to consume the entire meal and

that it was necessary to eat for the full 10-min time period. Energy contents of standardized meals were identical at baseline and on the postintervention test days. The breakfast test meal contained 25% of the subject's prescribed restricted daily energy and consisted of fat providing 35% of total energy (en%), carbohydrate at 49en%, and protein at 16en%. For example, if the subject's prescribed restricted daily energy amount was 1800 kcal, the breakfast meal contained 450 kcal. Breakfast calories were adjusted proportionately, thus, a 2200-kcal prescription received a breakfast meal with 550 kcal (**Supplemental Table 2**). After 10 min the plate was removed and the participants were permitted to watch movies on a VCR, read books or magazines, or do light written work (devoid of time and food cues). Postprandial blood draws were taken 20, 60, 120, 180, and 235 min after the completion of the breakfast meal (equivalent to −240, −200, −140, −80, and −25 min before test lunch was served). Approximately 245 min after the completion of the breakfast, subjects were served a standard lunch test meal. The standardized lunch meal consisted of a turkey sandwich, potato chips, a small garden salad, sliced apples, and water (Supplemental Table 2). The participants were asked to consume the entire meal in 15 min. This test meal contained 40% of the subject's prescribed restricted daily calorie intake with macronutrient distribution matched to that of the standard breakfast: fat at 35en%, carbohydrate at 49en%, and protein at 16en%. For example, if the subject's prescribed restricted daily calorie amount was 1800 kcal, the lunch meal contained 720 kcal. Lunch energy content was adjusted proportionately, thus, a 2200-kcal prescription received a lunch meal with 880 kcal. Postprandial blood draws were taken at 5, 20, 40, 60, 90, 120, 150, 180, 210, 240, 270, and 300 min after the completion of the lunch test meal. The catheter was removed immediately after the final blood draw and subjects were allowed to leave the WHNRC at ∼18:00. In addition to the blood collection, an appetite assessment protocol was followed throughout the day and is described in further detail below.

Test Day 2.

The purpose of Test Day 2 was to collect data on self-selected food intake, without subjecting participants to confounding variables related to Test Day 1 (e.g., repeated blood sampling or all-day relegation to their rooms). Two days after completion of Test Day 1, subjects returned to the WHNRC in the overnight-fasted state and as before were asked to remove watches and turn off cellular phones. An identical meal prescription to that given on Test Day 1 was provided. Both the breakfast and lunch test meals were matched in macronutrient and food composition and were offered at the same times as on Test Day 1. On Test Day 2, subjects were not required to remain in the research center for the remainder of the morning after the breakfast meal, but were told to refrain from eating any caloric, carbonated, or caffeinated food or beverage during this free time. Four hours later, the subjects returned to the WHNRC and, similar to Test Day 1, were admitted to a room in the metabolic research unit, equipped with a chair, desk, recliner, and bathroom. The standard lunch meal was served, and upon completion, the subjects were permitted to comingle with other study participants or make use of a larger shared living room. Because capturing hunger-induced intermeal interval from spontaneous hunger cues as opposed to from factors like boredom was critical to the design of the protocol, participants were kept occupied for short periods in the afternoon. Stressful, strenuous, or lengthy activities were avoided so as to not interfere with normal physiological hunger cues. At 16:00 the subjects were sequestered to their private rooms and were told to inform staff when they were ready to eat dinner. Until the time they requested dinner, they were allowed to be occupied with reading books or magazines, playing board games, or answering questionnaires and other tasks that were part of the study and centered on other outcomes. Upon the dinner request, the clock time was noted (to calculate the intermeal interval) and a cart containing 40 hot and cold fresh food items in excess of that which could normally be eaten (with lids and packaging removed) was delivered to the subject's room within 10 min (**Supplemental Figure 1**A, B). Food and beverage items with varying degrees of energy density were offered, totaling ∼8500 kcal. Multiple-sized plates, bowls, and serving utensils were provided. Upon presentation of the food, the subjects were given instructions to *1*) eat anything on the cart, *2*) let a staff member know if they ran out of any food item and would like more, *3*) take as long as they wanted to complete the meal, and *4*) let a staff member know when they were finished. Finally, they were asked not to throw anything away and to leave all food they were served, but did not eat, on their plate.

When the subjects completed the meal, the cart was removed from the room. All foods, including those from the test breakfast and lunch plus all buffet items (before and after the dinner meal), were weighed using a Mettler Toledo PB5001-S/FACT Classic Plus digital scale. At 19:45 the participants were permitted to leave the WHNRC. The food intake analysis for the buffet meal was performed using NDS-R software (University of Minnesota, Nutrition Coordinating Center). Intermeal interval (the time between cessation of the standard lunch meal and the request of the buffet meal) and meal duration (the time between initiation of the buffet meal and the point at which the subject informed the staff of meal completion) were recorded for each participant. The same procedures performed at the baseline test days were repeated at either week 14 or week 15 of the study (equivalent to week 11 or 12 of the weight loss intervention).

Anthropometrics.

Height and weight were measured using a wall-mounted stadiometer (Ayrton Stadiometer model S100) and an electronic scale (Scale-tronic model 6002), respectively. BMI was calculated.

Blood processing and satiety hormone assays.

All assays and the test meal protocol (including blood collection timing) were validated in pilot studies in which a separate group of adult volunteers consumed the standard breakfast and lunch meals. From these pilot studies that assessed a variety of vendors and kits (31), hormone assays that performed adequately in terms of an ability to detect meal-associated hormone excursions, and in terms of acceptable technical variability, were identified and used herein. Blood was collected at room temperature and allowed to clot to produce serum, whereas for plasma EDTA-coated vacutainers were collected on ice and contained the following additives: aprotinin (200 kIU/mL blood; G-Biosciences), dipeptidyl peptidase-4 inhibitor (100 μM; MilliporeSigma, EMD Millipore Corporation), and a protease inhibitor cocktail [AEBSF: 4-(2-aminoethyl)benzenesulfonyl fluoride hydrochloride] 20 μM, bestatin 1.3 μM, E-64 0.14 μM, leupeptin 0.01 μM; Sigma Millipore). To obtain serum and plasma, tubes were centrifuged at 1300 × *g* for 10 min at 4 °C and aliquots stored at −80°C until analyzed. The aliquot for acylated ghrelin was acidified before freezing (to 0.1 M HCl). Ghrelin was determined using a 96-well ELISA kit (Millipore/Linco). The kit measures human acylated ghrelin in serum or plasma as a sandwich ELISA. CCK was analyzed using a Euria-CCK RIA kit (Euro Diagnostica); a substitution for the plasma extraction used Strata C18-E columns from Phenomenex.

Glucose and triglycerides were measured on the Hitachi 902 instrument using Roche Diagnostics reagents (Roche). Amylin was analyzed using a 96-well ELISA kit (Millipore/Linco) monoclonal antibody–based sandwich immunoassay. The captured antibody recognizes human amylin, amylin acid (deamidated amylin), a 1-20 fragment of amylin, but not reduced amylin. Plasma PYY_{3-36} was determined using an I^{125}-labeled RIA kit (Millipore Corporation). GLP-1 was determined using a 96-well ELISA kit (Millipore Corporation) for quantification of biologically active forms of GLP-1 (7-36 amide and 7-37 amide). It is highly specific for the immunologic measurements of active GLP-1 and will not detect other forms of GLP-1 (such as 1-36 amide, 1-37, 9-36 amide, or 9-37). Plasma GIP and insulin were multiplexed using the human gut hormone panel LincoPlex kit (Millipore/Linco) on a Luminex instrument (BioPlex™, Bio-Rad). Serum leptin was assayed using the Human Serum Adipokine Lincoplex Kit (Panel B, Millipore/Linco) on the Bio-Plex™. Adiponectin was also measured using a LincoPlex kit (Linco) on the Bio-Plex™.

TABLE 1 Circulating concentrations of hormones and analytes and subjective appetite scores in overnight-fasted adult female and male study volunteers before and after an ~12-wk weight loss intervention[1]

	Total ($n = 65$)		LD ($n = 34$)		AD ($n = 31$)	
	BL	PI	BL	PI	BL	PI
Satiety factors						
Amylin, pM	9.23 ± 1.71	10.0 ± 1.58	6.13 ± 0.932	6.39 ± 0.987	12.7 ± 3.42	14.1 ± 3.07
GLP-1, pM	3.15 ± 0.347	3.42 ± 0.335	2.79 ± 0.285	2.96 ± 0.354	3.56 ± 0.660	3.94 ± 0.583
Insulin,*,[a] mIU/mL	7.24 ± 0.427	5.76 ± 0.365	7.54 ± 0.604	5.64 ± 0.492	6.91 ± 0.603	5.90 ± 0.546
GIP, pg/mL	35.9 ± 3.67	30.9 ± 3.01	38.6 ± 5.55	32.2 ± 4.46	33.0 ± 4.71	29.5 ± 4.03
Ghrelin,[a] pg/mL	242 ± 11.6	291 ± 11.3	266 ± 16.9	293 ± 12.1	214 ± 15.0	288 ± 19.8
PYY_{3-36}, pg/mL	55.9 ± 2.46	52.6 ± 2.26	57.3 ± 3.19	54.0 ± 3.32	54.3 ± 3.82	51.0 ± 3.04
CCK, pg/mL	1.23 ± 0.0834	1.36 ± 0.0802	1.23 ± 0.122	1.23 ± 0.110	1.23 ± 0.113	1.50 ± 0.116
Leptin,[a] ng/mL	33.3 ± 2.14	25.0 ± 1.93	25.6 ± 2.50	17.7 ± 1.81	40.6 ± 3.19	32.0 ± 3.13
Adiponectin, ng/mL	14.3 ± 0.658	14.9 ± 0.0652	14.1 ± 1.03	14.8 ± 1.01	14.5 ± 0.835	15.1 ± 0.837
Glucose, mg/L	91.0 ± 0.528	92.0 ± 0.508	91.5 ± 0.712	91.5 ± 0.597	90.5 ± 0.786	92.5 ± 0.841
Triglyceride,[a] mg/dL	92.6 ± 2.71	86.8 ± 2.53	92.5 ± 3.97	88.7 ± 3.64	92.8 ± 3.69	84.8 ± 3.50
VAS scores, mm						
Hunger	49.7 ± 2.13	54.6 ± 2.11	50.2 ± 2.93	56.5 ± 3.03	49.2 ± 3.12	52.6 ± 2.91
Fullness	13.3 ± 1.28	12.7 ± 1.26	14.0 ± 1.78	10.1 ± 1.26	12.5 ± 1.86	15.6 ± 2.21
Desire to eat[a]	46.1 ± 2.00	54.4 ± 2.01	46.0 ± 2.56	57.4 ± 2.89	46.1 ± 3.14	51.0 ± 2.73
Prospective consumption[a]	47.1 ± 1.47	51.8 ± 1.48	47.0 ± 2.09	55.9 ± 1.99	47.1 ± 2.06	47.3 ± 2.09

[1] Values are means ± SEMs. Model 1: effect of dairy group and weight loss. *Significant group effect ($P < 0.05$); significant week effect ($P < 0.05$); [a]significant change after weight loss ($P < 0.05$). No interaction effects were seen. Model 3: effect of weight loss, irrespective of dairy group. AD, adequate dairy; BL, baseline; CCK, cholecystokinin; GIP, gastric inhibitory peptide; GLP-1, glucagon like peptide-1; LD, low dairy; PI, postintervention; PYY_{3-36}, peptide YY_{3-36}; VAS, visual analog scale.

Appetite assessment log.

Visual analog scale (VAS) ratings of hunger, fullness, desire to eat, and prospective consumption were recorded on an electronic data device (Palm model Z22, Palm, Inc.) (32, 33). The VAS software was created using the Satellite Forms Software development platform, version 6.1 (Thacker Network Technologies Inc.). These responses were provided by study participants on Test Day 1, but not on Test Day 2, to avoid cueing feelings of hunger before the buffet meal. For example, participants were asked to respond to the question, "How hungry are you feeling right now?" by selecting a point along the scale between the anchors "not at all hungry" and "extremely hungry." This same approach was used for the remaining questions: fullness, desire to eat, as well as prospective consumption. Responses were recorded 19 times during the test day relative to the lunch meal at 0 min: VASs were done at −295 and −285 min for fasting; −240, −200, −140, −80, and −25 min for postbreakfast measures; and 5, 20, 40, 60, 90, 120, 150, 180, 210, 240, 270, and 300 min for postlunch measures.

Statistical analyses

The current results stem from a stand-alone set of experiments [albeit using the same cohort as that of Van Loan et al. (29)] and is not considered a secondary analysis. In our archiving efforts for the data from the clinical trial, we retained randomization information for the protocols for 65 of the total enrolled 71 participants. These 65 ($n = 31$, AD; $n = 34$, LD) were included in the final analyses. Missing data (~15% of total data points) were imputed using the Amelia II package in R. This package performs multiple imputation using the expectation maximization algorithm with bootstrapping. Briefly, this algorithm creates a bootstrapped version of the data, then fills in the missing data, and uses the maximum likelihood estimate to determine the best imputed data to match the data distribution and parameter estimates, while accounting for unobserved/latent relations within the data. Such an approach is ideal for the given data set (34). All data were evaluated for normality using quantile-quantile plots. Data not normally distributed were transformed using either log, cube, Johnson normalizing, or square root; transformed data were used in subsequent analyses. For fasted values, a mean of the 2 same-day fasting blood draw values was used for each individual. AUC was calculated using the trapezoidal rule by splitting data up into phases of the day: postbreakfast (5 time points) and postlunch (12 time points). The AUC for any given hormone for each participant was calculated as the total area under the concentration curve; thus, even a postprandial reduction of a given analyte (e.g., acylated ghrelin) still yielded a positive integer AUC. This method also is an indirect index of total systemic exposure to a hormone over a defined period of the day. To evaluate a treatment effect of a dairy food–rich intervention diet we used mean fasted values, AUC postprandial values, and buffet ad libitum challenge outcomes in linear mixed-model analyses with subject as random effect, week (baseline compared with postintervention) and treatment (LD compared with AD) as fixed effects (model 1), and a week × treatment interaction. Building on model 1, we evaluated if body weight change (which occurred postrandomization, even though participants were matched for body weight when being randomly assigned into groups at baseline) was a significant covariate (model 2). In order to understand the effect of weight loss on appetite factors, irrespective of intervention diet, mean fasting and AUC postprandial values were evaluated in a modified model 1, by leaving out treatment effect but retaining the other components (model 3). All analyses were done in the R statistical program (R Core Team) (35) and JMP Pro 14 (SAS Institute).

Results

In this subset of individuals, mean ± SEM weight loss was 6.2 ± 0.5 kg in the AD group and 6.0 ± 0.5 kg in the LD group. Body fat was reduced by (mean ± SEM) 2.7% ± 0.4% in the AD group and 3.7% ± 0.5% in the LD group. There was no difference in these changes by treatment group (**Supplemental Table 3**), consistent with observations in the larger cohort that were reported previously (29).

Table 1 presents an overview of the fasting endocrine and satiety variables by group at baseline and postintervention. **Supplemental Tables 4–6** present the mean differences between baseline and postintervention, SEs, and upper and lower 95% CIs by group for all variables. Overall, these aligned with the results we observed using linear mixed models, which are discussed here in greater depth. As would be anticipated after body weight and body fat loss, leptin was lower in both AD and LD

postintervention than at baseline ($P < 0.001$). Fasting insulin had an intervention ($P = 0.049$) and week effect ($P < 0.001$), but no interaction, suggesting a group difference at baseline and postintervention; fasting insulin was lower postintervention in both cases. Fasting acylated ghrelin ($P < 0.001$), triglycerides ($P = 0.003$), VAS desire to eat ($P = 0.006$), and VAS prospective consumption ($P = 0.037$) had week effects, but no group effects or interactions. Whereas acylated ghrelin, VAS desire to eat, and VAS prospective consumption increased postintervention, triglycerides were reduced. Fasting CCK showed a trend for a week difference ($P = 0.086$, numerically higher in AD postintervention than in LD), but no other differences were identified.

When weight loss effects on endocrine hormones and VAS scores were evaluated irrespective of dairy group, fasting insulin ($P = 0.001$), leptin ($P = 0.022$), and triglycerides ($P = 0.002$) were reduced significantly after weight loss, whereas acylated ghrelin ($P < 0.001$), VAS desire to eat ($P = 0.006$), and VAS prospective consumption ($P = 0.039$) were significantly higher after weight loss (all $P < 0.05$) (Table 1). Fasting CCK ($P = 0.084$) and glucose ($P = 0.087$) showed a trend toward being different between baseline and postintervention.

Figure 2 presents the circulating hormones represented as AUCs after breakfast and AUCs after lunch; **Supplemental Figures 2** and **3** present the time course excursions. In Figure 2, only parameters that displayed significant differences are presented. No differences were observed in the postbreakfast AUC period for any appetite markers. Postlunch AUC acylated ghrelin was significantly different between the LD and AD groups ($P = 0.045$) at both weeks, as was postlunch AUC hunger ($P = 0.050$); LD was higher than AD. There was a main effect of week in postlunch AUC insulin ($P = 0.054$), suggesting an effect of weight loss, but not of dairy intervention, postintervention was lower than at baseline. When weight loss effects on endocrine hormones and VAS scores were evaluated irrespective of dairy, AUC postbreakfast acylated ghrelin ($P = 0.047$) was significantly higher after weight loss, whereas AUC postbreakfast ($P = 0.052$) and postlunch ($P = 0.048$) insulin were significantly lower after weight loss. We calculated the satiety index (36) [calculated as (VAS desire to eat premeal − postmeal)/energy content of meal (kcal)]. There were no intervention group or week effects in the satiety index (breakfast meal: LD: 6.6 ± 0.5/kcal, AD: 6.6 ± 0.6/kcal; lunch meal: LD: 4.0 ± 0.3/kcal, AD: 3.9 ± 0.3/kcal).

Body weight change was a significant covariate for postbreakfast VAS AUC hunger ($P = 0.006$), VAS desire to eat score ($P = 0.029$), and VAS prospective consumption ($P = 0.004$), but not for any other fasting or postprandial measures. Other intervention or week effects or their interactions remained unaffected by adding body weight change as a covariate.

Figure 3 and **Supplemental Figure 4** provide the buffet intake summary. There were no differences between AD or LD groups at baseline or postintervention in total energy and macronutrients consumed or in the intermeal interval. However, the mean ± SEM energy intake consumed from the buffet was 57.3% ± 1.5% of the prescribed energy intake amount, an excess compared with the 45% of daily energy intake that was provided with the controlled intervention diet. When evaluated without dairy intervention groups, there was a trend for intermeal interval to be shorter postintervention than before ($P = 0.059$). In other parameters, neither intervention nor week significantly affected buffet energy intake or macronutrient intakes.

Taken together, the fasting, postbreakfast, and postlunch results indicate that subjective and endocrine responses were not different in persons consuming LD and AD diet patterns over ~12 wk.

Discussion

Given their unique lipid and protein profiles, and evidence from acute experiments, dairy foods have been hypothesized to play a role in long-term appetite regulation, although to our knowledge no randomized controlled trials have been conducted to demonstrate this effect. Furthermore, a comprehensive evaluation of hunger, satiety, and satiation phenotypes, coincident with multihormone endocrine profiling, in the context of weight loss is lacking in humans. Although weight loss resulted, as expected, in increased perceptions of hunger and an endocrine profile consistent with an increased drive to eat, a dairy food–rich diet had no significant impact on these effects.

The results reported here suggest that a dairy food–rich diet pattern in the context of calorie restriction has no effect on endocrine patterns. The acute effect of dairy on satiety has been summarized in a recent meta-analysis that included 13 clinical trials (28). A 500-mL dairy (milk or yogurt) preload before mixed-meal paradigms was shown to reduce subjective ratings of hunger and prospective food consumption scores, and to increase fullness scores, in addition to reducing energy consumption in a subsequent meal, compared with fruit drink, cola, or chocolate bar preloads. The long-term effect of dairy foods on body weight and weight loss has been evaluated (37), via both observational epidemiological studies (38–41) as well as randomized clinical trials (19, 21, 23, 42–44). The evidence is controversial, with some studies finding no associations, whereas others find a positive or an inverse association. However, to our knowledge, the study herein is the first report of the long-term or "repeated exposure" effect of a diet rich in dairy foods on a comprehensive panel of subjective and objective satiety measures, in the context of a weight loss intervention. The lack of a greater impact of dairy food intake on satiety supports results from the parent study which reported that a dairy food–rich diet did not have an influence on weight loss in this same cohort (29). Our test day diets were devoid of dairy foods (with the exception of butter) to avoid confounding diet effects with meal effects. Thus, future analyses are needed to determine the potential acute effects of dairy-containing meals on postprandial hormones and hunger cues.

An additional consideration is the possibility that weight loss per se affects satiety more strongly than dietary dairy composition. Under this working model, factors associated with long-term negative energy balance may overpower regulators that are specific to dietary patterns. Consistent with this concept, we identified several weight loss–associated changes independent of LD/AD status, including *1*) very modest but statistically significant reductions in fasting and postprandial insulin excursions, *2*) increased fasting acylated ghrelin, *3*) a greater magnitude of postprandial acylated ghrelin reductions, *4*) increased ratings (in the overnight fasted state) of desire to eat and prospective consumption, and *5*) reduced fasting leptin and triglycerides.

Weight loss alone resulted in changes in the fasting and postprandial endocrine milieu. Even modest weight loss can reduce satiety (45, 46), which may contribute to the weight regain after dietary weight loss interventions that is

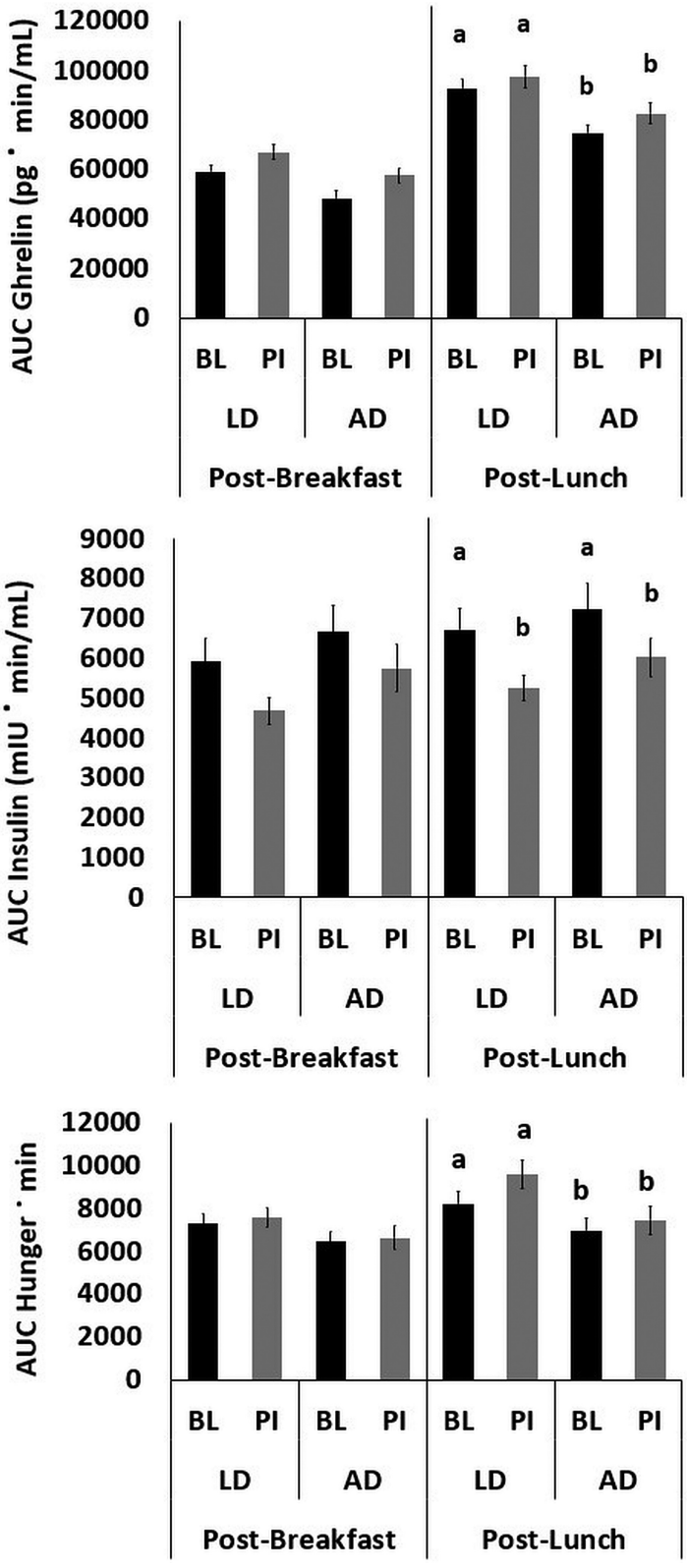

FIGURE 2 AUCs for ghrelin (A), insulin (B), and visual analog scale hunger score (C) of adult female and male study volunteers before and after a ~12-wk weight loss intervention that showed differences as a result of the intervention, measured 5 times between breakfast and lunch (postbreakfast) and 12 times after lunch (postlunch). All data are means ± SEMs, $n = 34$ (LD) or $n = 31$ (AD). Relative to the lunch meal at 0 min, blood draws were done at −295 and −285 min for fasting; −240, −200, −140, −80, and −25 min for postbreakfast measures; and 5, 20, 40, 60, 90, 120, 150, 180, 210, 240, 270, and 300 min for postlunch measures. Labeled means without a common letter differ by weeks or by treatment group, $P < 0.05$. For ghrelin, note that postprandial concentrations dropped; the AUC represents the magnitude of the reductions. AD, adequate dairy; BL, baseline; LD, low dairy; PI, postintervention.

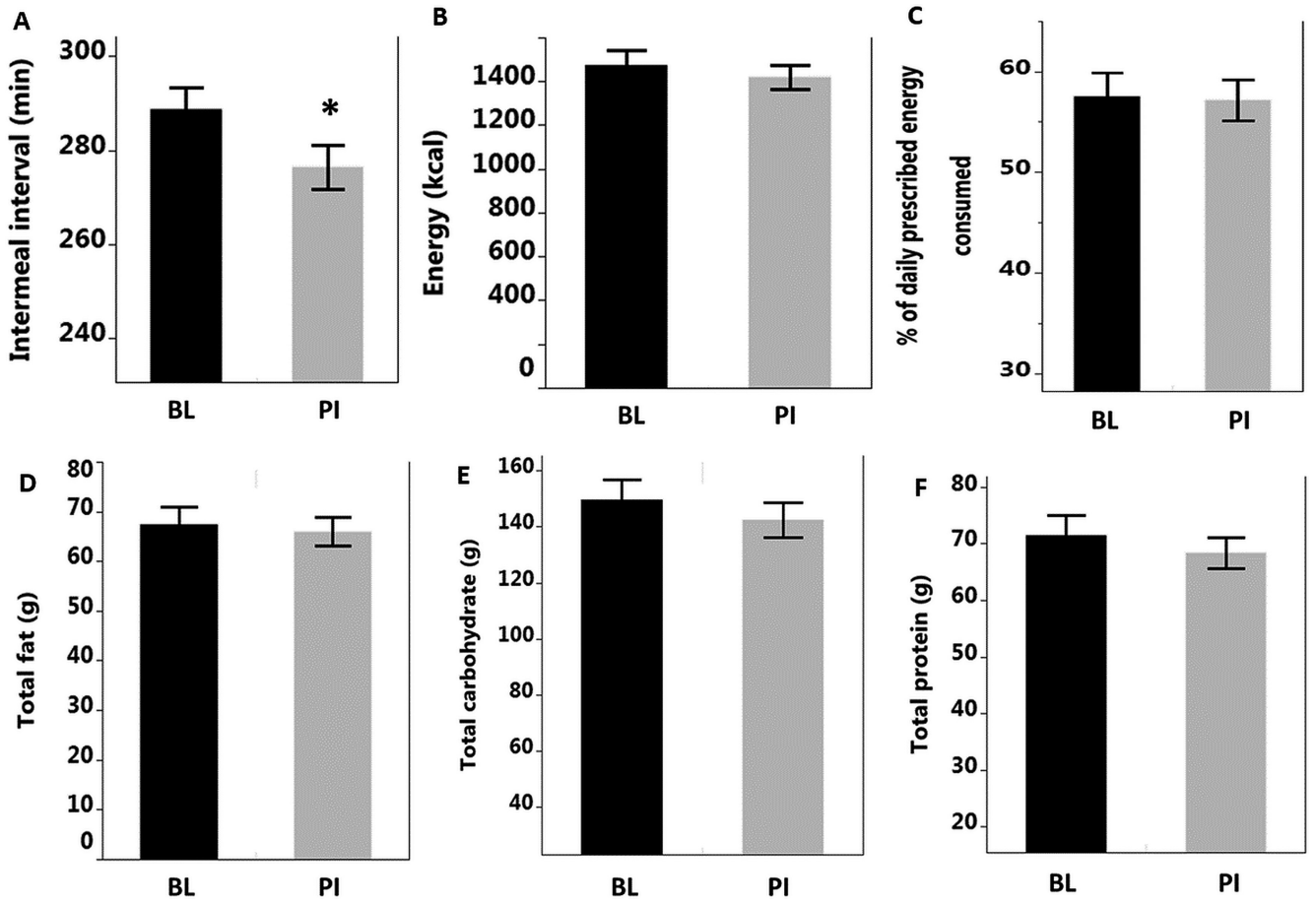

FIGURE 3 Buffet parameters irrespective of dairy intervention group of adult female and male study volunteers before and after a ~12-wk weight loss intervention. (A) Intermeal interval, (B) energy intake, (C) percentage of prescribed daily energy consumed, and (D) total fat, (E) total carbohydrate, and (F) total protein intakes. All data are means ± SEMs, $n = 34$ (low dairy) or $n = 31$ (adequate dairy). *PI tended to differ from BL, $P = 0.06$. Percentage of daily prescribed energy consumed indicates the percentage of prescribed treatment energy (500-kcal restriction) consumed during the buffet. BL, baseline; PI, postintervention.

observed in ~90% of individuals (47). The compensatory increase in appetite, drop in satiety, and reduction in resting energy expenditure combine synergistically to bring about this recidivism (48). Weight loss has been associated with an increase in fasting and postprandial ghrelin (7). We did observe that ghrelin was higher postintervention while fasting, and postprandial ghrelin concentrations summarized as AUC after lunch decreased less after weight loss. Ghrelin is an orexigenic satiety hormone and has also been shown to decrease insulin secretion (49), which is aligned with our observation that postprandial insulin was reduced after weight loss. Other weight loss studies have observed reductions in PYY_{3-36} (50), GLP-1 (51), and CCK (52), evaluated between 120 and 240 min past a mixed macronutrient meal challenge (7, 50, 51). Our results are not consistent with these studies, because we did not find any significant differences in fasting or postprandial PYY_{3-36}, CCK, or GLP-1. Our protocol design included a breakfast meal and a lunch meal with the idea of observing the second meal effect that has been observed in other studies. This second meal effect has been attributed to action in the lower gut when fermentable material is present and can specifically affect PYY_{3-36} and/or GLP-1 (53). These hormones are secreted in pulses in response to meal ingestion. Keeping in mind that identical meals were served before and after weight loss, and the dietary fiber components of both LD and AD diets were similar, the lack of change in these hormones that we observed might be expected. A myriad of other reasons might underlie the different findings between studies including meal composition, satisfaction (liking) of the meal, familiarity of the meal, timing of the meal, or other feeding paradigms or factors that are not consistent across studies.

Notably, we did not detect any weight loss– or dietary intervention–associated difference in buffet energy intakes. Albeit, the calorie consumption at the buffet exceeded the energy content of the dinner meal that was provided in the controlled diet. These results suggest to us that the presentation of a buffet like this one was not a good test of satiety; once sensory-specific satiety occurred the participant could simply move to another offering. It also suggests that the hedonic motivators, such as the endocannabinoids or orexin, may have overtaken the physiological signals, such as leptin. We observed a reduction in fasting leptin in both groups. Finally, we did observe that the lunch-to-dinner intermeal interval was shorter postintervention, perhaps as a result of increased hunger or desire to eat specifically before the buffet. Given that observation, along with the fact that the postintervention standard meals provided a greater proportion of energy needs because of weight loss, it might be speculated that subjects were eating to satisfy something other than physiological hunger.

Limitations, conclusions, and future directions

A uniform 500-kcal/d energy deficit was chosen as opposed to the deficit being scaled for percentage energy requirements for the sake of being able to compare across other literature reporting dairy–weight loss studies. Alternate means to induce weight loss may have yielded different results, which can be evaluated in future research. By design, we evaluated subjective appetite ratings and endocrine measures on a different day than the ad libitum buffet challenge. This was done to avoid subjects' behavior from being modified before they consumed food from an ad libitum buffet. However, this also makes it challenging to draw conclusions between subjective and objective appetite ratings and the buffet challenge outcomes. Further, owing to the necessity of strictly following a set test schedule for each study cohort, the menopausal or menstrual cycle phases were not monitored or recorded. Another limitation of this study was that the sample size and power calculation for the weight loss study was made based on body weight change and not satiety parameters. Despite these limitations, the current experiment is the first, to our knowledge, to report on a day-long comprehensive milieu of appetite hormone and VAS changes in persons before and after healthy weight loss; these daily patterns may be most relevant to overall physiology and weight management. We also leveraged an ad libitum buffet and intermeal-interval paradigm to provide an objective measure of food intake behavior. The latter measures were unaffected in the weight-reduced state when compared with preintervention and, as aforementioned, the LD/AD status also did not affect outcomes. The current observations provide important insights into the fundamental regulation of human food intake. Yet, there are many avenues for future inquiry. For instance, there is interest to determine if temporal patterns of and person-to-person difference in putative food intake–regulating hormones associate with subjective and objective indicators of satiety, satiation, and hunger. Other efforts could examine how more severe weight loss, differing dietary components beyond dairy, or alterations in physical activity and fitness affect postprandial phenotypes. These studies, and others, will complement our current findings, which suggest that homeostatic systems regulating food intake are persistent.

Acknowledgments

This study would not have been possible without the efforts of University of California Davis Clinical and Translational Science Center nursing staff for assistance with blood draws and the University of California metabolic food laboratory at the WHNRC for meal preparation. The authors' responsibilities were as follows—MDVL, NLK, SHA, ECS, LRW, APT, MGW, WFH, ERG, and BDP: were responsible for the research design, study oversight, or specimen collection and data acquisition; SK: was responsible for the data organization, statistical analysis, and worked with NLK and SHA on the manuscript preparation; and all authors: provided edits and feedback on and read and approved the final manuscript.

References

1. Hays NP, Bathalon GP, McCrory MA, Roubenoff R, Lipman R, Roberts SB. Eating behavior correlates of adult weight gain and obesity in healthy women aged 55–65 y. Am J Clin Nutr 2002;75(3):476–83.
2. de Graaf C, Blom WA, Smeets PA, Stafleu A, Hendriks HF. Biomarkers of satiation and satiety. Am J Clin Nutr 2004;79(6):946–61.
3. Blundell J, de Graaf C, Hulshof T, Jebb S, Livingstone B, Lluch A, Mela D, Salah S, Schuring E, van der Knaap H, et al. Appetite control: methodological aspects of the evaluation of foods. Obes Rev 2010;11(3):251–70.
4. Coutinho SR, Rehfeld JF, Holst JJ, Kulseng B, Martins C. Impact of weight loss achieved through a multidisciplinary intervention on appetite in patients with severe obesity. Am J Physiol Endocrinol Metab 2018;315(1):E91–E8.
5. Lean ME, Malkova D. Altered gut and adipose tissue hormones in overweight and obese individuals: cause or consequence? Int J Obes 2016;40(4):622–32.
6. Austin J, Marks D. Hormonal regulators of appetite. Int J Pediatr Endocrinol 2009:141753.
7. Sumithran P, Prendergast LA, Delbridge E, Purcell K, Shulkes A, Kriketos A, Proietto J. Long-term persistence of hormonal adaptations to weight loss. N Engl J Med 2011;365(17):1597–604.
8. Nymo S, Coutinho SR, Jorgensen J, Rehfeld JF, Truby H, Kulseng B, Martins C. Timeline of changes in appetite during weight loss with a ketogenic diet. Int J Obes 2017;41(8):1224–31.
9. Nymo S, Coutinho SR, Eknes PH, Vestbostad I, Rehfeld JF, Truby H, Kulseng B, Martins C. Investigation of the long-term sustainability of changes in appetite after weight loss. Int J Obes 2018;42(8):1489–99.
10. Plata-Salaman CR. Regulation of hunger and satiety in man. Dig Dis 1991;9(5):253–68.
11. Salleh SN, Fairus AAH, Zahary MN, Bhaskar Raj N, Mhd Jalil AM. Unravelling the effects of soluble dietary fibre supplementation on energy intake and perceived satiety in healthy adults: evidence from systematic review and meta-analysis of randomised-controlled trials. Foods 2019;8(1):15.
12. Warrilow A, Mellor D, McKune A, Pumpa K. Dietary fat, fibre, satiation, and satiety—a systematic review of acute studies. Eur J Clin Nutr 2019;73(3):333–44.
13. Heden TD, Liu Y, Sims L, Kearney ML, Whaley-Connell AT, Chockalingam A, Dellsperger KC, Fairchild TJ, Kanaley JA. Liquid meal composition, postprandial satiety hormones, and perceived appetite and satiety in obese women during acute caloric restriction. Eur J Endocrinol 2013;168(4):593–600.
14. Potier M, Darcel N, Tome D. Protein, amino acids and the control of food intake. Curr Opin Clin Nutr Metab Care 2009;12(1):54–8.
15. Stevenson JL, Clevenger HC, Cooper JA. Hunger and satiety responses to high-fat meals of varying fatty acid composition in women with obesity. Obesity 2015;23(10):1980–6.
16. Mehrabani S, Salehi-Abargouei A, Asemi M, Mehrabani S, Feizi A, Safavi SM. Effect of low-fat milk consumption compared to apple juice and water on the energy intake among 10–12-year-old obese boys: a three-way cross-over clinical trial. Int J Prev Med 2014;5(11):1405–11.
17. Anderson GH, Luhovyy B, Akhavan T, Panahi S. Milk proteins in the regulation of body weight, satiety, food intake and glycemia. Nestle Nutr Workshop Ser Pediatr Program 2011;67:147–59.
18. Gilbert JA, Joanisse DR, Chaput JP, Miegueu P, Cianflone K, Alméras N, Tremblay A. Milk supplementation facilitates appetite control in obese women during weight loss: a randomised, single-blind, placebo-controlled trial. Br J Nutr 2011;105(1):133–43.
19. Zemel MB, Thompson W, Milstead A, Morris K, Campbell P. Calcium and dairy acceleration of weight and fat loss during energy restriction in obese adults. Obes Res 2004;12(4):582–90.
20. Zemel MB. The role of dairy foods in weight management. J Am Coll Nutr 2005;24(6 Suppl):537S–46S.
21. Zemel MB, Richards J, Milstead A, Campbell P. Effects of calcium and dairy on body composition and weight loss in African-American adults. Obes Res 2005;13(7):1218–25.
22. Song Q, Sergeev IN. Calcium and vitamin D in obesity. Nutr Res Rev 2012;25(1):130–41.
23. Jones KW, Eller LK, Parnell JA, Doyle-Baker PK, Edwards AL, Reimer RA. Effect of a dairy- and calcium-rich diet on weight loss and appetite during energy restriction in overweight and obese adults: a randomized trial. Eur J Clin Nutr 2013;67(4):371–6.
24. Dougkas A, Minihane AM, Givens DI, Reynolds CK, Yaqoob P. Differential effects of dairy snacks on appetite, but not overall energy intake. Br J Nutr 2012;108(12):2274–85.

25. Dove ER, Hodgson JM, Puddey IB, Beilin LJ, Lee YP, Mori TA. Skim milk compared with a fruit drink acutely reduces appetite and energy intake in overweight men and women. Am J Clin Nutr 2009;90(1):70–5.
26. DellaValle DM, Roe LS, Rolls BJ. Does the consumption of caloric and non-caloric beverages with a meal affect energy intake? Appetite 2005;44(2):187–93.
27. Soenen S, Westerterp-Plantenga MS. No differences in satiety or energy intake after high-fructose corn syrup, sucrose, or milk preloads. Am J Clin Nutr 2007;86(6):1586–94.
28. Onvani S, Haghighatdoost F, Surkan PJ, Azadbakht L. Dairy products, satiety and food intake: a meta-analysis of clinical trials. Clin Nutr 2017;36(2):389–98.
29. Van Loan MD, Keim NL, Adams SH, Souza E, Woodhouse LR, Thomas A, Witbracht M, Gertz ER, Piccolo B, Bremer AA, et al. Dairy foods in a moderate energy restricted diet do not enhance central fat, weight, and intra-abdominal adipose tissue losses nor reduce adipocyte size or inflammatory markers in overweight and obese adults: a controlled feeding study. J Obes 2011:989657.
30. Institute of Medicine (US) Panel on Macronutrients, Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary Reference Intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington (DC): National Academies Press; 2005.
31. Woodhouse LR, Adams SH, Blankenship J, Freytag T, Keim N, Littlefield ES, Tengonciang M, Van Loan M. Gut hormone response to a mixed meal: post-prandial changes and intra-individual variation. FASEB J 2007;21(6):A1322.
32. Flint A, Raben A, Blundell JE, Astrup A. Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. Int J Obes 2000;24(1):38–48.
33. Blundell J, Bellisle F, editors. Satiation, satiety and the control of food intake: theory and practice. Cambridge (UK): Woodhead Publishing; 2013.
34. Honaker J, King G, Blackwell M. Amelia II: a program for missing data. J Stat Soft 2011;45(7):1–47.
35. R Core Team. R: a language and environment for statistical computing. Vienna (Austria): R Foundation for Statistical Computing; 2013.
36. Green SM, Delargy HJ, Joanes D, Blundell JE. A satiety quotient: a formulation to assess the satiating effect of food. Appetite 1997;29(3):291–304.
37. Van Loan M. The role of dairy foods and dietary calcium in weight management. J Am Coll Nutr 2009;28 (Suppl 1):120S–9S.
38. Mirmiran P, Esmaillzadeh A, Azizi F. Dairy consumption and body mass index: an inverse relationship. Int J Obes 2005;29(1):115–21.
39. Marques-Vidal P, Gonçalves A, Dias CM. Milk intake is inversely related to obesity in men and in young women: data from the Portuguese Health Interview Survey 1998–1999. Int J Obes 2006;30:88–93.
40. Rajpathak SN, Rimm EB, Rosner B, Willett WC, Hu FB. Calcium and dairy intakes in relation to long-term weight gain in US men. Am J Clin Nutr 2006;83(3):559–66.
41. Rosell M, Håkansson NN, Wolk A. Association between dairy food consumption and weight change over 9 y in 19,352 perimenopausal women. Am J Clin Nutr 2006;84(6):1481–8.
42. Thompson WG, Rostad Holdman N, Janzow DJ, Slezak JM, Morris KL, Zemel MB. Effect of energy-reduced diets high in dairy products and fiber on weight loss in obese adults. Obes Res 2005;13(8): 1344–53.
43. Bowen J, Noakes M, Clifton PM. Effect of calcium and dairy foods in high protein, energy-restricted diets on weight loss and metabolic parameters in overweight adults. Int J Obes 2005;29(8): 957–65.
44. Zemel MB, Richards J, Mathis S, Milstead A, Gebhardt L, Silva E. Dairy augmentation of total and central fat loss in obese subjects. Int J Obes 2005;29(4):391–7.
45. Mars M, de Graaf C, de Groot LC, Kok FJ. Decreases in fasting leptin and insulin concentrations after acute energy restriction and subsequent compensation in food intake. Am J Clin Nutr 2005;81(3):570–7.
46. Cornier MA. Is your brain to blame for weight regain? Physiol Behav 2011;104(4):608–12.
47. MacLean PS, Bergouignan A, Cornier M-A, Jackman MR. Biology's response to dieting: the impetus for weight regain. Am J Physiol Regul Integr Comp Physiol 2011;301(3):R581–600.
48. Rosenbaum M, Leibel RL. Adaptive thermogenesis in humans. Int J Obes 2010;34(Suppl 1):S47–55.
49. Poher AL, Tschöp MH, Müller TD. Ghrelin regulation of glucose metabolism. Peptides 2018;100:236–42.
50. Essah PA, Levy JR, Sistrun SN, Kelly SM, Nestler JE. Effect of weight loss by a low-fat diet and a low-carbohydrate diet on peptide YY levels. Int J Obes 2010;34(8):1239–42.
51. Adam TC, Jocken J, Westerterp-Plantenga MS. Decreased glucagon-like peptide 1 release after weight loss in overweight/obese subjects. Obes Res 2005;13(4):710–6.
52. Chearskul S, Delbridge E, Shulkes A, Proietto J, Kriketos A. Effect of weight loss and ketosis on postprandial cholecystokinin and free fatty acid concentrations. Am J Clin Nutr 2008;87(5):1238–46.
53. Covasa M, Stephens RW, Toderean R, Cobuz C. Intestinal sensing by gut microbiota: targeting gut peptides. Front Endocrinol 2019; 10:82.