

Accepted Manuscript

Daily pattern of energy distribution and weight loss

Hollie A. Raynor, Fan Li, Chelsi Cardoso



PII: S0031-9384(18)30097-0
DOI: doi:[10.1016/j.physbeh.2018.02.036](https://doi.org/10.1016/j.physbeh.2018.02.036)
Reference: PHB 12096
To appear in: *Physiology & Behavior*
Received date: 30 November 2017
Revised date: 31 January 2018
Accepted date: 16 February 2018

Please cite this article as: Hollie A. Raynor, Fan Li, Chelsi Cardoso , Daily pattern of energy distribution and weight loss. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Phb(2018), doi:[10.1016/j.physbeh.2018.02.036](https://doi.org/10.1016/j.physbeh.2018.02.036)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Daily Pattern of Energy Distribution and Weight Loss**Hollie A. Raynor,^a Fan Li,^a and Chelsi Cardoso^a**

^a1215 Cumberland Avenue, 229 JHB, University of Tennessee, Knoxville, TN 37996-1920;

hraynor@utk.edu; fli22@vols.utk.edu; chelsicecelia2@gmail.com

Corresponding author: Hollie A. Raynor, 1215 Cumberland Avenue, 229 JHB, University of

Tennessee, Knoxville, TN 37996-1920; p: 865-974-6259; f: 865-974-3491; email:

hraynor@utk.edu

Declarations of Interest: HA Raynor is part of the Scientific Advisory Board of SlimmingWorld.

Funding Source: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Abstract

Timing of energy intake, a temporal dietary pattern, may enhance health. Eating a greater amount of energy earlier and a smaller amount of energy later in the day, a behavioral circadian rhythm, may assist with chronoenhancement. Chronoenhancement seeks to enhance entrainment (synchronization) of biological and behavioral circadian rhythms. In humans, research reports that eating a greater amount of energy early and a smaller amount of energy later in the day increases dietary induced thermogenesis, improves cardiometabolic outcomes, and enhances weight loss. However, little human research has examined if this eating pattern enhances regularity of biological circadian rhythm. In a randomized controlled 8-week pilot study, the influence of energy distribution timing on weight loss and regularity of sleep onset and wake times (marker for biological circadian rhythm) was examined. Within an hypocaloric, three-meal prescription, participants ($n = 8$) were assigned to either: 1) Morning: 50%, 30%, and 20% of kcal at breakfast, lunch, and dinner, respectively; or 2) Evening: 20%, 30%, and 50% of kcal at breakfast, lunch, and dinner, respectively. Percent weight loss and regularity of sleep onset and wake times were significantly ($p < 0.05$) greater for Morning than Evening. To enhance understanding of the influence of energy distribution timing on health, longer studies conducted in free-living participants, with dietary intake assessed using time-stamped methods, that include measures of the circadian timing system are needed. This small review is based upon a symposium presentation at the Society of the Study of Ingestive Behavior in 2017.

Keywords: Circadian, Energy, Temporal, Distribution, Pattern, Weight loss

Highlights

Timing of energy intake, a temporal dietary pattern, may enhance health.

Eating more energy earlier and less energy later in the day may enhance weight loss.

A regular energy distribution pattern may entrain the circadian timing system.

1.1 Introduction

Human nutrition research has traditionally examined the impact of a nutrient, such as a macro- or micronutrient, or type of food (i.e., fruits and vegetables) on health outcomes.¹ Currently, there is greater emphasis on examining dietary patterns, such as eating occasions, multiple food groups, and/or multiple nutrients, in relation to health outcomes.² Within this approach, there is also recognition that time of day of consumption may be an important factor in the relationship between nutrition and health, thus research has started to examine temporal patterns of intake.^{1,3}

One temporal pattern that has recently been examined that may affect health is timing of energy intake, and particularly the distribution of energy intake throughout the day.^{1,4-7} National surveillance data indicate that since the 1970's the pattern of intake of meals and snacks has changed over time, with a decrease in the percentage of adults that report eating breakfast,³ and an increase in the number of and amount of energy intake from snacks consumed per day.^{3,8} Furthermore, self-reported time of breakfast shows that it is being consumed later in the day.³ This temporal pattern, a reduction in breakfast consumption, consuming breakfast later in the day, and more energy consumed from snacks, suggests that the distribution of energy intake in the day may have shifted such that less energy is being consumed earlier in the day and more energy is consumed later in the day.

Recent data examining the temporal pattern of energy intake does indicate that adults in the US appear to be consuming a very small amount of total energy intake earlier in the day. For example, data from 1999-2004 National Health and Nutrition Examination Survey (NHANES)

show that for the majority of adults, the first and second largest daily consumption event is occurring after 10 am.¹ Another study used a smartphone to collect the daily temporal pattern of energy intake in 156 healthy, free-living participants using digital images.⁹ The time-stamp of the images allowed the temporal aspect of eating to be examined.⁹ Results indicated that less than 25% of total energy intake was consumed before noon, while 37.5% of total energy intake was consumed after 6 pm. These studies indicate that adults are consuming a small percentage of their total energy early in the day, leaving most of energy intake to occur later in the day.⁹ This temporal eating pattern is now hypothesized to be problematic for weight management and cardiovascular health as it may negatively influence the circadian timing system (CTS).^{5,10-13}

1.2 The circadian timing system, circadian disruption, and health

The CTS provides an intrinsically-generated nearly 24-hour signal that is typically entrained to the geophysical properties of earth's rotation, primarily daylight and darkness.¹⁴ The suprachiasmatic nuclei (SCN) in the hypothalamus function as the master clock of the mammalian CTS, coordinating the sleep-wake cycle, metabolic and hormonal processes, and the overall temporal organization of physiological processes within the body.^{5,10,11,13,14} The SCN also coordinates peripheral oscillators located in cells and organs (e.g., lung, liver, etc.), so that physiological systems function harmoniously.^{11,13,14}

A direct pathway from the retina carries photic information of environmental light/dark cycles to the SCN, which serves as the principal zeitgeber (synchronizer) to the CTS.¹⁴ Several nonphotic stimuli have also been shown to serve as zeitgebers, including daily behavioral patterns of eating.¹⁴⁻¹⁸ Daily patterns of eating do not completely override the light-dark cycle input to the SCN, but feeding has been shown to act as a potent zeitgeber of the peripheral oscillators.¹⁴⁻¹⁸ If pattern of eating is not aligned to the output of the SCN, the peripheral

oscillators may be out of phase with the SCN, resulting in internal desynchrony, i.e., chronodisruption [CD].¹⁴ This type of CD may be thought of as a result of a disconnection of temporal organization between biological, originating from the SCN, and behavioral circadian rhythms.^{5,11-13} The loss of coordination between biological (SCN) and behavioral circadian rhythms impacting on peripheral oscillators is related to negative health outcomes, including obesity and weight gain, metabolic syndrome, cardiovascular disease, cognitive impairment, and mood disorders.¹⁰

Chronotherapy, a chronobiological-based intervention, can moderate CD.¹⁴⁻¹⁹ This type of intervention can focus on adjusting the CTS, and traditionally these interventions have focused on changing exposure to light or darkness or modifying sleep and wake times, which influence the SCN. Another approach can target adjustment of behavioral circadian rhythms, using interventions that change the timing and/or regularity of other misaligned behaviors that may be influential in synchronizing the peripheral oscillators.¹⁴ These interventions can then enhance the alignment of biological and behavioral circadian rhythms (chronoenhancing), entraining the SCN and the peripheral oscillators.¹⁴⁻¹⁹ Interventions altering the behavioral circadian rhythm of eating via moving intake to occur earlier in the day may assist with entraining the CTS by enhancing synchronization between the peripheral oscillators and the SCN, improving overall health.

1.3 Timing of energy intake and metabolic and hormonal response

To improve physiological parameters related to cardiometabolic and weight-related health, timing of energy intake would need to influence cardiometabolic and metabolic response. Laboratory-based experimental designs do demonstrate an enhanced favorable cardiometabolic and metabolic response when a greater amount of energy is consumed earlier, rather than later, in

the day.²⁰⁻²² For example, in a randomized cross-over trial, twenty healthy participants were randomized to receive the same standard meal, 30% energy from protein, 31% energy from fat, 39% energy from carbohydrates, providing 1168 kcal, on two different days at two different times.²¹ On one day, the meal was served at 8 am, and 7 days later, the meal was served at 6 pm, or vice versa. Dietary induced thermogenesis was significantly greater, and glucose and insulin response was significantly lower after the morning, as compared to the evening, meal.²¹ Similarly, another study examined differences in dietary induced thermogenesis when identical meals, which provided 33.3% of calculated energy needs, were provided at “breakfast” (one hour after scheduled wake time) and “dinner” (13 hours after scheduled wake time).²² Results indicated that dietary induced thermogenesis was 44% lower with the evening as compared to the morning meal, even though the meals were identical in nutrient composition.²² Finally, 10 healthy women participated in a randomized cross-over trial in which after receiving two weeks of standardized meals, participants completed a 1-day protocol that contained three meals.²⁰ The three meals were identical in the two conditions; the only difference was the timing of the second meal. In one condition, the meals were served at 8 am, 1 pm, and 6 pm (Early), while in the other condition the meals were served at 8 am, 4:30 pm, and 6 pm (Late). Post-prandial glucose response following the second meal was significantly greater in the Late condition as compared to the Early condition.²⁰ These studies indicate that eating a greater amount of energy earlier in the day enhances dietary induced thermogenesis, which can enhance overall energy expenditure, and improves the glycemic response. This physiological response to eating a greater amount of energy earlier in the day could enhance outcomes related to weight management and cardiometabolic health.

1.4 Timing of energy intake and weight loss

Three observational studies have explored the relationship between timing of energy intake and weight reduction.^{6,23,24} A retrospective observational study, the Adventist Health Study 2, a relatively healthy North American cohort comprised of over 50,000 adults, investigated if the timing of when the largest meal of the day was consumed was related to weight change over 7 years.²³ Both the timing of when the largest meal was consumed and height and weight were self-reported. Compared to participants who reported consuming their largest meal at dinner, those consuming their largest meal at breakfast experienced a significant decrease in body mass index (BMI).²³ Two prospective observational studies, with participants from Spain with overweight or obesity, examined whether taking the mid-day meal early or later in the day was associated with weight loss.^{6,24} One study examined the relationship between meal timing and weight loss during a 20-week weight loss program,⁴ while the other study examined excess weight loss over 6 years of follow-up following bariatric surgery.²⁴ In both studies, late and early lunch eating were defined based on time of lunch, the main meal of the day in Spain, with early eating consuming lunch prior to 3 pm and later eating consuming lunch after 3 pm. Late lunch eaters lost significantly less weight than early lunch eaters during the 20 week weight loss program.⁶ The difference in weight loss between early and late lunch eaters occurred at week 5 and was maintained during the remaining 15 weeks of the program.⁶ Following bariatric surgery, those participants who had the poorest weight loss response to the surgery over the 6-year follow-up had the highest percentage of participants who consumed a late lunch.²⁴ These observational studies suggest that having the largest or main meal of the day earlier in the day may enhance reductions in weight.

There is very little experimental research conducted on the relationship between timing of energy intake and weight loss. Two randomized controlled trials have been conducted in this

area.^{25,26} One study randomized 42 women with overweight or obesity to one of two hypocaloric diets (600 kcal/day reduction) over three months.²⁵ In one intervention (G1), participants were instructed to consume 70% of their energy for breakfast, morning snack, and lunch, and 30% of their energy for afternoon snack and dinner. In the second intervention (G2) participants were instructed to consume 55% of their energy for breakfast, morning snack, and lunch, and 45% of their energy for afternoon snack and dinner. Participants met with a dietitian to assist with compliance to the prescription. While analyses were not conducted regarding adherence to the specific goals for eating occasions up to lunch and then after lunch, analyses of breakfast and dinner from food records indicated a different pattern of intake that matched the prescriptions (G1: 35% energy and 20% energy for breakfast and dinner, respectively; G2: 30% energy and 45% energy for breakfast and dinner, respectively), but significant differences were not reported. However G1 did have significantly greater weight loss than G2 (-8.2 ± 3.0 kg vs -6.5 ± 3.4 kg, $p < 0.05$). Reduction in homeostasis model assessment–estimated insulin resistance (HOMA-IR) was significantly greater ($p < 0.05$) in G1 than G2.

In another study, 93 women with overweight or obesity and metabolic syndrome were randomized to one of two, 3-month obesity interventions.²⁶ In this investigation, Participants in both interventions were prescribed a diet containing 1,400 kcal /day and met with a dietitian to check for compliance during the intervention. In one intervention (Breakfast), participants were instructed to consume 50% of their energy at breakfast, 36% at lunch, and 14% at dinner. In the other intervention (Dinner), participants were instructed to consume, 14% of their energy at breakfast, 36% at lunch, and 50% at dinner. Participants were also provided with times of when to eat the meals, with breakfast at 6 to 9 am, lunch at 12 to 3 pm, and dinner at 6 to 9 pm. No diet results were reported. For weight loss, Breakfast lost significantly more weight than Dinner

(-8.7 ± 1.4 kg vs -3.6 ± 1.5 kg, $p < 0.0001$). Interestingly, the difference in weight loss between the two groups became significantly different early in the intervention (week 4) and remained significantly different throughout the remaining time of the intervention. At 3 months, fasting glucose, insulin, and HOMA-IR decreased in both groups, but Breakfast decreased to a greater extent ($p < 0.0001$) than Dinner in these outcomes. Oral glucose tolerance tests also showed that at 3 months, both groups had significantly lower glucose and insulin excursions as compared to baseline, but Breakfast again had a significantly ($p < 0.0001$) greater reduction in glucose and insulin excursions from baseline than Dinner (glucose: -22% vs -15% ; insulin: -58% vs -30%).

At week two in the investigation, participants consumed their meals in a lab setting for one day, and measures of insulin, glucose, ghrelin, and hunger and fullness were taken throughout the day.²⁶ Results found that Breakfast had significantly lower ($p < 0.05$) area under the curve for glucose, insulin, ghrelin, and hunger, and significantly greater ($p < 0.05$) area under the curve for fullness than Dinner.

Results of these observational and experimental investigations indicate that eating a greater amount of energy earlier in the day may be helpful for weight management. In particular, during obesity treatment, this eating pattern appears to enhance weight loss, with the effect occurring early in treatment and maintained over time. While evidence is limited, cardiometabolic enhancements were found when greater energy intake occurred earlier, as compared to later, in the day, with these enhancements showing prior to when differences in weight loss were apparent. While these investigations examined if eating earlier in the day is helpful for weight management and cardiometabolic health, they did not examine if this eating pattern assists with entrainment of biological and behavioral circadian rhythms.

1.5 Timing of energy intake, sleep, and weight loss: Pilot study

To better understand if consuming a larger portion of energy earlier and a smaller portion later in the day is an eating pattern that enhances weight loss via synchronization of biological and behavioral circadian rhythms, we conducted an 8-week pilot study that examined if the amount of energy consumed and the time of day it is consumed (behavioral circadian rhythm) enhanced weight loss and regularity of sleep and wake times (marker for biological circadian rhythm). In this pilot study, within the context of an 8-week lifestyle intervention for obesity treatment, two isocaloric, energy distribution patterns were examined. Both energy distribution patterns instructed participants to consume only three meals per day. One pattern, Morning, prescribed an energy distribution pattern of 50% of energy in the first meal, 30% in the second meal, and 20% in the last meal. The second pattern, Evening, prescribed an energy distribution pattern of 20% in the first meal, 30% in the second meal, and 50% in the last meal. Measures of diet, via three-day food records, were taken at 0 and 8 weeks to assess behavioral circadian rhythm. Measures of sleep, via accelerometry, to assess biological circadian rhythm, were taken at 0 and 8 weeks. Percent weight loss over the course of the 8 weeks was determined. This study was approved by the Institutional Review Board at the University of Tennessee and was registered with ClinicalTrials.gov (Identifier: NCT02204735).

1.5.1 Methods

For this pilot, participants were recruited via flyers. Participants were adults who had a body mass index between 27 and 45 kg/m², a self-reported daily (weekday and weekend) wake-up time between 5 am and 8 am, and self-reported at least six total hours of sleep ≥ 5 nights per week. Participants were ineligible if they could not walk at least 2 blocks without stopping; were participating in a weight loss program and/or taking weight loss medication or lost $> 5\%$ of body weight during the past 6 months; were diagnosed with type 1 or 2 diabetes; had bariatric surgery;

were pregnant, lactating, < 6 months post-partum; were on medication to aid in sleep; or were shift workers/alternative shift workers that work outside of 7 am and 7 pm.

In 2014, a total of 46 participants were phone-screened for eligibility and those participants who were initially eligible were invited to an in-person orientation, in which informed consent was obtained by research staff. Eleven potential participants attended the orientation and signed consents, with eight of these potential participants completing baseline assessments. These eight participants were randomized, using a random numbers table, to one of the two tested interventions. Participants were informed of the intervention they were assigned to at their first intervention session.

Morning and Evening received an 8-week standard lifestyle intervention for obesity, which consisted of 30-minute weekly, individual meetings, delivered by M.S.- and Ph.D.-level research staff. In each meeting, participants were weighed, self-monitoring records of diet and physical activity were reviewed, and a behavioral lesson was presented. Behavioral lessons covered topics such as self-monitoring, goal setting, stimulus control, pre-planning, and problem-solving and were based upon previous trials. Participants were instructed to consume an energy- and fat-restricted diet (1,200-1,500 kcal/day, < 30% kcal from fat). Participants were instructed to eat a total of three eating occasions each day, with the first occasion to occur within one hour of awakening and to consume their second and third eating occasions within five or six hours of their previous occasion. Participants were instructed to have at least one hour prior to going to sleep with no eating. Participants were instructed to incrementally build up their physical activity to a goal of 200 min (recommended as 40 min, five days per week) of moderate-intensity physical activity per week, with no guidance provided regarding what time of day physical activity should occur.

Participants randomized to Morning were instructed to consume 50% of their energy intake in their first meal, 30% in their second meal, and 20% in their meal (i.e., for 1200 kcal/day, 600 kcal in the first meal, 360 kcal in the second meal, and 240 kcal in the third meal). Evening was instructed to consume 20% of their energy intake in their first meal, 30% in their second meal, and 50% in the third meal. Participants were provided with sample meal plans meeting their intervention prescription.

Measures were collected at 0 and 8 weeks, unless otherwise described, by trained research assistants blinded to randomization assignment. Overall energy intake and meal energy intake was assessed by 3-day (2 weekdays and 1 weekend) food records. Eating occasions were participant defined. Nutrition Data System for Research (NDS-R) software developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, Minnesota was used to determine energy intake.

At 0 weeks, self-reported measures on risk of self-apnea (STOP BANG)²⁷ and sleep quality (Women's Health Initiative Insomnia Rating Scale [WHIIRS])²⁸ were collected. Data on basic sleep quality and overall amount of sleep obtained was collected using the SenseWear® armband from BodyMedia®. Participants were instructed to wear the armband for 23 hours a day for each of the 7-day period assessments at 0 and 8 weeks. The body monitoring system of the SenseWear® armband continuously records skin temperature, Galvanic skin response, and metabolic equivalent values. The SenseWear® has been shown to be a reliable measurement for total sleep time in both individuals with and without obstructive sleep apnea,²⁹ and a valid and reliable measure of total sleep time and sleep efficiency in adolescents.³⁰ The armband reports total minutes of lying down and total minutes wake/sleep during the lying down time, allowing sleep efficiency to be calculated. Mean minutes of sleep per 24 hours and mean sleep efficiency

was calculated from the 7 days of measures. Participants completed a sleep diary during the seven days that the armband was worn. Sleep onset and wake times from the diary, which were compared to output from the SenseWear® armband, were used to quantify sleep regularity. Regularity was calculated using guidelines from the Social Rhythm Metric.^{15,16} A score of 0 to 7 was calculated to assess the mean regularity of sleep onset and wake times. Regularity was defined as the number of times sleep onset and wake times occurred within the same 45 min each day during the assessed week. A score of 0 indicates none of the scored events occurred within the same 45 min period during the week (no regularity), while 7 represents all scored events occurred within the same 45 min period during the week (perfect regularity). The Social Rhythm Metric has been found to be a valid and reliable measure of rhythms.^{15,16} In addition to measuring sleep, the armband measured moderate- to vigorous-intensity physical activity minutes.³¹

Weight was assessed by an electronic scale, and height was assessed using a stadiometer, using standard procedures, with participants wearing light clothing, without shoes. Weight was measured weekly, while height was measured at baseline only. Percent weight loss was calculated from baseline weight.

Adherence to the intervention was evaluated by attendance to sessions and mean weekly compliance to the dietary prescriptions in regards to timing of meal intake and amount consumed at meals from self-monitoring forms. Each week, one random day was selected from the self-monitoring records to review and meals that were consumed within one hour of their designated prescription time were counted as being consumed at the correct time and meals that were ± 50 kcal of their energy goals were counted as being the correct size.

Baseline characteristics between the two interventions were examined for differences

using chi-square and independent t-tests for nominal/ordinal data and interval data, respectively. Mixed analyses of variance, with intervention as the between-subjects factor and time as the within-subjects factor, were used to examine differences between the interventions across time for all variables except percent weight loss, which was analyzed with an independent t-test. For mixed analyses of variance, significant interactions were followed with post hoc pairwise comparisons using Bonferroni corrections to determine where differences occurred. Greenhouse-Geisser corrections were used when appropriate for repeated measures to adjust for sphericity. Attendance and compliance to energy distribution timing prescriptions were examined with independent t-tests. Analyses were conducted using SPSS 23.0 (SPSS, Inc). Alpha-level was set at 0.05.

1.5.2 Results

Eight women (53.1 ± 6.4 years, 36.0 ± 2.4 kg/m², 75% non-Hispanic Whites – see Table 1) were randomized to Morning or Evening (no significant differences occurred between the two interventions in demographic, and baseline diet, sleep, physical activity, or anthropometric variables). Self-report measure of risk of sleep-apnea indicate low to intermediate risk,²⁷ and self-report measure of sleep quality is below the cut-off considered to indicate poor quality.²⁸

Changes in diet are shown in Table 2. Energy intake significantly decreased from 0 to 8 weeks (1812 ± 373 kcal/day vs 1433 ± 331 , $d = 1.07$, $F(1,6) = 6.01$, $p = 0.049$), with no significant differences between the interventions. In regards to patterns of intake, the number of eating occasions decreased significantly from 0 to 8 weeks (4.5 ± 1.2 occasions/day vs 3.1 ± 0.6 occasions/day, $d = 1.5$, $F(1,6) = 27.5$, $p = 0.002$), with no significant differences between the interventions. Additionally, how energy was distributed throughout the day changed over the course of the intervention, with Breakfast showing the greatest percent of energy intake

Table 1. Demographic characteristics of Morning and Evening

	Morning (n=4)	Evening (n = 4)
Age ^a (yrs)	51.0 ± 5.9, 45-59	55.3 ± 6.9, 45-59
Body mass index ^a (kg/m ²)	35.7 ± 4.8, 32-43	36.3 ± 2.5, 34-40
Women (%)	100.0	100.0
Race (%)		
White	100.0	50.0
Black	0.0	50.0
Hispanic (%)	0.0	0.0
STOP BANG ^a	2.3 ± 1.0, 1-3	3.3 ± 1.3, 2-5
WHIIRS ^a	6.8 ± 2.6, 3-9	6.3 ± 2.6, 4-10
Moderate- to vigorous physical activity ^a (hrs/day)	0.43 ± 0.22, 0.16-0.64	0.23 ± 0.13, 0.40-0.33

^aReported in M ± SD, Minimum value-Maximum value. WHIIRS = Women's Health Initiative Insomnia Rating Scale.

occurring in the first meal of the day and the smallest percent of energy intake occurring in the last meal of the day at 8 weeks, and Dinner showing the smallest percent of energy intake occurring in the first meal of the day, with the second and third meals being larger than the first meal, but similar in percent of energy take, at 8 weeks. There was a significant interaction ($F(1,6) = 23.7, p = 0.003$) for percent of energy intake at the first meal, with Breakfast consuming a

significantly greater ($F(1,6) = 56.2, p < 0.001$) percentage of energy in the first meal than Dinner at 8 weeks ($d = 5.3$).

In regards to how the three meals were spaced during the day, there was a significant decrease in hours from self-reported awake time and the first meal from 0 to 8 weeks, with no significant differences between the interventions (1.39 ± 0.35 hrs vs 0.89 ± 0.45 hrs, $d = 1.2, F(1,6) = 14.5, p = 0.009$). A significant increase in hours between meal 1 and meal 2 from 0 to 8 weeks occurred, with no significant difference between the interventions (4.45 ± 0.87 hrs vs 5.28 ± 0.82 hrs, $d = 0.9, F(1,6) = 7.3, p = 0.036$). No significant change in hours between meal 2 and meal 3 occurred from 0 to 8 weeks (5.66 ± 0.63 hrs vs 5.08 ± 0.52 hrs, $d = 1.0, F(1,6) = 5.59, p = 0.056$). A significant increase in hours from the last eating occasion to self-reported sleep onset occurred from 0 to 8 weeks, with no significant difference between the interventions (3.27 ± 1.51 hrs vs 3.98 ± 0.84 hrs, $d = 0.6, F(1,6) = 8.1, p = 0.029$).

Taken together, these results show that the two groups differed in their energy distribution timing, with Breakfast consuming a greater proportion of energy earlier in the day and Evening consuming a greater proportion of energy later in the day. Also, in both interventions the eating pattern shifted in which eating started closer to awakening in the morning, with a longer period of no eating prior to sleep onset. Eating occasions also occurred approximately every 5 hours when awake.

Sleep outcomes are shown in Table 3. For sleep, there were no significant changes in hours of sleep from 0 to 8 weeks (6.37 ± 0.77 hrs vs 6.85 ± 0.87 hrs, $d = 0.5, F(1,6) = 3.9, p = 0.097$). At 0 weeks, mean sleep time for Morning was 23:31 hr:min (range: 22:56 hr:min - 23:41 hr:min) and Evening was 00:10 hr:min (range: 23:50 hr:min - 00:55 hr:min). At 0 weeks, mean wake time for Morning was 06:04 hr:min (range: 05:47 hr:min - 06:15 hr:min) and Evening was

Table 2. Dietary intake of Morning and Evening at 0 and 8 weeks^a

	Morning (n = 4)	Evening (n = 4)
Energy (kcal/day) ^b		
0 weeks	1849 ± 141, 1660-1973	1776 ± 550, 1000-2172
8 weeks	1423 ± 156, 1209-1570	1544 ± 568, 939-1772
Number of eating occasions per day ^b		
0 weeks	4.9 ± 0.8, 4.0-6.0	4.1 ± 1.5, 3.0-6.3
8 weeks	3.0 ± 0.0, 3.0-3.0	3.3 ± 1.0, 2.7-4.7
First meal percent of daily energy ^c		
0 weeks	15.5 ± 6.7, 7.7-22.4	21.4 ± 8.7, 13.6-33.2
8 weeks	44.5 ± 6.7*, 39.0-54.2	14.3 ± 4.5*, 8.9-18.3
Second meal percent of daily energy		
0 weeks	22.4 ± 8.7, 12.0-30.6	33.9 ± 14.9, 17.0-41.7
8 weeks	30.3 ± 4.4, 24.6-34.5	41.3 ± 18.8, 26.7-57.9
Third meal percent of daily energy		
0 weeks	36.7 ± 8.3, 30.1-48.6	35.3 ± 17.5, 20.2-50.5
8 weeks	25.0 ± 4.9, 21.2-32.0	42.0 ± 10.0, 32.1-52.1
Time from awakening to first meal (hrs) ^b		
0 weeks	1.19 ± 0.33, 0.82-1.42	1.59 ± 0.28, 1.42-2.00
8 weeks	0.95 ± 0.46, 0.56-1.58	0.82 ± 0.50, 0.31-1.33
Time from first to second meal (hrs) ^b		
0 weeks	4.82 ± 0.26, 4.47-5.07	4.08 ± 1.15, 3.17-5.75
8 weeks	5.03 ± 0.79, 3.91-5.78	5.53 ± 0.88, 4.26-6.50

Time from second to third meal (hrs)

0 weeks $5.50 \pm 0.71, 4.88-6.45$ $5.83 \pm 0.59, 5.31-6.51$

8 weeks $5.40 \pm 0.29, 5.00-5.67$ $4.76 \pm 0.52, 4.04-5.17$

Time from last eating occasion to sleep
(hrs)^b

$2.71 \pm 0.55, 1.95-3.25$ $3.84 \pm 2.04, 1.61-6.33$

0 weeks

$3.93 \pm 0.51, 3.22-4.44$ $4.03 \pm 1.18, 2.52-5.08$

8 weeks

^aReported in $M \pm SD$, Minimum value-Maximum Value, ^bSignificant main effect of time ($p < 0.05$), ^cSignificant interaction ($p < 0.05$). *Significantly different ($p < 0.001$).

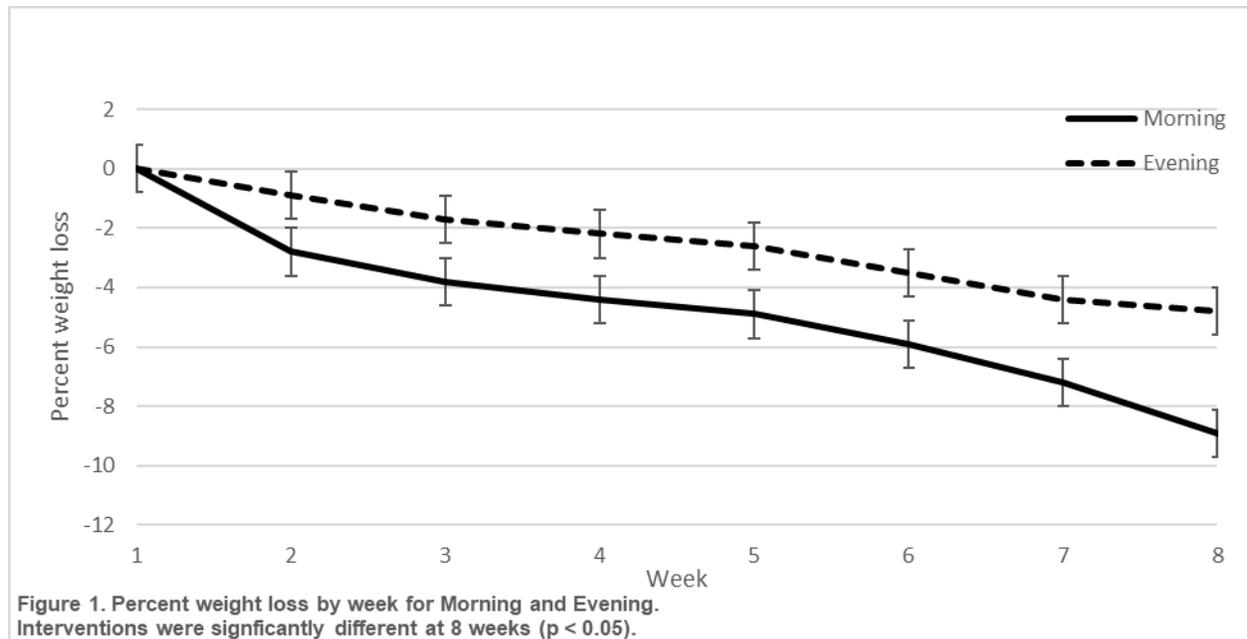
06:40 hr:min (range: 05:20 hr:min - 07:30 hr:min). At 8 weeks, mean sleep time for Morning was 23:20 hr:min (range: 22:56 hr:min - 23:41 hr:min) and Evening was 23:22 hr:min (range: 22:13 hr:min - 00:26 hr:min). At 8 weeks mean wake time for Morning was 06:12 hr:min (range: 05:49 hr:min - 06:36 hr:min) and Evening was 06:47 hr:min (range: 06:16 hr:min - 07:00 hr:min). There was a significant interaction ($F(1,6) = 8.6, p < 0.026$) for sleep efficiency, however posthoc comparisons did not show a significant difference between Morning and Evening at 8 weeks or a significant difference between 0 and 8 weeks for either intervention. There was also a significant interaction ($F(1,6) = 6.4, p = 0.045$) for sleep onset and awakening regularity, with Morning have significantly greater ($F(1,6) = 6.8, p = 0.04$) regularity than Evening at 8 weeks ($d = 1.8$).

Table 3. Sleep measures for Morning and Evening at 0 and 8 weeks^a

	Morning (n = 4)	Evening (n = 4)
Sleep (hrs)		
0 weeks	5.97 ± 0.38, 5.67-6.52	6.87 ± 0.84, 6.06-8.00
8 weeks	6.51 ± 0.73, 5.61-6.96	7.18 ± 0.96, 6.25-8.26
Percent sleep efficiency ^b		
0 weeks	79.2 ± 9.8 [#] , 67.4-91.1	85.7 ± 4.9 [#] , 79.7-90.5
8 weeks	83.3 ± 7.1 [#] , 73.7-90.7	81.4 ± 6.6 [#] , 72.5-87.3
Sleep regularity ^b		
0 weeks	5.0 ± 1.1, 4.0-6.5	4.3 ± 1.0, 3.0-5.0
8 weeks	5.6 ± 0.9 [*] , 4.5-6.5	3.9 ± 1.0 [*] , 2.5-5.0

^aReported in M ± SD, Minimum value-Maximum Value ^bSignificant interaction (p < 0.05). [#]Not significantly different (p > 0.05). ^{*}Significantly different (p < 0.05).

Percent weight loss for each intervention by week is shown in Figure 1. There was a significant difference (t (6) = 3.4, p = 0.014) between the interventions in percent weight loss at 8 weeks with Morning showing a greater decrease in percent weight loss than Evening (-8.9 ± 1.4% vs -4.8 ± 1.3%, d = 3.0).



Daily hours of moderate- to vigorous-intensity physical activity did not significantly change from 0 to 8 weeks (0.33 ± 0.20 hrs/day vs 0.40 ± 0.38 hrs/day, $d = 0.2$, $F(1,6) = 0.6$, $p = 0.476$), with no significant differences between interventions. There were no differences in the interventions in regards to attendance (Morning: 8.0 ± 0.0 , Evening: 7.8 ± 0.5 , $t(6) = 1.00$, $p = 0.356$), and number of meals per day compliant to meal timing goals (Morning: 2.6 ± 0.4 , Evening: 2.4 ± 0.4 , $t(6) = 0.919$, $p = 0.394$), and number of meals per day compliant to meal size goals (Morning 2.2 ± 0.2 , Evening: 2.1 ± 0.1 , $t(6) = 0.870$, $p = 0.418$).

The results from this pilot study indicate that during a brief lifestyle intervention, an eating pattern in which a greater percentage of energy is consumed earlier in the day, as compared to an eating pattern in which a greater percentage of energy is consumed later in the day, enhanced sleep onset and awakening regularity. This may suggest an improvement of synchronization of behavioral and biological circadian rhythms. Furthermore, this potentially chrono-enhancing eating pattern dramatically increased percent weight loss (this pilot study found

percent weight loss was enhanced by > 80%). However, it is important to underscore limitations of this pilot study. As the sample is all women and middle-aged, menopausal status may influence outcomes and this information was not collected from participants. The sample size is very small, which may hamper ability to detect baseline difference between the interventions, and significant findings are found only in areas with very large effect sizes. Dietary intake and sleep diaries are self-reported (sleep diaries were compared to SenseWear® armband output), and a biomarker of biological circadian timing was not collected.

1.6 Conclusion

A temporal pattern of energy intake, energy distribution timing, is a newly identified dietary pattern that appears to impact health outcomes. In particular, consuming a greater amount of energy earlier in the day and a smaller amount of energy later in the day appears to improve cardiovascular health, enhance dietary induced thermogenesis, and increase weight loss. These improvements may be due to greater entrainment of the CTS, in which the synchronization of biological and behavioral circadian rhythms are improved.

As this area of research is in its infancy, with few studies conducted in free-living participants, several areas of research are needed to better understand how timing of energy intake influences health outcomes and the mechanisms of action. Intervention studies conducted with larger samples over longer time periods are needed. Importantly, within these studies, to better ascertain timing of energy intake, dietary assessment should incorporate methodologies, other than self-report, that help measure amount and time of energy intake. This may involve the use of technology, such as digital imaging, accelerometry (i.e., bite counter), and/or continuous blood glucose monitoring, as these methods can time stamp eating occasions and potentially help with quantifying size of the eating occasions. Additionally, along with measures of behavioral

circadian rhythms, studies should measure biological markers of circadian rhythm, such as morning-evening cortisol difference, daily profile of wrist temperature, and dim-light melatonin onset. Finally, the moderating influence of chronotype on compliance to this type of prescription and weight loss should be examined. These types of investigation will provide greater insight into the ability of participants to implement and maintain this type of dietary pattern over time, its influence on health outcomes, and its effect on CTS entrainment.

References

1. Eicher-Miller HA, Khanna N, Boushey CJ, Gelfand SB, Delp EJ. Temporal dietary patterns derived among the adult participants of NHANES 1999-2004 are associated with diet quality. *Journal of the Academy of Nutrition and Dietetics*. 2016;116:283–291.
2. Reedy J, Wirfalt E, Flood A, et al. Comparing 3 dietary pattern methods—cluster analysis, factor analysis, and index analysis—with colorectal cancer risk: The NIH–AARP Diet and Health Study. *American Journal of Epidemiology*. 2010;171:479–487.
3. Kant AK, Graubard BI. 40-year trends in meal and snack eating behaviors of American adults. *Journal of the Academy of Nutrition and Dietetics*. 2015;115:50-63.
4. Arble D, Bass J, Laposky A, Vitaterna M, Turek F. Circadian timing of food intake contributes to weight gain. *Obesity*. 2009;17:2100-2102.
5. Garaulet M, Gómez-Abellán P. Timing of food intake and obesity: A novel association. *Physiology & Behavior*. 2014;134:44-50.
6. Garaulet M, Gomez-Abellan P, Alburquerque-Bejar JJ, Lee YC, Ordovas JM, Scheer FA, J. L. Timing of food intake predicts weight loss effectiveness. *International Journal of Obesity*. 2013;37:604-611.

7. Wang JB, Patterson RE, Ang A, Emond JA, Shetty N, Arab L. Timing of energy intake during the day is associated with the risk of obesity in adults. *Journal of Human Nutrition and Dietetics*. 2014; Suppl 2:255-262.
8. Dunford EK, Popkin BM. Disparities in snacking trends in US adults over a 35 year period from 1977 to 2012. *Nutrients*. 2017;9:809.
9. Gill S, Panda S. A smartphone app reveals erratic diurnal eating patterns in humans that can be modulated for health benefits. *Cell Metabolism*. 2015;22:789–798.
10. Corbalan-Tutau MD, Gomez-Abellan P, Madrid JA, Canteras M, Ordovas JM, Garaulet M. Toward a chronobiological characterization of obesity and metabolic syndrome in clinical practice. *Clinical Nutrition*. 2015;34:477-483.
11. Garaulet M, Ordovas JM, Madrid JA. The chronobiology, etiology and pathophysiology of obesity. *International Journal of Obesity*. 2010;34:1667-1683.
12. Summa KC, Turek FW. Chronobiology and obesity: interactions between circadian rhythms and energy regulation. *Advances in Nutrition*. 2014;5:312S-319S.
13. Garaulet M, Madrid JA. Chronobiological aspects of nutrition, metabolic syndrome and obesity. *Advanced Drug Delivery Reviews*. 2010;62:967-978.
14. Salgado-Delgado R, Osorio AT, Saderi N, Escobar C. Disruption of circadian rhythms: a crucial factor in the etiology of depression. *Depression Research and Treatment*. 2011. doi:10.1155/2011/839743.
15. Monk TH, Flaherty JF, Frank E, Hoskinson K, Kupfer DJ. The social rhythm metric: an instrument to quantify the daily rhythms of life. *Journal of Nervous and Mental Disease*. 1990;178:120-126.

16. Monk TH, Kupfer DJ, Frank E, Ritenour AM. The social rhythm metric (SRM): measuring daily social rhythms over 12 weeks. *Psychiatry Research*. 1991;36:195-207.
17. Monk TH, Petrie SR, Hayes AJ, Kupfer DJ. Regularity of daily life in relation to personality, age, gender, sleep quality and circadian rhythm. *Journal of Sleep Research*. 1994;3:196-205.
18. Frank E, Swartz HA, Kupfer DJ. Interpersonal and social rhythm therapy: managing the chaos of bipolar disorder. *Biological Psychiatry*. 2000;48:593-604.
19. Litinski M, Scheer FAJL, Shea SA. Influence of the circadian system on disease severity. *Sleep Medical Clinics*. 2009;4:143-163.
20. Bandín C, Scheer FAJL, Luque AJ, et al. Meal timing affects glucose tolerance, substrate oxidation and circadian-related variables: A randomized, crossover trial. *International Journal of Obesity*. 2015;39:828–833.
21. Bo S, Fadda M, Castiglione A, et al. Is the timing of caloric intake associated with variation in diet-induced thermogenesis and in the metabolic pattern? A randomized cross-over study. *International Journal of Obesity*. 2015;39:1689–1695.
22. Morris CJ, Garcia JJ, Myers S, Yang JN, Trienekens N, Scheer FAJL. The human circadian system has a dominating role in causing the morning/evening difference in diet-induced thermogenesis. *Obesity*. 2015;23:2053–2058.
23. Kahleova H, Lloren JJ, Mashchak A, Hill M, Fraster GE. Meal frequency and timing are associated with changes in body mass index in adventist health study 2. *Journal of Nutrition*. 2017;147:1722-1728.

24. Ruiz-Lozano T, Vidal J, de Hollanda A, Scheer FAJL, Garaulet M, Izquierdo-Pulido M. Timing of food intake is associated with weight loss evolution in severe obese patients after bariatric surgery. *Clinical Nutrition*. 2016;35:1308-1314.
25. Lombardo M, Bellia A, Padua E, et al. Morning meal more efficient for fat loss in a 3-month lifestyle intervention. *Journal of the American College of Nutrition*. 2014;33:198–205.
26. Jakubowicz D, Barnea M, Wainstein J, Froy O. High caloric intake at breakfast vs. dinner differentially influences weight loss of overweight and obese women. *Obesity (Silver Spring)*. 2013;21:2504-2512.
27. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology*. 2010;108:812-821.
28. Levine DW, Kripke DF, Keplan RM, et al. Reliability and validity of the women's health initiative insomnia rating scale. *Psychological Assessment*. 2003;15:137-146.
29. Sharif MM, BaHamman AS. Sleep estimation using BodyMedia's SenseWear(TM) armband in patients with obstructive sleep apnea. *Annals of Thoracic Medicine*. 2013;8:53-57.
30. Roane BM, Van Reen E, Hart CN, R. W, Carskadon MA. Estimating sleep from multisensory armband measurements: validity and reliability in teens. *Journal of Sleep Research*. 2015;24:714-721.
31. Bond DS, Raynor HA, Phelan S, Steeves J, Daniello R, Wing RR. The relationship between physical activity variety and objectively measured moderate-to-vigorous physical activity levels in weight loss maintainers and normal-weight individuals. *Journal of Obesity*. 2012: doi:10.1155/2012/812414.