The Effect of Eating Frequency on Sleep Quality Among Healthy Adults: A Component of The Frequency of Eating and Satiety Hormones (FRESH) Study

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Abstract

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The relationship between sleep and health have been well documented, with scientific evidence supporting a positive association between high quality of sleep and health-related outcomes. Given the importance of sleep, the current paper explores the possible ways to improve sleep quality through eating frequency (EF). Data were provided by the Frequency of Eating and Satiety Hormones (FRESH) study conducted at the Fred Hutchinson Cancer Research Center. The FRESH study was a randomized, cross-over clinical trial where participants were randomly selected to follow a low EF (3 meals/day) and high EF (6 meals/day) meal plans for a 21-day period. Sleep quality was evaluated using the self-reported Pittsburg Sleep Quality Index (PSQI) survey at the end of each period. A total of 49 participants from the FRESH study fully completed the PSQI. A three-way ANOVA with repeated measures was performed to compare the mean PSQI scores after following the low and high EF interventions to determine the effects on sleep quality, controlling for BMI and gender. In conclusion, low EF resulted in a 0.5-point greater global PSQI than high EF. However, there was insufficient evidence to support a statistically significant difference in PSQI scores between the low and high EF when controlling for BMI and gender.

1. Introduction

Getting a good night of sleep plays a crucial role in living a healthy and productive life. There is ample scientific evidence to support that sleep can impact glucose metabolism, regulation of satiety hormones, and mental health.[1,2,3] Observational studies have found a strong and positive association between sleep restriction and impaired insulin sensitivity, with one experimental study that demonstrated a 19-25% reduction in insulin sensitivity after just a single night of restricted sleep.[1] Proper sleep can also play a critical role in helping to maintain a healthy weight by regulating satiety hormones such as ghrelin. Ghrelin is a potent hormone that promotes food intake by stimulating appetite.[4] It has been reported that an acute 3 hour reduction in sleep duration can increase ghrelin concentrations by 14.9%, independent of BMI, age, and sex.[2] Additionally, sleep quality and duration can have dramatic impacts on an individual's motivation, mental acuity, and energy levels. A study of participants enrolled in an employee wellness program found that those who report worse sleep quality were less likely to maintain a new healthy behavior over time such as stress management, weight management, physical activity, and smoking cessation.[3]

Despite the proposed positive benefits of sleep, it appears that there is a growing trend of sleep disorders among adults in the United States. According to the National Health Interview Survey, between 2002 and 2012 the prevalence of insomnia or trouble sleeping increased from 17.8% in 18.9%.[5] During the same period of time, the National Health Interview Survey also observed an increase in reported daytime sleepiness from 9.8% to 12.7% of the respondents.[5] This increase in daytime sleepiness presents a potential public health risk because employees with excessive daytime sleepiness are twice as likely to be involved in occupational accidents compared to those not reporting daytime sleepiness.[6] Daytime sleepiness is also strongly associated with motor vehicle accidents and "near-miss" incidents on the roadways. A cross-sectional study conducted on truck drivers in Italy found that those who report severe daytime sleepiness were two times more likely to be involved in an accident and three times more likely to be involved in near-miss incidents.[7] Given the potential increased risk that excessive daytime sleepiness poses to the public, it is imperative to find easily implemented methods to improve overall sleep quality.

Various behavioral factors can have great impact on an individual's sleep quality. Some factors associated with sleep include duration, intensity, and timing of physical activity, collective screen time throughout the day, bright light exposure in the evening, and caffeine consumption. Findings from a randomized clinical trial suggest that increasing physical activity can potentially resolve or mitigate insomnia in otherwise inactive patients. The study was conducted on physically inactive adults with insomnia and found that increasing aerobic activity over a 16 week period improved sleep quality by 4.8 points on the Pittsburg Sleep Quality Index (PSQI).[8] Screen time has also been identified as a behavioral factor that can impact a person's sleep quality. It has been observed that those who accrue more than 1.5 hours of screen time per day have a lower quality of sleep and an even more significant sleep quality reduction occurred when screen time is reported during habitual bedtime.[9] Aspects of an individual's diet and consumption schedule have also been reported to impact sleep, specifically the consumption of caffeine. One randomized clinical trial reported that consuming one cup of coffee as early as 6 hours before regular bedtime can disrupt sleep quality.[10]

An area that has been largely overlooked by the scientific community is eating frequency (EF), or the number of eating occurrences within 24 hours.[11] Eating small and frequent meals throughout the day is an increasingly common food behavior for individuals[12]; however, there is a lack of scientific evidence to support an optimal EF.[11] There is even less research devoted to exploring the potential impacts of EF on overall sleep quality. A pilot study with a design similar to the FRESH study found that high EF (6 meals/day) was associated with an increase in inflammatory markers related to disease and sensations of hunger.[13,14]

The present study sought to use data from the FRESH study to (1) characterize average sleep quality after following a low and high EF intervention for 21 days, (2) test the *a priori* hypothesis that a difference in EF will result in a change in overall sleep quality.

2. Methods

2.1 Trial Design

Data used for this study were collected as part of the Frequency of Eating and Satiety Hormones (FRESH) Study. The FRESH study was a randomized, crossover clinical trial conducted at the Fred Hutchinson Cancer Research Center in Seattle, Washington, USA. The purpose of the FRESH study was to determine whether eating frequency (EF) impacts blood-based biomarkers linked to inflammation, adiposity, and satiety. The study is registered at clinicaltrials.gov as NCT02392897. Full details of the study methods and procedures have been previously published.[11] In brief, 50 healthy adults were recruited from the Greater Seattle area from June 2015 to the Fall of 2018 and randomized into the study. The study was separated into two 21-day phases, during which participants were instructed to follow a low EF (3 meals/day) or high EF (6 meals/day) intervention during the first phase. Once the first phase ended, the participants returned to their regular diet for a 14-day washout period. After the washout the second phase directed participants to follow the opposite intervention than the one previously assigned to that individual.

Details regarding the eligibility and exclusion criteria for the participants of the FRESH study have been previously published.[11] In short, the study sample consisted of healthy males and females between the age of 18 and 50 years old. The three categories of BMI, normal (18.5 - < 25.0 kg/m^2), overweight (27.9 - 29.9 kg/m^2), and obese (30.0 - 40.0 kg/m^2), were represented in the study. All study procedures had IRB approval and all participants signed a written informed consent. At the end of the study, participants were compensated $300.00 for completing all study activities.

2.2 Intervention

Once eligibility was verified, anthropometric measurements and demographic characteristics were collected from all participants. Height and weight were measured by a staff member from the Fred Hutchinson Cancer Research Center. Demographic information was determined from a self-report survey. Participants were then randomized into the intervention protocol using a computer program to begin with either the low or high EF intervention phase. Before the start of each 21-day phase, a staff member provided participants with in-depth instructions on how to follow each intervention so as to minimize divergence. These instructions included details on the study activities, expectations for participation, specific instructions on their assigned eating pattern, and individually tailored calorie-level assignment.

All aspects of food intake were designed to be held constant across the two arms, with only the time and frequency of food intake varied. In each intervention participants were instructed to eat their first meal at 8am and finish their last meal by 6 pm. For the low EF intervention, participants were instructed to eat every 5 hours (8am, 1pm, and 6pm). During the high EF intervention, participants were instructed to eat every 2 hours (8am, 10am, 12pm, 2pm, 4pm, 6pm). Accommodations were made for specific hours to ease school and work schedules but the time between eating occasions remained the same (for example, participants could start at 7 am). All meals had to be completed within a 15- to 30-minute window. The two interventions were isocaloric based on each participant's daily energy requirement so that study results would not be confounded by changes in total energy intake nor type of food intake. A study nutritionist calculated the estimated daily energy requirements for each individual using the Mifflin equation.[15] The assigned calorie-level for each individual participant remained the same between the low and high EF interventions to prevent weight loss or gain, and to prevent any confounding of results. Participants were provided sample menus with varying energy needs for each intervention. The menus were based on the "food choice" system which offers guidelines on the timing and quantity of servings that should be consumed from each of the following categories: starch, milk, fruit, vegetables, fat, and protein. The "food choice" system ensured that each participant consumed a balanced meal based on current nutrition guidelines, while also providing some flexibility to accommodate for individual taste preferences.

Study staff from the Fred Hutchinson Cancer Research Center followed up with all participants regularly through the use of four in-person clinic visits and regular email and text message communication. The participants returned to the Fred Hutch Prevention Center 10 days into each phase for a midpoint visit. During these visits staff members could answer any of the participants' questions or concerns regarding the study protocol, while also monitoring their progress and making any necessary adjustments. Staff members also monitored the participants progress on a daily basis via online communication and food diaries. Every evening during each of the two phases participants received an email or text message with a link to their personalized meal plan checklist. The checklist contained a list of the different food groups they should have consumed that day per their assigned meal plan. Once the participant finished filling out the list, the data were sent directly to the study database where staff members monitored and tracked their progress. Members of the staff could then quickly follow up if they noticed a missing item from the list or if a participant failed to follow study protocol. Additionally, participants received occasional email and text message reminders containing words of encouragement to increase motivation and adherence to the protocol.

The remaining two in-person clinic visits occurred at the end of each phase for an endpoint visit. The participants returned to the Prevention Center to run various tests including completing a Pittsburg Sleep Quality Index (PSQI) survey. The PSQI is a self-reported retrospective questionnaire that assesses sleep quality over a 1-month period.[16] It contains 19-items that are then converted into seven component scores that address the different aspects of sleep quality. These seven components include: (1) Sleep Quality, (2) Sleep Latency, (3) Sleep Duration, (4) Habitual Sleep Efficiency, (5) Sleep Disturbances, (6) Use of Sleep Medications, (7) Daytime Dysfunction. Each component score is equally weighted and ranges from 0 to 3, with "0" signifying no difficulty and "3" signifying severe difficulty.[16] The sum of the component scores generate the Global PSQI Score, which reflects the overall quality of a person's sleep. The Global PSQI score ranges from 0 to 21, with higher scores reflecting poor sleep quality. Global PSQI scores above 5 indicate sleep disorders.[16]

Covariates included BMI and gender because previous studies have shown that differences in BMI and gender are associated with differences in sleep quality.[17,18,19]

2.3 Statistical Analysis

All analyses were performed using Rstudio version 1.1.456. The seven component and global PSQI scores were treated as discrete quantitative variables. The PSQI scores from the low and high EF conditions are presented as mean and standard deviation. Two different analyses were performed to compare the effect of EF on mean PSQI scores. The first compared the main effect difference between the two EF conditions on the PSQI component and global scores using the repeated measures ANOVA model. The second used a three-way ANOVA with repeated measures to compare the effects of EF on mean PSQI scores when controlling for the between-subject factors of BMI and gender. The significance level was set at $p < 0.05$ for both tests.

3. Results

3.a Baseline Characteristics

Table. 1: Baseline Characteristic			
	Count	% or Mean	SD
Age (years)	49	32.1	7.8
Sex			
Women	39	80%	
Men	10	20%	
BMI			
Normal [18.5 to <25.0 kg/m^2]	42	84%	4.9%
Overweight [27.9 to 29.9 kg/m^2]	1	2%	2%
Obese [30.0 to 40 kg/m^2]	6	12%	12%
Race			
Asian	10	20%	6.1%
African American	2	4%	2.8%
Caucasian	34	69%	6.7%
More Than One	3	6%	3.4%

The table above shows the participants' mean age in years along with standard deviation. Percentages were used to represent the proportion of participants that were male, and that fell within each BMI and race categories.

A total of 49 healthy adults from the FRESH study fully completed the PSQI survey. The sample of participants primarily consisted of women (n = 39) and the average age was 32.1 years (± 7.8). 84% of the participants fell within the normal weight category (n=42) with 2% in the overweight (n=1), and 12% in the obese category (n=6). Based on the self-reported race survey 68% of participants identified as Caucasian (n=34), 20% Asian (n=10), 4% Black or African American (n=2), and 6% identified with more than one race (n=3).

3.c Outcomes and estimation of eating frequency on sleep quality

Table 2 -Pittsburg Sleep Quality Index (PSQI) scores of FRESH participants [mean (SD)]		
N=49	**Low EF**	**High EF**
Global PSQI Score	5.32 (2.28)	4.88 (2.41)
Subjective Sleep Quality	0.796 (0.499)	0.735 (0.569)
Sleep Latency	0.898 (1.16)	0.857 (0.979)
Sleep Duration	0.184 (0.441)	0.286 (0.540)
Habitual Sleep Efficiency	0.490 (1.02)	0.367 (0.782)
Sleep Disturbances	2.16 (0.921)	1.96 (0.978)
Use of Sleep Medications	0.163 (0.553)	0.082 (0.449)
Daytime Dysfunction	0.633 (0.602)	0.592 (0.610)

EF refers to eating frequency; low EF = 3 meals per day; high EF = 6 meals per day, N=sample size, SD = standard deviation

Table 3 – ANOVA for repeated measures comparing mean PSQI scores between low and high EF			
PSQI Scores	**MS**	**F-value**	**p-value**
Global Score	9.88	1.81	0.182
Subjective Sleep Quality	0.326	1.14	0.288
Sleep Latency	0.0711	0.064	0.801
Sleep Duration	0.0238	0.098	0.755
Habitual Sleep Efficiency	1.07	1.37	0.245
Sleep Disturbances	0.0485	0.053	0.819
Use of Sleep Medications	0.307	1.21	0.274
Daytime Dysfunction	0.119	0.347	0.557

ANOVA refers to analysis of variance; PSQI = Pittsburg sleep quality index; EF = eating frequency; MS = mean square
Response Variable: The eight total PSQI scores including the seven component and aggregate global score.
Independent Variable or Repeated Measure: EF meal plans – low vs. high

Significance level set to 0.05

The global PSQI score is an aggregate of the seven components of the survey, which are outlined in Table 2 and 3. Each component score is equally weighted and ranges from 0 to 3, while the global score ranges from 0 to 21. Higher scores correspond with poor sleep quality.

Table 2 provides the mean and standard deviation of the global PSQI and seven PSQI component scores after following the two intervention arms for 21 days. The global PSQI score after following the low EF was slightly greater than the high EF (5.32 vs. 4.88). The seven component scores representing the seven common aspects of sleep quality resulted in similar outcomes, with the high EF intervention scores slightly lower than the low EF intervention. Sleep duration was the only component score that had the opposite effect with high EF presenting a slighter greater PSQI component score than low EF (low EF mean[SD] = 0.184[0.441]; high EF mean[SD]= 0.286 [0.540]). In this case, the low EF resulted in slightly longer sleep duration than high EF.

Table 3 compares the absolute mean PSQI scores from the low and high EF interventions to determine whether there was a significant effect on sleep quality. An ANOVA for repeated measures model was used for this comparison. While Table 2 indicated that high EF had better global PSQI outcomes, along with six out of the seven components, the results were not statistically significant. In addition, the positive effects that low EF had on sleep duration was not statistically significant (p-value = 0.755).

Table 4 – 3-way ANOVA for repeated measures comparing the main effects of EF, gender, and BMI on sleep quality			
Source	**MS**	**F-value**	**p-value**
Global Score			
EF	9.88	1.75	0.189
Gender	0.678	0.120	0.730
BMI	5.34	0.947	0.333
Subjective Sleep Quality			
EF	0.326	1.08	0.303
Gender	0.0148	0.049	0.825
BMI	0.0369	0.122	0.728
Sleep Latency			
EF	0.0711	0.060	0.808
Gender	0.0224	0.019	0.891
BMI	0.0561	0.047	0.829
Sleep Duration			
EF	0.0238	0.100	0.753
Gender	0.586	2.46	0.121
BMI	0.0619	0.260	0.612
Habitual Sleep Efficiency			
EF	1.07	1.40	0.240
Gender	0.484	0.635	0.428
BMI	5.29	6.94	0.00995**
Sleep Disturbances			
EF	0.0485	0.053	0.819
Gender	2.66	2.90	0.0921
BMI	2.23	2.43	0.123
Use of Sleep Medications			
EF	0.307	1.17	0.282
Gender	0.0382	0.146	0.703
BMI	0.177	0.679	0.412
Daytime Dysfunction			
EF	0.119	0.367	0.546
Gender	0.642	1.98	0.163
BMI	0.163	0.501	0.481

ANOVA refers to analysis of variance; EF = eating frequency; MS = mean square, BMI = body mass index
Response variable: The eight total PSQI scores including the seven component scores and aggregate global score
Repeated measure: EF meal plan – low (0) vs. high (1)
Additional independent variables: Gender – male (0) vs. female (1); BMI (continuous variable)

Significance level set at 0.05
*Significance codes: * = 0.05; ** = 0.01; *** = 0.001*

Table 4 shows the results from the three-way ANOVA with repeated measures which compared the absolute mean PSQI scores from the low and high EF interventions controlling for the between-subject variables of BMI and gender. The model indicates that BMI may be a confounder in the relationship between EF and sleep efficiency as it was statistically significant in the model (F-value = 6.94, p-value <0.01). The PSQI survey determines habitual sleep efficiency by calculating the percent of time in bed is spent sleeping. Those who are sleeping 85% or more of their time in bed have no problem with habitual sleep efficiency, while those who spend less than 65% of their time in bed asleep would have a severe difficulty with sleep efficiency.[16]

4. Discussion

The present study aimed to characterize average sleep quality after following a low and high EF and compare the effects of EF on sleep quality in healthy adult subjects. The evidence did not support the hypothesis that a change in EF would differentially affect sleep quality. Moreover, comparing the effects of EF on sleep quality when controlling for BMI and gender, only BMI appeared to have a potential confounding effect on habitual sleep efficiency; however, this finding should be interpreted with caution due to potential multiple testing issues.

The global PSQI score is an aggregate of the seven component scores of the PSQI survey and evaluates an individual's overall sleep quality. Each of the component scores assesses a different feature of sleep. The global PSQI score ranges from 0 to 21, with higher scores representing worse sleep quality and score greater than 5 indicating a possible sleep disorder.[16] The mean PSQI global score after following the low EF intervention was slightly greater than the high EF intervention; 5.32 vs. 4.88, respectively (Table 1). While these scores are generally low overall, the low EF is approximately 0.5 points greater than the high EF intervention. The mean PSQI scores for the low and high EF were analyzed using the repeated measures ANOVA model (Table 3). However, contrary to the hypothesized prediction, the difference in mean global PSQI scores between the low and high EF was not statistically significant (F-value = 1.80, p-value = 0.182). Furthermore, a three-way ANOVA verified no statistically significant association between global PSQI scores and EF when controlling for BMI, and gender (Table 4).

The difference in absolute mean PSQI scores between the low and high EF for each of the seven components of the survey were also analyzed using repeated measures ANOVA model (Table 3). The analysis found no effect between EF and PSQI score when controlling for BMI and gender in six out of the seven component scores (components 1, 2, 3, 5, 6, 7). BMI was identified as a potential confounding variable between EF and habitual sleep efficiency scores (F-value = 6.94, p-value= 0.0095). A Kruskal-Wallis test found a non-linear relationship between BMI and habitual sleep efficiency; however, the association was insignificant (chi-sq. = 4.23, df = 2, p-value = 0.121). The data were most likely skewed due to a single participant in the overweight category (Table 1). The significant results from the three-way ANOVA for repeated measure was most likely due to the single observational being influential and the potential that multiple tests can yield significant tests by chance. Therefore, the results should be interpreted with caution.

To our knowledge, the current study is the first of its kind. There are a limited number of randomized clinical trials that have explored the impacts of eating frequency on health, and none that have isolated the study variable to only sleep quality. Based on the findings in this paper, it is unclear whether there is a relationship between EF and sleep quality. The mean global PSQI score after following the low and high EF interventions was generally low (5.32 and 4.88, respectively). Given that a global score greater than 5 indicates a potential sleep disorder, it appears that the high EF mostly resulted in positive sleep related outcomes, while there could be a potential association between low EF and sleep disorders. These results align with an observational study that examined sleep quality and daily meal frequency in Japanese medical students. Fuji, et al., found that students who consumed at least three meals a day or more reported higher sleep quality as measured by the PSQI survey.[20]

As observed, the participants generally had low global mean scores after following both EF interventions. One potential explanation for the low mean scores despite changes in EF could stem from both meal plans having the same feeding window over 24 hours. For both experimental arms, participants were instructed to consume their first meal at 8 am and begin eating their last meal at 6 pm, resulting in a 14-hour energy restriction period. Having similar feeding windows between the two different EF meal plans was necessary for the purpose of the current study to control for EF; however, it might have contributed to the overall low scores. A scientific review examining meal frequency and health found that periods of intermittent energy restriction of approximately 16-hours were associated with positive health indicators related to reducing disease risk.[21]

Additionally, restricting meals before habitual bedtimes may also contribute to the low mean scores. The present study controlled for meal size and eating intervals, eliminating any foods after the last meal at 6 pm. A study looking into the eating and sleeping habits of university students reported a positive association between the number of sleep disturbances and consuming a meal within 3 hours of bedtime.[22] Chung, et al., reported an approximate 40% increase in the odds of nocturnal awakening when participants consumed their last meals within 3 hours of their habitual bedtime compared to those who consumed their last meal more than 3 hours before going to sleep.[22] .

The FRESH study was a randomized, cross-over clinical trial that provides many strengths in the overall study design, notwithstanding some limitations. The main limitation in the current study is the reliance on self-reported data collected from the PSQI survey. The PSQI is a retrospective survey that analyzes sleep quality over a 1-month period.[16] It is possible that some of the participants may have misreported their sleep quality over that time frame. Generalizability of the findings is another major limitation of the study. All participants were recruited from a single area, which may not be indicative of the effects of eating frequency and sleep quality in other areas of the world. In addition, the participants were able and willing to complete the study protocol. Evidence suggests that those who are willing to partake in a scientific study are inherently different than those who choose not to participate.[23] Additionally, a majority of the study sample identified as female and Caucasian, further limiting the generalizability of the findings to other populations.

There are several strengths provided by the FRESH study design. The primary including the use of a randomized, cross-over clinical trial, which allowed for each participant to act as their own control and eliminated potential contamination commonly found in other paired trials. The second is the methods used to increase compliance. Compliance was improved due to the free-living meal plans, which provided some flexibility to accommodate for an individual's taste preference. Additionally, staff members monitored compliance through the use of an online daily meal-plan checklist. Lastly, the study retained many of their participants through the use of 4 different visits to the clinic and motivational messages. The staff members frequently checked-in with the participants to answer any of their questions or concerns during the clinic visits, and quickly made adjustments to their meal plan if needed. The online motivational messages also served to keep the participants excited and willing to complete the study. In the end many of the participants completed both phases of the study. A total of 49 participants fully completed the PSQI survey after each phase, allowing for a sufficient power for statistical analysis.

In summary, there was insufficient evidence to support that a change in EF effects sleep quality. There was also no association found between sleep related outcomes and EF after controlling for BMI and gender. In general, the participants in the study demonstrated a low mean global PSQI score, which could lead to future studies examining the effects of intermittent energy restriction and/or the timing of meals around bedtimes and sleep quality.

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