THE PENNSYLVANIA STATE UNIVERSITY
SCHREYER HONORS COLLEGE

DEPARTMENT OF BIOBEHAVIORAL HEALTH

ASSOCIATION OF HABITUAL SLEEP VARIABLITY WITH ABDOMINAL OBESITY IN ADOLESCENTS

LUCIA LIAO
SPRING 2015

A thesis
submitted in partial fulfillment
of the requirements
for a baccalaureate degree in Science
with honors in Biobehavioral Health

Reviewed and approved* by the following:

Duanping Liao
Professor and Chief of Epidemiology
Thesis Supervisor

David Vandenbergh
Associate Professor of Biobehavioral Health
Honors Adviser

Lori Francis
Associate Professor of Biobehavioral Health
Faculty Reader

* Signatures are on file in the Schreyer Honors College.

ABSTRACT

Poor sleep habits have often been considered a risk factor for obesity. The present study investigates the association between habitual sleep variability (HSV) and abdominal obesity in a population-based sample of adolescents. The study further examines the potential mediating role of physical activity and nutritional intake in the relationship between HSV and abdominal obesity.

The study population consists of 304 adolescents who participated in the Penn State Child Cohort follow-up examination. HSV was calculated using actigraph-measured sleep duration on 7 consecutive nights. Dual-energy x-ray absorptiometry (DEXA) was used to determine abdominal obesity measurements, including android/gynoid ratio (AGR waist/hip ratio), android/whole body proportion (AWP), gynoid/whole body proportion (GWP), subcutaneous fat (SAT), visceral fat (VAT), and total fat (TAT) areas. Actigraph recordings over the course of one week were used to measure physical activity. The study used the Youth/Adolescent Food Frequency Questionnaire to obtain nutritional profiles.

After adjusting for major confounders and habitual sleep duration, linear regression models showed a highly significant association between HSV and multiple abdominal obesity measures. With a 1-hour increase in HSV, TAT and VAT increased by 32.5 (12.1) cm^2 and 6.85 (2.82) cm^2 respectively. Mediation models showed that nutritional intake is a weak mediator between HSV and abdominal obesity association, whereas physical activity is not a mediator.

In conclusion, this study achieves a better understanding of childhood obesity, a leading risk factor in early death and heart disease, by providing insight into the mechanism between

sleep variability and obesity in adolescents. The results suggest that the mechanism between HSV and abdominal obesity can be partially explained by higher food intake but not by lower physical activity.

TABLE OF CONTENTS

LIST OF TABLES

ACKNOWLEDGEMENTS

I would like to extend a sincere thank you to Dr. Duanping Liao for so kindly allowing me to work on his project. He has been an exceptional mentor and I'm very grateful for his support of my college career these past 3 years. I would like to acknowledge Fan He who so generously dedicated his time and efforts to guide me through this project. I cannot explain how grateful I am for every helpful email he has sent me. I could not have done it without your insight and kindness.

I would also like to thank Drs. Lori Francis and David Vandenbergh for generously supporting me on this project as my honors advisors.

Introduction

The obesity epidemic is the most well-known public health burden in the United States. In 2007 to 2008, 32% of US children and adolescents were classified as overweight or obese (1). It is more alarming that the prevalence of pediatric obesity in the United States has risen dramatically in the last three decades. Specifically, the amount of overweight children has doubled and the number of obese children has tripled in the United States (2). Comorbidities associated with being overweight are similar in both children and adults. Obesity is frequently associated with increased risk of death, dyslipidemia, type 2 diabetes, elevated blood pressure, and certain cancers (2-3). Moreover, longitudinal studies have shown that over half of obese school age children, particularly adolescents remain obese into their adult years (4). Mortality and morbidity are increased in the adult population if these individuals were overweight during adolescence, regardless if they lose extra weight in adulthood (4-5). The current obesity epidemic necessitates the understanding of lifestyle behaviors and prevention measures that can influence obesity.

This obesity rise in the past 30 years coincides with a decline in the sleep duration of both children and adults (6-7). According to a survey by the U.S. Centers for Disease Control and Prevention (CDC), 35.9% of adults reported an average of less than 7 hours of sleep in 2009, in contrast to 29% in the 2004-2006 National Health Interview Survey (8-9). Recent studies have shown that children have self-reported an average nightly sleep duration of 9.5 hours (10-11), which is below expert recommendations of 10-11 hours a night (12). Many studies have found short sleep duration to be positively associated with BMI in participants of all ages (13-18) and

with increased food consumption and cravings (19-20). It has been suggested that insufficient sleep duration results in increased ghrelin and decreased circulating leptin, which promote hunger and food intake (21-22). However, the majority of these studies used self-reported sleep duration measurements (13-16), which may be confounded by reporting error, sleep disturbance, and emotional distress rather than represent actual sleep loss (23-24). Fewer studies have used actigraph-measured sleep duration (12-13).

Night-to-night sleep variability, rather than sleep duration, has been increasingly reported to predict general obesity (6-8, 25-28). Patel and coworkers found that each 1-hour increase in irregularity of sleep duration increased the odds of BMI-measured obesity 1.63-fold (25). Studies with similar results have hypothesized that HSV (habitual sleep variability) and obesity are associated via physical activity and nutritional intake (25-27). It has been suggested that children with more variable sleep patterns were subject to more hectic households with poorer dietary habits, less regular mealtimes and fewer opportunities to exercise (26). Researchers have hypothesized that increased HSV primarily resulted from children catching up on sleep during weekends, which consequently lowered their physical activity during weekends (25). According to a study, weekend-weekday sleep irregularity leads to overall decrease in physical activity in adolescents (27).

Although much attention has been directed to general obesity, much fewer studies have focused on abdominal adipose tissue distribution. A meta-analysis of data from over 88,000 individuals determined that abdominal obesity is a better discriminator of cardiovascular disease and diabetes risk than body mass index (BMI) (29-30). Therefore, I carried out this present study to investigate the independent relationship between HSV and abdominal obesity. I further

investigated the potential mediating role of nutritional intake and physical activity in the association between HSV and abdominal obesity.

Methods

Study Population

This study used data from 421 adolescents who completed the longitudinal Penn State Child Cohort study (PSCC). All participants in the baseline study were recruited from Dauphin County, Central Pennsylvania and examined at the Clinical Research Center at Penn State College of Medicine. Recruitment and examination methods for the PSCC baseline study have been reported elsewhere (31-32). Out of the 700 subjects in the baseline study, 421 returned to complete the follow-up examination between 2010-2013 with a response rate of 60%. The follow-up exam was completed an average of 7.70 years after the baseline exam. Loss of follow-up subjects occurred primarily due to subjects moving out of the central Pennsylvania area. However, no major difference was found in the demographic characteristics between participants who continued the study and those who did not. Dual-energy x-ray absorptiometry scan was used to measure participants' abdominal obesity, and afterwards, participants were connected to Holter monitors to measure beat-to-beat ECG for 39 hours. Complete physical examinations and neuropsychological tests were performed on the participants. Participants were held overnight on day 1 and underwent a 9-hour polysomngraphy from 10 PM on day-1 to 7 AM on day-2. After the participants returned home from the sleep lab, they wore actigraphs for 7 days to measure physical activity. After day-8, the Holter monitor, nutrition questionnaires, and actigraph were

collected from subjects. This study protocol was approved by the Penn State University College of Medicine Institutional Review Board 98-228. Written informed consents were obtained from participants and parents or legal guardians if the subject was under age 18.

Sleep variables

Subjects wore actigraphs on the wrist of their non-dominant hand during bedtime to objectively measure their sleep duration. Participants also self-documented their bed time and waking time every night. Habitual sleep duration (HSD) and HSV were calculated based on actigraph data and verified using the subjects' daily sleep logs. HSD was calculated as the average of their sleep duration for the seven consecutive nights after they left the sleep lab, i.e. Night-2 to Night-8. HSV was determined by taking the standard deviation of their sleep duration across the seven days. 94 participants, who had less than 5 nights of documented sleep data, were removed from the sample set.

Abdominal Obesity Variables

Subjects underwent whole-body DXA scans using Hologic Discovery W scanner (Hologic Inc., Walthma, MA) to measure adipose tissue distribution in the abdominal region. With the participant lying in a supine position, a constant X-ray source with 2 main energy peaks was passed through the subject's body tissue. The ratio of the attenuation at the lower energy beam relative to the attenuation of the higher energy beam was used to define fat-free and fat tissue areas (33). Android region, gynoid region, visceral adipose tissue (VAT), and subcutaneous adipose tissue (SAT) were selected as regions of interests (ROI) and identified by

Hologic APEX 4.0 software (Hologic Inc., Bedford, MA). An experienced investigator visually verified all ROIs. Total fat area in the abdominal region (TAT) was calculated as the sum of VAT and SAT areas. Android/gynoid fat mass ratio (AGR), android/whole body fat mass proportion (AWP), gynoid/whole body fat mass proportion (GWP), VAT, SAT, and TAT areas were used as abdominal obesity measures in this report.

Physical Activity Variables

Participants were asked to complete a physical activity questionnaire. Physical activity variables were also measured using actigraph GT3X (Actigraph LLC, Pensacola, FL) worn by the subjects for 7 days. To avoid misclassification, subjects were asked to wear the actigraph, which records number of accelerations in three axes, around their waist area while awake. The study examined three primary physical activity variables based on actigraph measurements. Axis 1 measured the amount of vertical axis acceleration picked up by the actigraph. The count of acceleration in axis 1 was standardized on a one-minute basis (Axis 1 CPM), as calculated by the total number of acceleration/total recording time. Total time in sedentary bouts was determined by the amount of minutes the participant recorded less than 150 vertical axis accelerations per minute. And total time in sedentary breaks was calculated as the sum of the time between sedentary bouts. When analyzing total time in sedentary bouts and breaks, I adjusted for the amount of total recording time to account for the fact that the participants had different lengths of actigraph recordings.

Nutritional Intake Variables

The Youth/Adolescent Questionnaire completed by the subjects was to measure the subjects' daily nutrition intake (34-35). Participants were asked the frequency they consumed 152 food items over one year before the study. This frequency of their consumption of the 152 food items was analyzed by their nutrient indices to provide an estimate of their daily total calorie, fat, carbohydrate, and protein intake.

Other Covariates

Demographic variables, such as age, race, gender, smoking status, and medical history, were obtained by a self-administered questionnaire. BMI was calculated based on measured height and weight. BMI percentile was determined by 2000 CDC growth charts and adjusted for age and gender. Participants were categorized as normal, overweight, or obese based on BMI percentile values of <85, ≥ 85 and <95, and ≥ 95.

Statistical Analysis

Although 421 participants completed the follow-up exam, I excluded 116 of them due to insufficient documented sleep data (n=94), missing data on DXA variables (n=1), and/or missing data on physical activity variables (n=22). The sample size for statistical analysis therefore consisted of 307 participants. I determined the summary statistics such as the mean and standard deviation of demographic and study variables across different BMI classifications. Linear regression models were used to examine the relationship between HSV and abdominal obesity.

Regression models were then adjusted for nutrition intake and physical activity variables to determine their effect on the relationship. Major confounder variables, such as age, sex, and BMI percentile, were also adjusted for in the regression models. HSD was also adjusted in the model.

To further examine potential mediators, I used the R package "mediation" (36) to precisely determine the mediating effect that physical activity and nutritional intake had on the association between HSV and abdominal obesity. Mediation models were run with 5000 Monte Carlo simulations for reliable results. All analyses were performed using RStudio 2 (Version 0.98.1091).

Results

Demographic characteristics of the population are shown in **Table 1**. The overall mean (SD) age was 16.71 (2.26) years old. 52.46 percent of the population was male and 79.69 percent was white. I also examined the difference of these variables across 3 BMI percentile categories: normal, overweight, and obese. There was no significant difference in age or sex across BMI percentile defined classes. However, in terms of race, there were a larger proportion of white subjects in the normal (81.41%) and overweight (85.45%) categories than in the obese category (60.78%). The means (SD) of HSV and HSD were 1.19 (0.61) hours and 7.00 (0.83) hours. As expected, the obesity variables measured by the DXA scan were highly significantly associated with the BMI categories. As BMI increased, the means of AGR, AWP, SAT, TAT, and VAT areas increased significantly. I unexpectedly found GWP areas to be to be negatively

correlated with BMI percentile. BMI percentile was not found to be associated with the variables of physical activity or nutritional intake.

Table 2 shows linear regression analysis of the dependence of individual DXA variables on HSV with adjustment for nutritional intake. The regression coefficient estimates the impact of one-hour increase of HSV on the respective DXA variable. I found that TAT area was strongly associated with HSV with a regression coefficient (SE) of 32.4 (12.07) cm^2. With a 1-hour increase in HSV, there is a 25.60 (9.57) cm^2 increase in SAT area. Even after controlling for HSD, the regression coefficient and SD of the association between HSV and DXA variables remained similar. I also tried to determine if the association between HSV and abdominal obesity differs by age. However, no significant difference was found when the entire sample was dichotomized by age (>16 years vs.≤16 years, data not shown). I found a consistent difference in the regression coefficients between male and female populations (**Table 3**). HSV had a significantly larger effect on all the DXA variables in the female sample (n=144) than in the male sample (n=160). For example, the regression coefficient for the association between HSV and TAT area was 43.06 (16.55) in the female population, which was significantly greater than the regression coefficient 13.93 (17.50) in the male population.

I also adjusted for nutritional intake in **Table 2** to examine if those variables were mediators. The regression coefficients were significantly changed after controlling for total caloric intake, total fat intake, and total carbohydrate intake. For example, after adjusting for carbohydrate intake, the regression coefficient in the association between HSV and AGR changed by 17% from 0.018 to 0.015 (Model 2c). The regression coefficient in the association between HSV and VAT changed 19% from 6.84 to 5.52 after adjusting for carbohydrate intake.

In Table 4, I show that physical activity produced a smaller difference in the magnitude of association between HSV and DXA measurements than what is produced by nutritional intake. For instance, controlling for Axis1 increased the regression coefficient in the association between TAT and HSV by 6% from 32.46 cm^2 to 34.42 cm^2.

I performed a mediation analysis to quantify the direct effect, mediation effect, and total effect of 1-hour increase in HSV on VAT area. The mediator-adjusted regression coefficients, 95% confidence intervals, and P values are found in **Table 5**. Total carbohydrate and caloric intake had the greatest mediation effect. The carbohydrate mediation effect was 1.33 cm^2 out of the total effect (6.85 cm^2), meaning carbohydrate intake was responsible for around 19% of the relationship between HSV and abdominal obesity. I found no mediation effect in the three physical activity variables (all $p>0.05$).

Discussion

A majority of studies have focused on short sleep duration as a risk factor in obesity (13-18, 37-39). Nixon and coworkers found that 7-year olds who slept less than 7 hours a night had a threefold risk of obesity than those who slept over 9 hours a night, based on one night of actigraphy data (40). A study using children between 11-16 years showed that each additional hour of actigraph-measured sleep decreased obesity risk by 80% (41). Sleep variability, on the other hand, is less investigated, especially in association with abdominal obesity (6-8, 25-28). HSV was found to be associated with altered insulin levels and greater health risk in overweight children (42). Other studies have also connected HSV to general obesity through the parameter

BMI (25). In contrast, this report concentrates on the specific relationship between HSV and abdominal obesity by adjusting for BMI percentile and HSD in the models.

Many studies have attributed the association between HSV and obesity to increased food consumption and decreased physical activity (26-27, 29). Kjeldsen and coworkers found that increased sleep variability was associated with increased intake in energy-dense foods and sugar-sweetened beverages (26). In contrast, this study found that less than 19% of the association could be attributed to increased energy intake and none to physical activity. However, there is a lack of association between physical activity and abdominal obesity in this study's sample of otherwise healthy adolescents. Interestingly, my results show a stronger correlation between HSV and all DEXA variables in females than in males. Similarly, another study found HSD affected DEXA-measured obesity in females more strongly than in males (44).

Other etiological pathways have been suggested to explain the lack of sizeable mediating effect by physical activity and nutritional intake. A plausible mechanism is that sleep-related physiological comorbidities, such as emotional stress, depression, and anxiety are linking HSV to obesity (45). There is consistent evidence that shows a bidirectional association between obesity and depression (46). In a longitudinal study, participants with higher levels of depression increased in both abdominal obesity and BMI more quickly than those with lower levels of depression (47). In addition, it is possible that HSV could be related to abdominal obesity through irregular eating habits. Although the food intake could be the same amount, subjects with increased HSV may be more prone to skipping breakfast. Irregular eating times have been shown to be associated with metabolic syndrome, a cluster of coronary heart disease risk factors that include central obesity, diabetes, and hypertension (40). Mouse model studies have found that circadian dysfunction induced by genetic or environmental manipulation can cause

metabolic consequences that induce obesity. Increased night-to-night variability may possibly disrupt the body's underlying circadian rhythm and lead to metabolic consequences by disturbing the close relationship between the body's metabolic processes and molecular clock (49-50).

This study has several strengths. First of all, I used data from DXA scans to obtain a more precise measurement of central fat distribution. I controlled for possible confounding effects by adjusting for BMI percentile, HSD, age, race, and sex in the linear regression and mediation models. The mediation model allowed me to precisely quantify direct and mediating effects of HSV on abdominal obesity. I also used actigraphs to obtain an objective measurement of sleep and physical activity data over the course of a week to reflect the participants' sleeping habits in their natural setting. In addition, adjusting for BMI percentile and HSD enabled me to examine the exclusive relationship between HSV and abdominal obesity.

This present study does have some limitations. Participants may have forgotten to wear their actigraphs or switch to the wrist of their non-dominant hand during sleep. However, subjects with less than 5 out of 7 nights of recorded sleep data were excluded from the data analysis. Physical activity data may also be inaccurate by inconsistent wearing of the actigraph. Actigraphs can sometimes be an incomplete measurement of physical activity as they use motion from the waist to monitor activity of the whole body. This study also examines a study population of a small age range in adolescence and the results may not extend to a wider age range. In addition, the response rate for this follow-up study was 60%. Some selection bias could have occurred between those who continued on to complete the follow-up examination and those who did not. However, no significant difference in demographic characteristics between the two groups was found. Lastly, since this was a cross-sectional analysis, it is possible that reverse causation is responsible for this study's findings and that the irregular sleep patterns are

in fact a result of increased adiposity (51). Studies have found that obesity leads to excessive sleep, sleep apnea, and daytime sleepiness, but did not find sleep apnea to be a risk factor for obesity (24, 52).

In conclusion, high degree of habitual sleep variability is significantly related to abdominal obesity in adolescents. The association between HSV and abdominal obesity can be partially explained by increased food intake, especially carbohydrate and caloric intake. However, there is lack of evidence of a strong mediating effect by physical activity. And a large proportion of association between HSV and abdominal obesity could not be explained by food intake. Therefore, further research is needed into the causal link between night-to-night HSV and abdominal obesity through other physiological pathways.

Appendix A:

Tables

Table 1: Demographic characteristics of study population

	Overall N=304	Normal Weight N=199	Overweight N=54	Obese N=51	P value
Age (years)	16.71 (2.26)	16.69 (2.20)	16.89 (2.62)	16.58 (2.10)	0.76
Male (%)	52.46	51.76	50.91	56.86	0.78
White (%)	78.69	81.41	85.45	60.78	<0.01
HSV (hours)	1.19 (0.61)	1.18 (0.57)	1.13 (0.65)	1.30 (0.71)	0.29
HSD (hours)	7.00 (0.83)	7.04 (0.81)	7.05 (0.75)	6.80 (0.96)	0.17
BMI percentile	66.01 (28.07)	51.07 (23.54)	90.67 (3.04)	97.74 (1.44)	<0.01
AGR	0.36 (0.11)	0.31 (0.07)	0.40 (0.09)	0.51 (0.11)	<0.01
AWP (%)	6.30 (1.52)	5.64 (1.05)	6.97 (1.28)	8.25 (1.28)	<0.01
GWP (%)	18.01 (2.40)	18.54 (2.50)	17.55 (1.88)	16.44 (1.62)	<0.01
VAT area (cm^2)	59.87 (39.42)	49.88 (15.89)	74.00 (25.15)	122.91 (43.38)	<0.01
TAT area (cm^2)	282.79 (192.47)	183.75 (91.98)	368.75 (135.66)	578.23 (188.21)	<0.01
SAT area (cm^2)	222.92 159.01)	143.87 (85.73)	294.75 (119.82)	455.32(153.73)	<0.01
Total caloric intake (kcal)	1776.71 (652.57)	1814.95 (649.04)	1581.34 (654.54)	1841.52 (636.79)	0.61
Total fat intake (g)	64.21 (26.28)	66.12 (26.32)	57.80 (26.83)	63.66 (24.80)	0.25
Carbohydrates intake (g)	233.98 (87.76)	238.69 (86.56)	203.13 (84.93)	249.59 (89.47)	0.89
Protein intake (g)	70.47 (27.39)	71.34 (27.95)	65.36 (26.16)	72.69 (26.30)	0.86
Total time in sedentary bouts (minutes)	3027.58 (933.18)	2997.06 (929.25)	2963.63 (978.71)	3214.37 (893.46)	0.21
Total time in sedentary breaks (minutes)	6726.10 (1371.73)	6812.92 (1338.14)	6521.61 (1477.78)	6603.86 (1380.84)	0.20
Vertical axis activity acceleration (CPM)	393.50 (214.95)	398.59 (215.24)	403.86 (236.59)	362.62 (189.78)	0.37

Results are expressed as mean (SD) for continuous variables and as percentage for categorical variables.

Table 2. Regression coefficient, SE, and P value in association between DXA measurements and HSV, adjusted for nutritional intake

DXA measurements	***Model 1*** β (SE)	***Model 2*** β (SE)	***Model 2a*** β (SE)	***Model 2b*** β (SE)	***Model 2c*** β (SE)	***Model 2d*** β (SE)
TAT Area	32.46 (12.07)**	32.50 (12.09)**	29.93 (12.28)*	30.50 (12.22)*	27.75 (12.25)*	32.37 (12.16)**
VAT Area	6.84 (2.82)*	6.85 (2.82)*	6.02 (2.86)*	6.42 (2.85)*	5.52 (2.87)	6.68 (22.4)*
SAT Area	25.60 (9.57)**	25.60 (9.58)**	23.90 (9.74)*	25.10 (9.70)*	22.2 (9.78)*	2.57 (9.65)*
AGR	0.018 (0.008)*	0.018 (0.008)*	0.016 (0.008)*	0.016 (0.008)*	0.015 (0.008)*	0.017 (0.008)**
AWP	0.002 (0.001)*	0.002 (0.001)*	0.002 (0.001)	0.002 (0.001)*	0.002 (0.001)	0.002 (0.001)*

*: P value <0.05
**: P value <0.01

Model 1: adjusted for race, sex, BMI percentile, age
Model 2: Model1+HSD
Model 2a: Model 2+total caloric intake
Model 2b: Model 2+total fat intake
Model 2c: Model 2+carbohydrate intake
Model 2d: Model 2+protein intake

Table 3 Gender difference of the dependence of DXA variables on HSV

	Males (N=160)		**Females (N=144)**	
	β (SE)	P value	β (SE)	P value
TAT Area	13.93 (17.50)	0.43	43.06 (16.55)	0.01
VAT Area	1.75 (3.68)	0.64	9.97 (4.21)	0.02
SAT Area	12.18 (14.34)	0.40	33.10 (12.69)	0.40
AGR	0.012 (0.013)	0.34	0.019 (0.011)	0.06
AWP	0.001 (0.002)	0.44	0.003 (0.001)	0.08

Also adjusted for race, BMI percentile, age

Table 4: Regression coefficient, SE, and P value in association between DXA measurements and HSV, adjusted for physical activity

DXA measurements	***Model 1*** β (SE)	***Model 2*** β (SE)	***Model 2a*** β (SE)	***Model 2b*** β (SE)	***Model 2c*** β (SE)
TAT Area	32.46 (12.1)**	32.50 (12.1)**	33.00 (12.11)**	34.44 (12.17)**	34.42 (11.96)**
VAT Area	6.84 (2.82)*	6.85 (2.82)*	6.91 (2.84)*	6.94 (2.85)*	7.16 (2.81)*
SAT Area	25.6 (9.57)**	25.6 (9.58)**	26.06 (9.59)**	27.51 (9.64)**	27.26 (9.47)**
AGR	0.018 (0.008)*	0.018 (0.008)*	0.018 (0.008)	0.019 (0.008)*	0.019 (0.008)
AWP	0.002 (0.001)*	0.002 (0.001)*	0.002 (0.001)	0.002 (0.001)	0.002 (0.001)*

*: P value <0.05
**: P value <0.01

Model 1: adjusted for race, sex, BMI percentile, age
Model 2: Model1+HSD
Model 2a: Model 2+Sedentary Bouts
Model 2b: Model 2+Sedentary Breaks
Model 2c: Model 2+Axis 1 CPM

Table 5: Mediation model in the association between 1 hour increase in HSV and VAT area

Mediation Factor	Effect Type	β	95% CI	P value
Total caloric intake	Direct	6.02	-0.60, 12.43	0.08
	Mediation	0.83	-0.04, 2.36	0.08
	Total	6.85	0.06, 13.57	0.05
Total fat intake	Direct	6.42	-0.17, 13.15	0.06
	Mediation	0.43	-0.17, 1.73	0.25
	Total	6.85	0.09, 13.84	0.05
Carbohydrate intake	Direct	5.52	-1.15, 12.20	0.12
	Mediation	1.33	0.11, 3.04	0.02
	Total	6.85	-0.08, 13.97	0.05
Protein intake	Direct	6.68	0.10, 13.91	0.05
	Mediation	0.17	-0.33, 0.99	0.58
	Total	6.85	0.22, 14.03	0.04
Total time in sedentary breaks	Direct	6.84	0.22, 13.88	0.04
	Mediation	0.00	-0.46, 0.44	0.99
	Total	6.85	0.26, 13.79	0.04
Total time in sedentary bouts	Direct	6.89	0.04, 14.00	0.05
	Mediation	-0.04	-0.55, 0.35	0.84
	Total	6.85	0.02, 13.95	0.05
Axis_1_CPM	Direct	7.16	0.42, 14.13	0.03
	Mediation	-1.52	-6.60, 2.47	0.45
	Total	5.64	5.64, -2.00	0.17

BIBLIOGRAPHY

1. Hart CN, Cairns A, Jelalian E. Sleep and Obesity in Children and Adolescents. The Pediatric Clinics of North America. 2011;58:715-733
2. Deckelbaum RJ, Williams CL. Childhood Obesity: The Health Issue. Obes Res. 2001;9:239S-243S.
3. Nguyen, D, El-Serag, H. The Epidemiology of Obesity. March 2010;39(1): 1-7.
4. Moreno, L, Pigeot, I, Ahrens, W. Epidemiology of Children and Adolescents. 2011; 2: 1-35.
5. Cote AT, Harris KC, Panagiotopoulos C, Sandor GGS, Devlin AM. Childhood obesity and cardiovascular dysfunction. J Am Coll Cardiol. 2013;62:1309-1319.
6. Iglowstein, O.G. Jenni, L. Molinari, et al. Sleep duration from infancy to adolescence: reference values and generational trends. Pediatrics. 2003; 111:302
7. Dollman J, Ridley K, Olds T, Lowe E. Trends in the duration of school-day sleep among 10- to 15-year-old South Australians between 1985 and 2004. Acta Pædiatrica. 2007;96:1011-1014.
8. CDC Unhealthy sleep-related behaviors – 12 States, 2009. MMWR Morb Mortal Wkly Rep. 2011;60:233–238.
9. Schoenborn CA, Adams PF. Sleep duration as a correlate of smoking, alcohol use, leisure-time physical inactivity, and obesity among adults: United States, 2004--2006. Hyattsville, MD: National Center for Health Statistics; 2008.
10. Snell EK, Adam EK, Duncan GJ. Sleep and the body mass index and overweight status of children and adolescents. Child Dev. 2007;78(1):309–23.

11. Spilsbury JC, Storfer-Isser A, Drotar D, et al. Sleep behavior in an urban US sample of school-aged children. Arch Pediatr Adolesc Med. 2004;158(10):988–94.

12. Mindell JA, Owens J. A clinical guide to pediatric sleep: diagnosis and management of sleep problems. Philadelphia: Lippincott Williams & Wilkins; 2003

13. Cappuccio FP, Taggart FM, Kandala NB, et al. Metaanalysis of short sleep duration and obesity in children and adults. Sleep. 2008;31(5):619–26.

14. Jiang F. Sleep and obesity in preschool children. J Pediatr. 2009;154:814-818.

15. Chen X, Beydoun MA, Wang Y. Is sleep duration associated with childhood obesity? A systematic review and meta-analysis. Obesity (Silver Spring). 2008;16(2):265–74.

16. Hart CN, Cairns A, Jelalian E. Sleep and obesity in children and adolescents. Pediatr Clin North Am.2011;58(3):715–33.

17. Gupta NK, Mueller WH, Chan W, Meininger JC. Is obesity associated with poor sleep quality in adolescents?. Am J Hum Biol. 2002;14(6):762–8.

18. Nixon GM, Thompson JM, Han DY, et al. Short sleep duration in middle childhood: risk factors and consequences. Sleep. 2008;31(1):71–8.

19. Landis AM, Parker KP, Dunbar SB. Sleep, hunger, satiety, food cravings, and caloric intake in adolescents. J Nurs Scholarsh. 2009;41(2):115–23.

20. Weiss A, Xu F, Storfer-Isser A, Thomas A, IeversLandis CE, Redline S. The association of sleep duration with adolescents' fat and carbohydrate consumption. Sleep. 2010;33(9):1201–9.

21. C. Guilleminault, N.B. Powell, S. Martinez, et al. Preliminary observations on the effects of sleep time in a sleep restriction paradigm. Sleep Med, 4 (2003), p. 177

22. K. Spiegel, R. Leproult, M. L'Hermite-Baleriaux, et al. Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin J Clin Endocrinol Metab, 89 (2004), p. 5762

23. Vgontzas AN, Lin HM, Papaliaga M, et al. Short sleep duration and obesity: the role of emotional stress and sleep disturbances. Int J Obes (Lond). 2008;32(5):801-809.

24. Vgontzas AN, Fernandez-Mendoza J, Miksiewicz T, et al. Unveiling the longitudinal association between short sleep duration and the incidence of obesity: the Penn State Cohort. Int J Obes (Lond). 2014;38(6):825-832.

25. Patel SR, Hayes AL, Blackwell T, et al. The association between sleep patterns and obesity in older adults. International journal of obesity (2005). 2014;38:1159-1164.

26. Kjeldsen JS, Hjorth MF, Andersen R, et al. Short sleep duration and large variability in sleep duration are independently associated with dietary risk factors for obesity in danish school children. Int J Obes. 2014;38(1):32-39.

27. Stone MR, Stevens D, Faulkner GEJ. Maintaining recommended sleep throughout the week is associated with increased physical activity in children. Prev Med. 2013; 2012;56:112.

28. Shiromani P, Horváth T, Redline S, Van Cauter E, SpringerLink (Online service). Sleep Loss and Obesity: Intersecting Epidemics. New York, NY: Springer New York; 2012.

29. Rubenstein, J, Gastroenterology. March 2010; 38(5): S-387.

30. Lee CMY, Huxley RR, Wildman RP, Woodward M. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: A meta-analysis. J Clin Epidemiol. 2008;61(7):646-53.

31. Bixler EO, Vgontzas AN, Lin HM, et al. Blood pressure associated with sleep-disordered

breathing in a population sample of children. Hypertension. 2008;52(5):841-846

32. Liao D, Li X, Rodriguez-Colon SM, et al. Sleep-disordered breathing and cardiac autonomic modulation in children. Sleep Med. 2010;11(5):484-8.
33. Salamat M, Shanei A, Khoshhali M, Salamat A, Siavash M, Asgari M. Use of Conventional Regional DXA Scans for Estimating Whole Body Composition. ARCHIVES OF IRANIAN MEDICINE. 2014;17:674-678.
34. Rockett HR, Wolf AM, Colditz GA. Development and reproducibility of a food frequency questionnaire to assess diets of older children and adolescents. J Am Diet Assoc. 1995;95(3):336-340.
35. Rockett HR, Breitenbach M, Frazier AL, et al. Validation of a youth/adolescent food frequency questionnaire. Prev Med. 1997;26(6):808-816.
36. Imai K, Keele L, Tingley D, Yamamoto T (2010b). "Causal Mediation Analysis Using R." In HD Vinod (ed.), Advances in Social Science Research Using R, Lecture Notes in Statistics, pp. 129–154. Springer-Verlag, New York.
37. Hairston KG, Bryer-Ash M, Norris JM, et al. Sleep duration and five-year abdominal fat accumulation in a minority cohort: the IRAS family study. Sleep. 2010;33(3):289-295.
38. Yi S, Nakagawa T, Yamamoto S, et al. Short sleep duration in association with CT-scanned abdominal fat areas: the Hitachi Health Study. Int J Obes (Lond). 2013;37(1):129-134.
39. Theorell-Haglöw J, Berne C, Janson C, et al. Associations between short sleep duration and central obesity in women. Sleep. 2010;33(5):593-598.
40. Nixon GM, Thompson JM, Han DY, et al. Short sleep duration in middle childhood: risk factors and consequences. Sleep. 2008;31(1):71–8.

41. Gupta NK, Mueller WH, Chan W, Meininger JC. Is obesity associated with poor sleep quality in adolescents? Am J Hum Biol. 2002;14(6):762–8.

42. Spruyt K, Molfese DL, Gozal D. Sleep duration, sleep regularity, body weight, and metabolic homeostasis in school-aged children. Pediatrics. 2011;127:e345-e352.

43. Fuligni AJ, Hardway C. Daily variation in adolescents' sleep activities and psychological well-being. J Res Adolescence 2006;16(3): 353–378

44. Yu Y, Lu BS, Wang B, et al. Short sleep duration and adiposity in Chinese adolescents. Sleep. 2007;30(12):1688–97.

45. Faith MS, Matz PE, Jorge MA. Obesity-depression associations in the population. J Psychosom Res. 2002;53:935-942.

46. Preiss K, Brennan L, Clarke D. A systematic review of variables associated with the relationship between obesity and depression. Obesity Reviews. 2013;14:906-918.

47. Brady S. Link between depression and abdominal obesity. The Culvert Chronicles. 2010;5:9.

48. Sierra-Johnson, J., Undén, A.-L., Linestrand, M., Rosell, M., Sjogren, P., Kolak, M., De Faire, U., Fisher, R. M. and Hellénius, M.-L. (2008), Eating Meals Irregularly: A Novel Environmental Risk Factor for the Metabolic Syndrome. Obesity, 16: 1302–1307. doi: 10.1038/oby.2008.203

49. Shi SQ, Ansari TS, McGuinness OP, Wasserman DH, Johnson CH. Circadian disruption leads to insulin resistance and obesity. Curr Biol 2013; 23: 372–381.

50. Barclay JL, Husse J, Bode B, Naujokat N, Meyer-Kovac J, Schmid SM et al. Circadian desynchrony promotes metabolic disruption in a mouse model of shiftwork. PLoS One 2012; 7: e37150.

51. Vgontzas AN, Bixler EO, Tan TL, Kantner D, Martin LF, Kales A. Obesity without sleep apnea is associated with daytime sleepiness. Arch Intern Med1998; 158: 1333–1337.

52. Guan Z, Vgontzas AN, Bixler EO, Fang J. Sleep is increased by weight gain and decreased by weight loss in mice. Sleep 2008; 31: 627–633.

ACADEMIC VITA

Lucia Liao
1110 Donovan Way
Chester Springs, PA 19425
Lucy.Liao1@gmail.com

Education

Pennsylvania State University, University Park, PA

Schreyer Honors College
Bachelor of Science in General Science Expected Graduation Date: May 2015

Research Experiences:

Columbia School of Public Health New York, New York
Summer Institute for Biostatistics Student *May-July 2013*

- Conducted a research project on LDL management in patients with diabetes with Dr. Siqin Ye at New York Presbyterian Hospital
- Presented powerpoint presentation on research at Columbia CSIBS symposium
- Took graduate level introductory biostatistics and SAS programming course

Penn State Hershey Medical Center Hershey, PA
Clinical Research Intern *May-June 2012*
Sleep and cardio-metabolic risk factors: a prospective study of adolescents

- Attached Holter monitors to patients
- Explained trial's procedures to patients and families
- Set up air pollution monitors and Holter monitor equipment and data input

Department of Biochemistry and Molecular Biology Pennsylvania State University
Dr. Frank Pugh Eukaryotic Gene Regulation Lab *Dec 2011-Dec 2012*
Undergraduate researcher

- Studied transcription regulation mechanisms during chromatin construction
- Isolated genomic DNA to produce computational models of transcription machinery

Medical/Health Experiences:

Cardiac Care Mission trip to Ecuador Guayaquil, Ecuador
Health Care volunteer *Oct 2013*

- Participated in a volunteer trip to deliver life-saving medical care to pediatric patients with a cardiothoracic surgery team from Hershey Medical
- Translated medical instruction to patients and families in Spanish

Mount Nittany Medical Center University Park, PA
Emergency Department Volunteer *Jan 2013-May 2013*

- Transport patients from emergency room to test sites
- Restock IV pumps, blankets, ice packs, etc.

Global Medical Brigades Arimae, Darien, Panama
Medical Brigade Volunteer *Mar 10-20 2012*

- Fundraised money to finance the medication and medical care equipment of an indigenous community in Arimae, Panama
- Obtained patient history and symptoms and measured blood pressure, temperature, and height and weight in triage
- Educated patients on nutrition and hygiene

Other Experiences

Department of Biology Pennsylvania State University
Intro to Physiology Lecture Assistant *Aug-Dec 2013*

- *Lead* learning activities and answer questions during class lectures
- Host weekly office hours to teach physiology material to students and help them study

Phi Sigma Pi National Co-Ed Honors Fraternity Pennsylvania State University
Service and Philanthropy Chair *Aug 2012-present*

- Organize service events with local nursing homes, sustainability organizations, and animal shelters
- Fundraise for Penn State THON through canning trips, Thonvelopes, and bake sales

Member *Jan 2012-present*

- Designed and constructed a parade float for Penn State Homecoming
- Participated in Relay for Life and raised funds for Teach for America