OREGON HEALTH AND SCIENCE UNIVERSITY

The effect of social jetlag and chronotype on Healthy Eating Index (HEI) score, energy intake and body composition in non-shift workers aged 19-65, a NHANES 2017-2018 cross-sectional study

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Chapter 1: Specific Aims

People in modern industrialized societies are exposed to more irregular light-dark cycles than the people of the pre-electrical era.[1,2] Artificial light has given humans the capability to alter the timing of wakefulness, resulting in misalignment between the external sun clock and human biological clock.[3,4] Our biological clock, or circadian clock controls all levels of physiology that are in tune with daily environmental cycles.[5] Some evidence suggests a relationship between an individual's circadian preference and dietary intake but additional research is needed.

Individual circadian preference, or chronotype is a product of the daily synchronization between a person's internal biological clock with the 24-h light-dark cycle (i.e., entrainment) and is both genetically and highly age-dependent.[5] Chronotype can be quantified by either objectively measuring the midpoint time between the start and end of sleep during work-free days, or subjectively via questionnaire.[5] Individuals that prefer to awaken and go to sleep early are considered to have a morning/early chronotype and those that prefer a later timing of behaviors are considered to have a late chronotype.[5,6] As a byproduct of this physiologically-driven preference colliding with our societally-determined schedules, morning chronotypes typically experience longer sleep duration on workdays and shorter sleep duration on free days, while later chronotypes obtain shorter sleep duration on workdays and longer duration on free days.[5]

Circadian misalignment occurs when behaviors (i.e., wakefulness, eating, activity) occur at inappropriate circadian times. Examples of circadian misalignment are eating during the nighttime hours when internal circadian physiology is promoting sleep or attempting to sleep during the day.[5,7] One common form of recurrent circadian misalignment, social jetlag, occurs when an individual delays the timing of their behaviors on free days, such that they also delay their circadian timing, and thereby experience a misalignment upon returning to a work/school day.[5,8] Chronotype and social jetlag do not have a direct linear relationship.[5] However, social jetlag is typically greater in late chronotypes.[5] Social jetlag is also positively associated with perceived sleep debt.[8] Perceived sleep debt is defined as the difference between preferred weekday sleep duration and actual weekday sleep duration.[8] In subjects with type 2 diabetes, there is a significant association between higher perceived sleep debt and impaired glycemic control.[9] There is also evidence for an association between social jetlag and metabolic disorders.[10] However, the relationship between chronotype, social jetlag, and dietary patterns as measured by the Healthy Eating Index (HEI) of non-shift workers has not been fully examined.

The HEI was designed to measure how closely an individual dietary intake aligns with the Dietary Guidelines for Americans.[11] An HEI score of 100 closely aligns with current dietary guidelines and scores below 100 indicate deviation from these recommendations. The HEI-2015 includes 13 components that are scored separately and summed to obtain an overall HEI score.[11] Indicators of sleep patterns, measures of body composition and dietary patterns as measured by HEI score are collected as part of the National Health and Nutrition Examination Survey (NHANES). This study will take a cross-sectional look into the HEI scores of non-shift work individuals with social jetlag and/or late chronotype and examine their dietary patterns to determine if there a relationship between these factors and body composition. Our overall hypothesis is that a late chronotype and/or individuals with high social jetlag will consume a diet with a low HEI score, greater total calories and have a higher waist to hip ratio. We will test this hypothesis with the following specific aims:

Specific Aim 1: Determine the correlation between circadian timing as measured by chronotype and/or social jetlag and Healthy Eating Index score (HEI) among adults age 19-65 in the 2017-18 NHANES data.

Hypothesis: *Individuals with late chronotype and/or high social jetlag will consume a diet with a lower HEI score compared to individuals with early chronotype and/or low social jetlag.*

Specific Aim 2: Examine the relationship of circadian timing as measured by chronotype and/or social jetlag on total calorie intake among adults age 19-65 in the 2017-18 NHANES data.

Hypothesis: *Individuals with late chronotype and/or high social jetlag will consume more total calories per kilogram body weight compared to individuals with early chronotype and/or low social jetlag.*

Specific Aim 3: Describe the relationship of circadian timing as measured by chronotype and/or social jetlag on waist to hip ratio among adults age 19-65 in the 2017-18 NHANES data.

Hypothesis: *Individuals with late chronotype and/or high social jetlag will have a higher waist to hip ratio compared to individuals with early chronotype and/or low social jetlag.*

The impact of this study is to improve the understanding of how circadian misalignment is associated with diet quality and energy intake in adult non-shift workers. This study is cross-sectional and does not prove cause and effect but could lead to some additional hypothesis about how late chronotypes or extreme social jetlag may impact health.

Chapter 2: Background

The circadian system is a biological timekeeping system arising in the hypothalamus. This master circadian clock is fundamental in regulating the daily rhythms of sleep-wake cycle, hormonal secretions, and central and peripheral tissue metabolism.[12] Each body's internal clock is synchronized to the external light-dark cycle, relaying information in a coordinated and rhythmic way.[13] Inter-individual differences in the circadian phase relative to the light-dark cycle are referred to as chronotype.[14] Chronotypes are determined by a combination of how individual internal clocks respond to light and darkness and the duration of the individual's internal day, commonly referred to as a person's biological clock.[5] People are distinguished as "morning" and "evening" chronotypes based on their diurnal preferences.[6,14] The capability to extend wakefulness activities via electrical lighting has enabled humans to self-select their light-dark cycles.[15] Social, cultural and environmental cues also modulate chronotype.[1,2]

Extreme morning and evening chronotypes may shift circadian oscillations in body temperature, melatonin, cortisol, and other hormones by 2-3 hours.[14] These shifts characterize circadian misalignment which refers to the difference in biological night or day regulated by the endogenous circadian system and environmental night or day determined by the light-dark cycle.[14] Social jetlag is a common cause of chronic circadian misalignment and is correlated with chronotype. Social jetlag is measured by subtracting a person's midpoint of sleep on work days from their midpoint sleep on free days.[5] This measurement shows the discrepancy between a person's internal and social clocks.[16] High social jetlag is associated with increased hemoglobin A1c, c-reactive protein, and increased factors of metabolic syndrome.[14]

Chronotype Equation (MSF_{sc})

The following equation is how chronotype is calculated:

1. Calculate MSF: Mid-sleep time on free days (MSF)= (sleep onset + sleep duration)/2
2. Calculate MSFsc: Sleep-debt corrected MSF (MSF_{sc})= MSF – (sleep duration on free days – average weekly sleep duration)/2

Figure 1

a)

Sleep Time (assuming 8 hours)	Chronotype Classification
19:00-03:00 20:00-04:00	Extremely Early
21:00-05:00 22:00-06:00	Moderately Early
23:00-07:00 24:00-08:00	Intermediate
01:00-08:00	Slightly Late
02:00-10:00	Moderately Late
03:00-11:00 04:00-12:00 05:00-13:00 06:00-14:00 07:00-15:00	Extremely Late

b)

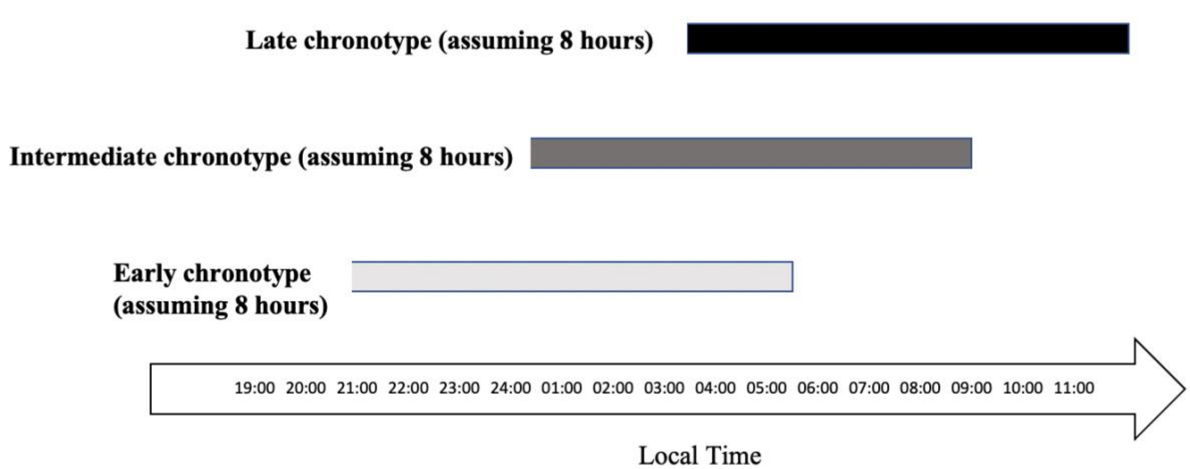


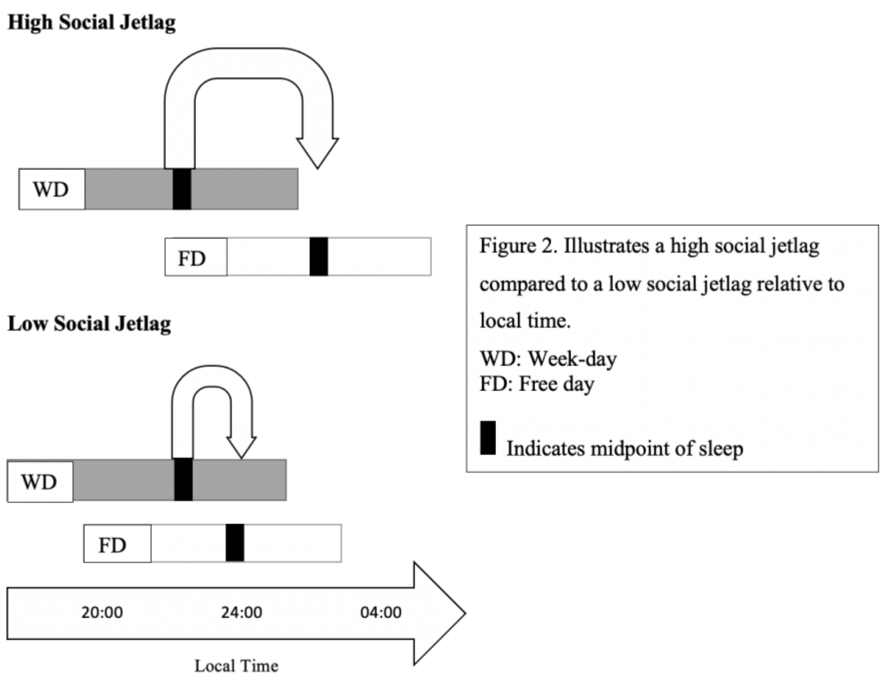
Figure 1. a) table representing sleep-wake cycles of different chronotype classifications, assuming 8-hour sleep times. b) illustrates chronotype classifications relative to local time.

Social Jetlag Equation

The following equation is how social jetlag is calculated:

Mid-sleep time on free days (MSF)- Mid-sleep time on weekdays

Figure 2



Ghrelin Regulation by Sleep and Circadian Rhythm

Ghrelin is a peptide and orexigenic hormone that is primarily secreted by the stomach.[17] Ghrelin plays an essential role in the complex signaling network of energy balance.[17] Acylation of ghrelin stimulates appetite with levels rising in a fasted state and decreasing after food ingestion.[17] Ghrelin is also regulated by circadian phase, independent of behavioral cycles.[18] Acylated ghrelin levels are higher in the biological evening than the biological morning along with increased postprandial hunger, how much food participants can eat, and appetites for meat, and sweets.[18] However, the relationship between hunger and fullness, acylated ghrelin and circadian phase remains obtuse with conflicting reports in the literature. Post-prandial acylated ghrelin significantly increased with circadian misalignment, but there were no changes in hunger and fullness.[18] This suggests that eating may be primarily altered through the food reward system during misalignment rather than hunger and fullness.[18]

In a randomized crossover study of nineteen healthy men, blood samples were taken to assess appetite-regulating hormones ghrelin, leptin, and pancreatic polypeptide during a standardized diet under normal sleep and sleep restriction.[19] Increased ghrelin levels were observed after sleep restriction compared with normal sleep.[19] Sleep restriction was also associated with an increase in 188-468 calories from snacks, primarily carbohydrates.[19] An increase in evening ghrelin during sleep restriction correlated with higher calorie intake from sweets.[19] Ghrelin impacts hunger and satiety and may be influenced by chronotype. Thus, some differences in eating behaviors by chronotype could be explained by physiological response to ghrelin but more research is needed to confirm this relationship.

Chronotype and Eating Behaviors

People who wake up earlier may have more flexibility in diet control in addition to greater control over food intake.[16] Evening types are more likely to skip breakfast than morning types and stay up late overeating.[16] One study found that people with an evening chronotype were twice as likely to experience eating disorders compared to people without an evening chronotype.[14] Food addiction may be indirectly associated with evening-type circadian preferences due to higher rates of insomnia and impulsivity.[20] Furthermore, late chronotype is correlated with higher rates of binge-eating disorder, especially in people over 40 years old and higher rates of night-eating syndrome.[16] Binge-eating disorder is when an individual has a loss of control over their eating which may occur at any time of day.[16] Night-eating syndrome is characterized by the inability to control eating during evening and nighttime.[16] Studies show that individuals that binge eat are also likely to experience uncontrolled eating at night and have a higher body mass index.[16]

The Influence of Food Timing on Metabolism

Food intake at an inappropriate circadian time may alter metabolism and increase the risk for adverse health outcomes.[15] Rhythmic feeding is key in synchronizing peripheral oscillators.[14] Therefore, altered feeding times may produce circadian system disruption and promote unhealthy metabolic outcomes such as higher fat mass, obesity, and poor glycemic control.[15] Individuals who consume a higher percentage of calories later in the biological night have a higher body fat percentage.[15] Higher fat mass may be a result of later meal timing due to a decreased thermic effect of food, or the decreased energy expended in response to food intake in the evening.[15] For example, one study found that the thermic effect of food response to a meal eaten at 10:30 pm decreased by approximately 4% compared to the same meal consumed at 6:30 pm.[21] The difference in morning-evening thermic response is primarily caused by the circadian system not external clock time.[15] Therefore, food intake during alterations in circadian alignment such as social jetlag may contribute to positive energy balance and weight gain over time.[15]

In addition, the enzyme lipoprotein lipase (LPL) follows a diurnal pattern with activity highest in the morning and lowest in the evening.[22,23] This extracellular enzyme is key in the metabolism of lipoproteins.[23] LPL increases activity in white adipose tissue in response to a meal.[23] If a meal occurs out of the diurnal LPL phase, particularly in the late evening, the individual may be at higher risk of storing free fatty acids in ectopic tissues.[23] This may contribute to nocturnal lipid intolerance, or impaired clearance of circulating triglycerides and impaired suppression of hepatic triglyceride synthesis due to decreased LPL in the late evening.[23] As a consequence, lipotoxicity may occur and lead to hepatic, pancreatic, or muscular comorbidities as well as metabolic syndrome.[23] Food timing may influence the metabolic response to feeding independent of the food composition.[24]

The Influence of Circadian Clocks on Peripheral Tissues

The expression of approximately 5-15% of mammalian genes have circadian oscillation driven by a molecular mechanism involving transcriptional and translational feedback loops.[22, 25] These feedback loops generate the basic rhythm driving gene expression.[22] However, in more than one tissue, relatively few genes share the same circadian expression profile.[22] These genes include those responsible for basic cell metabolism.[22] Because these genes share a common network, any upstream change in expression can significantly alter downstream elements of the same pathway.[22] Glycogen synthase 2 (GYS), lipoprotein lipase (LPL), peroxisome proliferator activated receptor gamma coactivators alpha and beta (PGC1a, PGC1b), 6-phosphofructo-2 kinase/fructose 2,6 bisphosphatase 3 (PFKFB3), and pyruvate dehydrogenase kinase isozyme 4 (PDK4) were all found to follow a daily oscillatory pattern in the liver.[22]

Adipose tissue also exhibits rhythmic clock gene expression in mice and humans.[26] In rat studies, diurnal variation in lipolysis rates and release of free fatty acids and glycerol into the blood correlate with rhythmic regulation of two genes encoding the lipolysis pacemaker enzymes, adipose triglyceride lipase (ATGL) and hormone-sensitive lipase (HSL).[26] Circadian clock$^{\Delta 19}$ mutant mice, which exhibit a long circadian period (28 hours) had low and nonrhythmic glycerol and free fatty acid blood content.[26] This indicates decreased lipolysis rates and increased sensitivity to fasting.[26] Mice with circadian disruption had an accumulation of triglycerides in white adipose tissue due to down-regulation of ATGL and HSL.[26] This leads to increased adiposity and adipocyte hypertrophy.[26] Furthermore, impaired clock gene expression in humans may lead to an imbalance in energy homeostasis, increased adiposity and development of obesity through these mechanisms.

Chronotype and Social Jetlag and Metabolism

Evening chronotypes have reported to have more health and behavioral problems compared to morning types.[14] Evening types are more likely to suffer from shorter sleep durations because they sleep later in the night but need to wake up earlier than their biological morning due to social influences.[14] Short sleep duration is a risk factor for obesity and poor glycemic control.[14,27]

Donga et al. found that a single night of restricted sleep resulted in a 22% increase in endogenous glucose production, indicating hepatic insulin resistance.[27] The rate of glucose disposal also decreased by approximately 20%, suggesting a decrease in peripheral insulin sensitivity.[27] In addition, plasma non-essential fatty acid levels increased by 19%, suggesting increased lipolysis.[27]

Independent of sleep duration, the evening chronotype is associated with significantly higher triglyceride levels, higher total body fat mass, and exaggerated inflammatory responses indicated by high C-reactive protein levels.[14] Yu et al. found that male evening types also tend to be associated with lower total body lean mass. The odds of having sarcopenia was 3.89 times higher in male evening types compared to male morning types.[14] Muscle tissue plays an important role in glucose regulation.[14] Therefore, sarcopenia is closely associated with adverse glucose metabolism and insulin resistance, resulting in higher fasting blood glucose.[14]

Yu et al. found that the odds of having diabetes was 2.98 times higher in male evening types compared to male morning types.[14] Pancreatic alpha cells normally secrete glucagon in response to low blood glucose.[7,28] Glucagon is tightly regulated by the behavioral cycle and is proportionately increased during biological night time food intake.[7] This is because pancreatic alpha cells also express MT_1, a melatonin receptor that facilitates glucagon secretion.[7] Melatonin levels are highest during the biological night.[7] Therefore, there is increased glucagon secretion in response to night time food intake.[7] Excess glucagon can lead to dysregulated glucose metabolism and contributes to insulin resistance.[7]

Chronotype and social jetlag may be associated with the development of metabolic syndrome. Metabolic syndrome is diagnosed based on the presence of having any three of the following criteria: abdominal obesity (men >102 cm; women >88 cm), triglyceride level ≥150 mg/dL, low HDL cholesterol (HDL-C) (men <40 mg/dL; women <50 mg/dL), high blood pressure ≥130/85 mmHg, and high fasting blood glucose ≥ 110 mg/dL.[29] In women, the odds of having metabolic syndrome were found to be 2.22 times higher in evening types compared to morning types.[14] Higher waist circumference, triglyceride and c-reactive protein levels, and total body fat (visceral and subcutaneous) were also observed in late chronotype females compared to other chronotypes.[14] Individuals with prediabetes and late chronotype were found to have higher triglycerides and hemoglobin A1c (HbA1c) levels after controlling for age, sex, BMI, alcohol use, sleep quality/duration, and social jetlag.[13] These findings may be attributed to decreased leptin levels, resulting in increased appetite, decreased energy expenditure, decreased insulin sensitivity and increased inflammation.[14]

Studies on social jetlag had similar findings, even after taking into account chronotype and sleep duration. Data suggest that there is a dose response between social jetlag and overweight phenotypes and metabolic dysfunction.[10] Participants with greater social jetlag scores were 1.3 times as likely to meet criteria for metabolic syndrome compared to participants with low, or no social jetlag.[10] Therefore, late chronotype and high social jetlag appear to increase risk of poor health outcomes such as obesity, metabolic syndrome. The relationship between chronotype and social jetlag and diet quality, quantified by HEI score, has not been reported.

Healthy Eating Index Score

The Healthy Eating Index (HEI) assesses dietary quality based on how close a set of foods align with the Dietary Guidelines for Americans (DGA).[11] Every 5 years, the DGA are updated, with an updated HEI reflective of those changes.[11,30] HEI-2015 is the most recently published index which includes 13 components (see Table 1).[11, 30] There are two categories of components, adequacy components and moderation components.[11] Adequacy components are food groups, subgroups and dietary elements that are encouraged.[11] Higher intakes of adequacy components are reflected in higher scores.[11] Moderation components are food groups and dietary elements that have recommended intake limits.[11] Higher intakes of moderation components are reflected in lower scores.[11] The total HEI is the sum of the 13 individual food component score and can be used as a measure of how closely the dietary intake follows the DGAs.[11] A key feature is that HEI scores reflect diet quality, not diet quantity by measuring nutrient density.[11] This is achieved by calculating the components as a food group amount per 1,000 calories in the total mix of foods.[11] Fatty acids are scored as a ratio of unsaturated to saturated fatty acids.[11] Scores have been used to examine prospective and cross- sectional associations between diet quality and health outcomes.[30]

Descending HEI scores have a graded increase in likelihood of obesity in men and women.[31] Men classified as having a poor diet (HEI <50) are twice as likely to have obesity compared to men classified as having a good diet (HEI >81).[31] Circadian misalignment and late chronotype is also a risk factor for obesity and can potentially influence HEI score due to unhealthy eating patterns such as binge-eating disorder, night-eating disorder, food addiction, and higher intakes of meat and sweets.[16,18,20]

Table 1. HEI-2015 Components and Scoring Standards

Component	Maximum Points	Standard for Maximum score	Standard for Minimum score of Zero
Adequacy:			
Total Fruits[1]	5	≥0.8 cup equivalent per 1,000 kcal	No Fruits
Whole Fruits[2]	5	≥0.4 cup equivalent per 1,000 kcal	No Whole Fruit
Total Vegetables[3]	5	≥1.1 cup equivalent per 1,000 kcal	No Vegetables
Greens and Beans[3]	5	≥0.2 cup equivalent per 1,000 kcal	No Dark Green Vegetables or Legumes
Whole Grains	10	≥1.5 ounce equivalent per 1,000 kcal	No Whole Grains
Dairy[4]	10	≥1.3 cup equivalent per 1,000 kcal	No Dairy
Total Protein Foods[3]	5	≥2.5 ounce equivalent per 1,000 kcal	No Protein Foods
Seafood and Plant Proteins[3,5]	5	≥0.8 ounce equivalent per 1,000 kcal	No Seafood or Plant Proteins
Fatty Acids[6]	10	(PUFAs + MUFAs)/ SFA ≥2 .5	(PUFAs + MUFAs)/ SFA ≤1.2
Moderation:			
Refined Grains	10	≤1.8 ounce equivalent per 1,000 kcal	≥4.3 ounce equivalent per 1,000 kcal
Sodium	10	≤1.1 grams per 1,000 kcal	≥2.0 grams per 1,000 kcal
Added Sugars	10	≤6.5% of energy	≥26% of energy
Saturated Fats	10	≤8% of energy	≥16% of energy

[1] Includes 100% fruit juice
[2] Includes all forms except juice
[3] Includes legumes (beans and peas)
[4] Includes all milk products, such as fluid milk, yogurt, and cheese, and fortified soy beverages
[5] Includes seafood; nuts, seeds, soy products (other than beverages), and legumes (beans and peas)
[6] Ratio of poly- and mono-unsaturated fatty acids (PUFAs and MUFAs) to saturated fatty acids (SFAs)

Previous studies have documented the effects of social jetlag and chronotype on health. However, the effect of social jetlag and chronotype on HEI score has not been addressed. It is clear that circadian misalignment influences dietary intake and nutrient metabolism. Therefore, this study was designed to determine how social jetlag and chronotype influence HEI score and body composition.

Chapter 3: Materials and Methods

The study dataset included participants from the 2017-2018 National Health and Nutrition Examination Survey (NHANES). NHANES data are released every two years and are collected continuously using stratified multistage cluster sampling probability design.[32] Participants are interviewed for general health, demographic, socioeconomic information. The questions were asked at the Mobile Examination Center (MEC), by trained interviewers, using the Computer-Assisted Personal Interview (CAPI) system.[32] Participants subsequently receive a comprehensive health examination conducted at the mobile examination center.[32] The Research Ethics Review Board of the National Center for Health Statistics approved the NHANES study protocol and all participants provided written informed consent.[32] We excluded participants under 19 years of age or over 65 years of age; those who had incomplete sleep, body composition, or dietary data; those with implausible total energy intake (10 kcal/kg/day) and shift-workers. After exclusions, a total of 2,785 participants remained in the analysis.

Sleep Variable – Chronotype

The responses to the following NHANES questions were used to determine chronotype by the equation listed below: 1) “What time do you usually fall asleep on weekdays or workdays?”, 2) “What time do you usually wake up on weekdays or workdays?”, 3) “What time do you usually fall asleep on weekends or non-workdays?”, 4) “What time do you usually wake up on weekends or non-workdays?” and 5) number of hours usually slept on weekdays /workdays and the 6) number of hours usually slept on weekends or non-workdays:

Mid-sleep time on free days on the weekend (MSF)= (sleep onset + sleep duration)/2

Sleep-debt corrected MSF (MSF_{sc})= MSF – (sleep duration on free days – average weekly sleep duration)/2

Sleep Variable – Social Jetlag

The responses to the following NHANES questions were used to determine social jetlag, or the midpoint difference between weekday and weekend sleep cycles: 1) “What time do you usually fall asleep on weekdays or workdays?”, 2) “What time do you usually wake up on weekdays or workdays”, 3) “What time do you usually fall asleep on weekends or non-workdays”, and 4) “What time do you usually wake up on weekends or non-workdays”

Dietary Variable – Total Caloric Intake

The response to Total Nutrient Intakes from the NHANES Dietary Recall Interview on day one and day two was averaged to determine the average caloric intake of each subject. Total caloric intake was standardized by assessing calories per kilogram of the participants body weight. Body weight in kilograms was obtained from the NHANES comprehensive health examination physical exam datafile.

Dietary Variable – Healthy Eating Index

To calculate HEI score, the nutrient data files from the NHANES Dietary Recall Interview (for both days of recall) were merged with the Food Patterns Equivalents Database. Intake of various food components of the HEI score were normalized per 1000 kcals. Scores for each of the 13 categories were calculated based on the HEI-2015 USDA guidelines. See scoring guidelines in Table 1. Total HEI was created by summing the 13 components. For each subject, an average HEI for the 2 days of recall was used in the analysis. HEI calculations were performed in JMP version 12.0 (SAS, Cary, NC).

Body Composition Variable – Waist to Hip Ratio

Waist to hip ratio was calculated by dividing waist circumference (cm) by hip circumference (cm). Waist circumference and hip circumference data was obtained from NHANES comprehensive health examination physical exam datafile.

Statistics

Analyses used Stata/IC 16.1(StataCorp; College Station, TX, USA). Mean and standard deviation for demographic variables were determined for the overall population for all adults (males and females) and males/females separately. T-tests were performed to assess if there was a significant difference between males and females. Descriptive statistics included mean, standard deviation and 95% confidence intervals. The distribution of the data was assessed for normality. A log transformation was performed on total calorie intake (kcal/kg) to normalize data. Continuous variables ratio of family income to poverty and minutes of sedentary activity were recoded to categorical variables. Missing data indicators were created for smoking status, education, ratio of family income to poverty and minutes of sedentary activity variables to account for the missing values in those particular variables in each linear regression model.

A simple linear regression was used to determine the association between chronotype and social jetlag to assess for co-linearity between out 2 primary predictors. The variables were not colinear. A multiple linear regression analysis was conducted to assess the association between HEI score and chronotype, social jetlag, age, gender, education, ratio of family income to poverty, depression, and smoking status. A multiple linear regression analysis was also used to assess the association between total calorie intake (kcal/kg) and chronotype, social jetlag, age, gender, education, ratio of family income to poverty, depression, smoking status, race and BMI. An additional multiple linear regression analysis was used to assess the association between waist to hip ratio and chronotype, social jetlag, age, gender, education, ratio of family income to poverty, depression, smoking status, race, and sedentary activity. Reduced models were conducted after excluding insignificant variables in each initial model. A *p*-value of <0.05 was considered statistically significant.

Figures and figure analyses used Prism 9.1.2 (GraphPad Software, LLC.). The Pearson correlation coefficient was used to measure the linear correlation between a primary predictive variables and the outcome. A one-way ANOVA test with Fisher's exact post-hoc analysis was performed to compare the variance categorical variables such as smoking and race and the outcome variable.

Table 2. National Health and Examination Survey (NHANES) Variables

Type of Data	Variable Name	SAS Label
Sleep Disorders Questionnaire	SLQ300	Usual sleep time on weekdays or workdays
	SLQ310	Usual wake time on weekdays or workdays
	SLQ320	Usual sleep time on weekends
	SLQ330	Usual wake time on weekends
	SLD012	Sleep hours- weekdays or workdays
	SLD013	Sleep hours- weekends
Dietary Interview	DS1TKCAL	First day energy (kcal)
	DS2IKCAL	Second day energy (kcal)
Body Measures	BMXWT	Weight (kg)
	BMXBMI	Body Mass Index (kg/m^2)
	BMXHIP	Hip circumference (cm)
	BMXWAIST	Waist circumference (cm)
Physical Activity	PAD680	Minutes of sedentary activity
Smoking Questionnaire	SMQ040	Do you now smoke cigarettes?
Depression Questionnaire	DPQ010	Have little interest in doing things
	DPQ020	Feeling down, depressed, or hopeless
	DPQ030	Trouble sleeping or sleeping too much
	DPQ040	Feeling tired or having little energy
	DPQ050	Poor appetite or overeating
Demographic Variables	RIAGENDR	Gender
	RIDAGEYR	Age in years at screening
	RIDRETH1	Race/Hispanic origin with non-hispanic asian
	DMDEDUC2	Education level- Adults 20+
	RIDEXPRG	Pregnancy status at exam
	INDFMIN2	Total annual family income or annual individual income
	INDFMPIR	Ratio of family income to poverty

SMQ040 Do you now smoke cigarettes was coded as 1 (every day), 2 (some days), or 3 (not at all)

DPQ010-DPQ050 was coded as 0 (not at all), 1 (several days), 2 (more than half the days), 3 (nearly every day)
Depression was assessed as the sum of the variables

DMDEDUC2 was coded as 1 (less than 9th grade), 2 (9th-11th grade), 3 (high school graduate/GED), 4 (some college/associates), 5 (college graduate or above)

Chapter 4: Results

Patient demographics

The demographics of the study participants are summarized in Table 2. The average age of the participants was 44 years, with slightly more females than males (52% vs. 48%). About one-third of the participants were Non-Hispanic White, while Non-Hispanic Black, Mexican American, Non-Hispanic Asian, Other Hispanic, and Other Race/Multi-racial represented about 25%, 15%, 14%. 10%, and 6%, respectively. Females had a significantly higher average BMI and HEI score, while males had a significantly higher average waist circumference, calories per kilogram (kcal/kg), total energy intake, and later chronotype.

Table 3. Characteristics of Study Participants

	All (n=2,875)	Male (n=1380)	Female (n=1495)
Characteristic	**mean (SD)**	**mean (SD)**	**mean (SD)**
Age (years)	44.0 (14.0)	44 (14.0)	43 (14)
Body Mass Index (kg/m^2)	29.6 (7.1)	29.3 (6.3)*	29.9 (7.6)
Waist Circumference (cm)	99.4 (17.2)	101.3 (16.7)*	97.5 (17.3)
Waist:Hip Ratio	0.9 (0.1)	1.0 (0.1)	0.9 (0.1)
Total Energy (kcal/day)	2128 (844.6)	2448.1 (926.7)*	1832.5 (630.7)
Kcal/kg	26.8 (12.0)	28.8 (13.2)*	25.0 (10.5)
Chronotype (clock time)	3:24 am (1 hour 42 minutes)	3:30am (1 hour 48 minutes)*	3:18 am (1 hour 42 minutes)
Social Jetlag (hours)	1.0 (1.3)	1.0 (.04)	1.0 (.03)
Healthy Eating Index Score (0-100)	55 (11.0)	54.4 (11.5)*	56.6 (11.4)
Smoking Status	***n (%)***		***n (%)***
Everyday	437 (39.9)	257 (39.5)	180 (40.4)
Some Days	109 (9.9)	72 (11.1)	37 (8.3)
Not At All	550 (50.2)	321 (49.4)	229 (51.4)
Race			
Mexican American	425 (14.8)	203 (14.7)	222 (14.9)
Other Hispanic	279 (9.7)	125 (9.1)	154 (10.3)
Non-Hispanic White	891 (31.0)	434 (31.5)	457 (30.6)
Non-Hispanic Black	708 (24.6)	327 (23.7)	381 (25.5)
Non-Hispanic Asian	415 (14.4)	209 (15.1)	206 (13.8)
Other Race/Multi-Racial	157 (5.5)	82 (5.9)	75 (5.0)

Results are expressed as mean ± standard deviation of the mean (SD). For each characteristic, groups were compared using an independent two-sample t test.* denotes a significant difference ($p < 0.05$) between males and females.

Healthy Eating Index

Social jetlag, but not chronotype, was associated with HEI score (Table 5. Model 1 & 2). Every 0.52 hour (31 minute) decrease in social jetlag was associated with a one-point increase in

HEI score (p<0.001). Age, gender, ratio of family income to poverty, depression, and smoking status were also associated with HEI. Figure 1 illustrates the four strongest correlations with HEI score. Age followed by smoking status had the strongest association with HEI score. There was a weak positive linear relationship (Pearson r = 0.18) between age and HEI score suggesting older participants had higher HEI scores (Figure 1a). Current smokers that reported smoking every day had a lower HEI score compared to participants who reported not smoking at all (Figure 1d). Males had lower HEI scores than females, 54.4 (95%CI: 53.8-55.0) and 56.5 (95%CI: 55.9 to 57.1), respectively (Table 4). A .31 increase in ratio of family income to poverty was associated with a 1-point increase in HEI score (Table 5. Model 2). Depression severity score was inversely related to HEI; a .42-point decrease in depression score was associated with a 1-point increase in HEI score (Figure 1c).

Table 4. Average Total HEI Score Multiple Linear Regression Model

		Model 1 (n=2,875)			**Model 2 (n=2,875)**	
	Coef.	**95% CI**	**p>|t|**	**Coef.**	**95% CI**	**p>|t|**
Variables						
Age (years)	0.1457	(0.1139, 0.1775)	0.000	0.1593	(0.1299, 0.1887)	0.000
Gender	1.8141	(0.9964, 2.6319)	0.000	1.8719	(1.0559, 2.6879)	0.000
Education	-0.0228	(-0.0483 , 0.0027)	0.080			
Ratio of Family Income to Poverty	0.3061	(0.1286, 0.4837)	0.001	0.3128	(0.1353, 0.4903)	0.001
Depression	-0.4788	(-0.6139 , -0.3437)	0.000	-0.4152	(-0.6004, -0.2299)	0.000
Smoking Status	0.5618	(0.4389, 0.6847)	0.000	0.5560	(0.4337, 0.6784)	0.000
Chronotype (clock time)	-0.1676	(-0.4367, 0.1016)	0.222			
Social Jetlag (hours)	-0.4639	(-0.7782, -0.1496)	0.004	-0.5199	(-0.8220, -0.2178)	0.001

Model 1 used a multiple linear regression model with all variables. Model 2 removed insignificant variables. A p<0.05 was considered statistically significant.

Figure 3

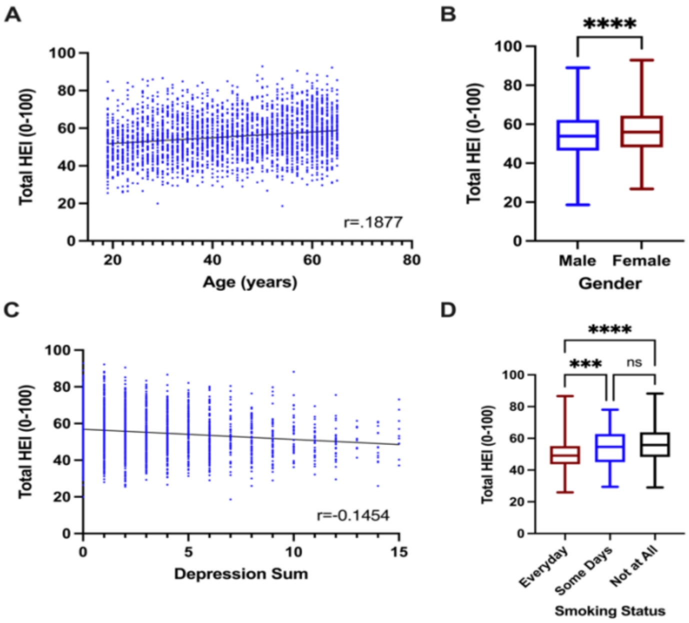


Figure 3. A) scatterplot of average total HEI score and age B) boxplot of average total HEI score and gender. Statistical analysis with unpaired t-test. **** denotes p<0.0001. C) scatterplot of average total HEI score and smoking status D) boxplot of average total HEI score and smoking status. Statistical analysis with one-way ANOVA and post-hoc analysis. **** denotes P<0.0001. *** denotes P<0.0003.

Total Energy Intake

Social jetlag, but not chronotype, was associated with total energy intake adjusted by body weight (kcal/kg; Table 6. Model 1 & 2). Every .02 hour (1.2 minute) increase in social jetlag was associated with an increase of 1 kcal/kg in total energy intake ($p<0.008$) suggesting a weak association between social jetlag and energy intake. Age, gender, education, race, and BMI were also associated with total energy intake. BMI had a strong inverse association with energy intake; a 0.89 reduction in BMI was associated with a 1 kcal/kg increase in energy intake. Males consumed greater calories per kilogram of body weight compared to females, 28.8 kcal/kg (95%CI: 28.1 to 29.5) and 25.0 kcal/kg (95%CI: 24.5-25.5), respectively (Table 4). A lower education level was also associated with increased calorie intake per kilogram of body weight ($p<0.003$).

Table 5. Total Energy Intake (kcal/kg) Multiple Linear Regression Model

	Model 1 (n=2,875)			Model 2 (n=2,875)		
	Coef.	95% CI	p>|t|	Coef.	95% CI	p>|t|
Variables						
Age (years)	-0.0017	(-0.0028, -0.0007)	0.001	-0.0019	(-0.0029, -0.0009)	0.000
Gender	-0.1187	(-0.1445, -0.0988)	0.000	-0.1234	(-0.1488, -0.0980)	0.000
Education	-0.0012	(-0.0020, -0.0004)	0.003	-0.0012	(-0.0020, -0.0004)	0.003
Ratio of Family Income to Poverty	-0.0025	(-0.0081, 0.0032)	0.388			
Smoking Status	-0.0030	(-0.0069, 0.0008)	0.125			
Race	-0.0166	(-0.0242, -0.0089)	0.000	-0.0163	(-0.0239, -0.0088)	0.000
BMI (kg/m^2)	-0.8833	(-0.9396, -0.8270)	0.000	-0.8851	(-0.9414, -0.8288)	0.000
Chronotype (clock time)	0.0064	(-0.0022, 0.0150)	0.144			
Social Jetlag (hours)	0.0181	(0.0081, 0.0282)	0.000	0.0200	(0.0104, 0.0297)	0.000

Model 1 used a multiple linear regression model with all variables. Model 2 removed insignificant variables. A $p<0.05$ was considered statistically significant.

Body composition

Chronotype, but not social jetlag, was associated with waist to hip ratio (Table 7. Model 1 & 2). An earlier chronotype was associated with a higher waist to hip ratio. A 10-second earlier chronotype was associated with a one unit increase in waist to hip ratio. Age, gender, education, ratio of family income to poverty, depression, smoking status and race were also associated waist to hip ratio. Gender followed by age had the strongest association with waist to hip ratio. Males had a greater waist to hip ratio compared to females, 1.0 (95%CI: 0.96-0.97) and 0.9 (95%CI: 0.89-0.96), respectively (Table 4). There was a positive association between age and depression severity and waist to hip ratio. More frequent smokers were associated with a higher waist to hip ratio. A lower education level and ratio of family income to poverty was correlated with a higher waist to hip ratio. Multiple linear regressions were performed with BMI as the body composition variable. Our data showed that social jetlag and chronotype accounted for less variability in BMI compared to waist to hip ratio.

Table 6. Waist to Hip Ratio Multiple Linear Regression Model

	Coef.	Model 1 (n=2,875) 95% CI	p>|t|	Coef.	Model 2 (n=2,875) 95% CI	p>|t|
Variables						
Age (years)	0.0018	(0.0016- 0.0020)	0.000	0.0018	(0.0016, 0.0020)	0.000
Gender	-0.0712	(-0.0762, -0.0661)	0.000	-0.0711	(-0.0761, -0.0661)	0.000
Education	-0.0002	(-0.0003, 0.0000)	0.017	-0.0002	(-0.0003, -0.0000)	0.018
Ratio of Family Income to Poverty	-0.0017	(-0.0028, -0.0006)	0.003	-0.0016	(-0.0027, -0.0006)	0.003
Depression	0.0023	(0.0015, 0.0031)	0.000	0.0023	(0.0015, 0.0031)	0.000
Smoking Status	-0.0017	(-0.0024, -0.0009)	0.000	-0.0013	(-0.0024, -0.0009)	0.000
Race	-0.0047	(-0.0062, -0.0032)	0.000	-0.0048	(-0.0062, -0.0033)	0.000
Sedentary Activity (minutes)	2.15E-06	(-1.64e-06, 5.94e-06)	0.266			
Chronotype (clock time)	-0.0031	(-0.0048, -0.0014)	0.000	-0.0028	(-0.0044, -0.0012)	0.000
Social Jetlag (hours)	0.0008	(-0.0011, 0.0027)	0.421			

Model 1 used a multiple linear regression model with all variables. Model 2 removed insignificant variables. A p<0.05 was considered statistically significant.

Figure 4

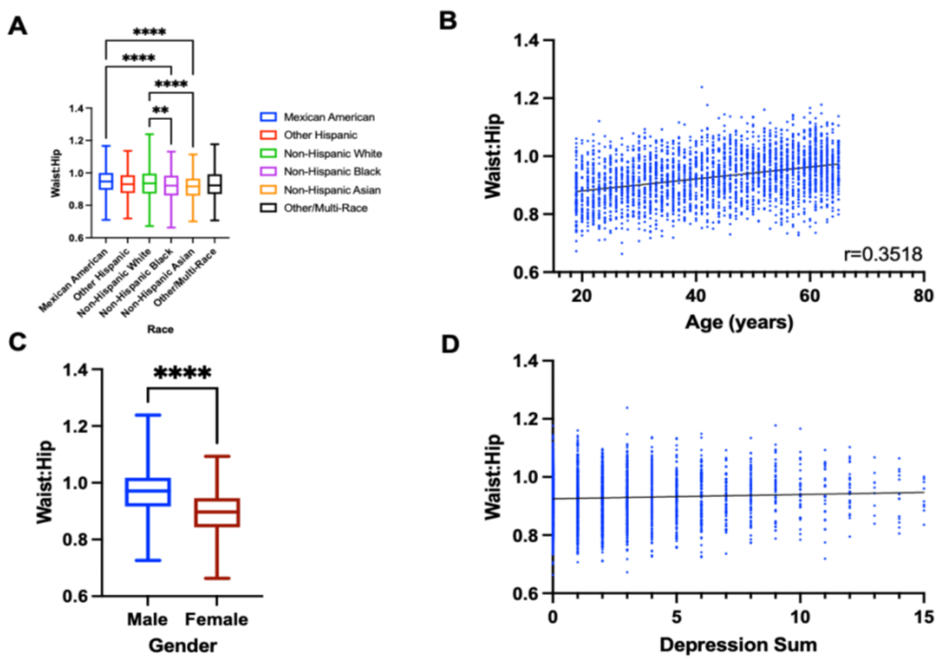


Figure 4. A) boxplot of waist to hip ratio and race. Statistical analysis with one-way ANOVA and post-hoc analysis. ** denotes p<0.0049. **** denotes p<0.0001 B) scatterplot of waist to hip ratio and age C) boxplot of waist to hip ratio and age. Statistical analysis with unpaired t-test. **** denotes p<0.0001. D) scatterplot of waist to hip ratio and depression sum.

Chapter 5: Discussion

In this cross-sectional study of NHANES 2017-2018 data, we found that higher social jetlag was associated with a lower HEI score and higher total energy intake adjusted by body weight (kcal/kg). These results align with existing literature that show that circadian misalignment is associated with increased postprandial active ghrelin levels and an increased appetite for energy-dense foods including sweets, salty food, dairy, and meat and lower intake of fruits and vegetables.[18, 33] Social jetlag can also result in sleep restriction, primarily during the weekday. Sleep restriction is associated with an increase in 188-468 calories from snacks, primarily carbohydrates.[19] The strongest correlation between HEI score was smoking status; everyday smokers had a significantly lower HEI score compared to some day smokers and non-smokers. This is consistent with previous research suggesting individuals with higher social jetlag were more likely to smoke. [34]

In contrast, earlier chronotype but not social jetlag was associated with waist to hip ratio. Social jetlag appears to be associated with diet quality and energy intake while chronotype appears to be associated with body shape. Differences in diet quality and quantity may be explained by circadian disruption, or the discrepancy between our internal clock and our external environment rather than chronotype, while chronotype may explain some features of body composition. These factors however are not completely independent; social jetlag is typically higher in late chronotypes. [5]

We observed that an earlier chronotype was associated with a higher waist to hip ratio which is inconsistent with current existing literature showing that a late chronotype is associated with a greater waist circumference. The reason our results differ from some previous literature is unknown but one potential explanation may be eating at inappropriate endogenous circadian times. Early chronotypes have an earlier biological night and therefore an earlier dim-light melatonin onset (DLMO; the time in which melatonin levels rise).[7] Eating dinner or snacking closer to or after DLMO produces a smaller thermic effect of food which could contribute to positive energy balance and higher body fat percentage associated with a higher waist to hip ratio. [7,15] In addition, peak lateness in chronotype is reached at age 18.4 years in females and 19.2 years in males with a sharp turn from increasingly later to increasingly earlier chronotype with advancing age.[35] Central adiposity also increases with age.[36] Therefore, older individuals with an earlier chronotype and greater central adiposity may be driving the association we observed.

One limitation to this analysis is that the retrospective study design only provides correlational data between sleep patterns and health parameters, and odds ratios were not calculated. In addition, sleep and dietary data were self-reported and are limited by participant recall, under-reporting of energy intakes, and perceptions of sleep patterns on the day of questionnaire administration. Our data showed that people with a higher BMI consumed less calories per kilogram of body weight. This association may be related to underreporting of food intake, especially from individuals with a higher BMI.[37]

The study findings aligned with our hypothesis that a higher social jetlag is associated with a lower HEI score and greater caloric intake. The study findings did not support our hypothesis that late chronotype is associated with a lower HEI score and increased energy intake. We observed that an earlier chronotype was associated with a higher waist to hip ratio which was the opposite of our hypothesized correlation. This association may be attributed to mistimed food intake. In addition, there was no relationship between social jetlag and body composition. NHANES added weekend or non-workday sleep data on the 2017-2018 cycle.

Additional research analyzing chronotype and social jetlag that includes future NHANES cycles could increase the power of data by increasing the number of participants.

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