

# Effects of Experimental Sleep Restriction on Weight Gain, Caloric Intake, and Meal Timing in Healthy Adults

Andrea M. Spaeth, MA<sup>1</sup>; David F. Dinges, PhD<sup>2</sup>; Namni Goel, PhD<sup>2</sup>

<sup>1</sup>Department of Psychology, School of Arts and Sciences, University of Pennsylvania, Philadelphia, PA; <sup>2</sup>Division of Sleep and Chronobiology, Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

**Study Objectives:** Examine sleep restriction's effects on weight gain, daily caloric intake, and meal timing.

**Design:** Repeated-measures experiments assessing body weight at admittance and discharge in all subjects (N = 225) and caloric intake and meal timing across days following 2 baseline nights, 5 sleep restriction nights and 2 recovery nights or across days following control condition nights in a subset of subjects (n = 37).

**Setting:** Controlled laboratory environment.

**Participants:** Two hundred twenty-five healthy adults aged 22-50 y (n = 198 sleep-restricted subjects; n = 31 with caloric intake data; n = 27 control subjects; n = 6 with caloric intake data).

**Interventions:** Approximately 8-to-1 randomization to an experimental condition (including five consecutive nights of 4 h time in bed [TIB]/night, 04:00-08:00) or to a control condition (all nights 10 h TIB/night, 22:00-08:00).

**Measurements and Results:** Sleep-restricted subjects gained more weight ( $0.97 \pm 1.4$  kg) than control subjects ( $0.11 \pm 1.9$  kg;  $d = 0.51$ ,  $P = 0.007$ ). Among sleep-restricted subjects, African Americans gained more weight than Caucasians ( $d = 0.37$ ,  $P = 0.003$ ) and males gained more weight than females ( $d = 0.38$ ,  $P = 0.004$ ). Sleep-restricted subjects consumed extra calories ( $130.0 \pm 43.0\%$  of daily caloric requirement) during days with a delayed bedtime (04:00) compared with control subjects who did not consume extra calories ( $100.6 \pm 11.4\%$ ;  $d = 0.94$ ,  $P = 0.003$ ) during corresponding days. In sleep-restricted subjects, increased daily caloric intake was due to more meals and the consumption of  $552.9 \pm 265.8$  additional calories between 22:00-03:59. The percentage of calories derived from fat was greater during late-night hours (22:00-03:59,  $33.0 \pm 0.08\%$ ) compared to daytime (08:00-14:59,  $28.2 \pm 0.05\%$ ) and evening hours (15:00-21:59,  $29.4 \pm 0.06\%$ ;  $P_s < 0.05$ ).

**Conclusions:** In the largest, most diverse healthy sample studied to date under controlled laboratory conditions, sleep restriction promoted weight gain. Chronically sleep-restricted adults with late bedtimes may be more susceptible to weight gain due to greater daily caloric intake and the consumption of calories during late-night hours.

**Keywords:** Caloric intake, gender, late-night eating, macronutrients, meal timing, race, sleep restriction

**Citation:** Spaeth AM; Dinges DF; Goel N. Effects of experimental sleep restriction on weight gain, caloric intake, and meal timing in healthy adults. *SLEEP* 2013;36(7):981-990.

## INTRODUCTION

The 2004-2007 National Health Interview Survey revealed that approximately 28.3% of adults report sleeping 6 h or less per night,<sup>1</sup> and other studies have indicated that the prevalence of short sleepers (adults who report an average of  $\leq 6$  h of sleep within a 24-h period) has significantly increased in recent decades.<sup>1,2</sup> Reported associations between short sleep duration and energy homeostasis suggest the former may be a risk factor for a higher body mass index (BMI)<sup>3-5</sup> and prospective cohort studies have identified short sleep duration as a predictor of greater weight gain.<sup>6-9</sup> This relationship may be stronger for men than for women.<sup>10,11</sup> However, no controlled laboratory studies have experimentally examined the effect of sleep restriction (SR) on weight gain in a large, diverse sample of men and women.

Laboratory studies have elucidated possible behavioral and physiological mechanisms underlying the relationship between sleep duration and weight gain. Spiegel and colleagues<sup>12</sup> found that subjects undergoing 2 nights of SR (4 h time in bed [TIB]/

night) with controlled energy intake via an intravenous glucose infusion exhibited increased levels of ghrelin (an orexigenic hormone released from the stomach) and decreased levels of leptin (an anorexigenic hormone released from adipocytes). These neuroendocrine changes were accompanied by significant increases in self-reported ratings of hunger and appetite, specifically for foods with high carbohydrate content.<sup>12</sup> Other experiments have also shown that sleep loss increased ghrelin levels and decreased leptin in calorically-restricted humans.<sup>13,14</sup> By contrast, in laboratory studies using *ad libitum* food access, which mimics a more natural environment, sleep loss was associated with either no change in ghrelin or leptin or an increase in leptin levels.<sup>15-20</sup> Such *ad libitum* experiments, however, demonstrated that sleep loss was associated with increased caloric intake.<sup>15,21-23</sup> These investigations collectively indicate that humans compensate (or over-compensate) for sleep loss by increasing energy intake.

Sleep restriction also affects macronutrient intake and meal frequency. Adolescents who habitually slept less than 8 h per night consumed a higher proportion of calories from fat and a lower proportion of calories from carbohydrates and protein than those who slept 8 h or more per night.<sup>24</sup> In adults, SR has been associated with increased craving for foods high in carbohydrate content,<sup>12</sup> greater consumption of calories from carbohydrates<sup>16</sup> or fats,<sup>22</sup> and increased caloric intake derived from snacks.<sup>16,25</sup>

In addition to daily caloric intake, meal timing is an important contributor to weight gain.<sup>26,27</sup> Baron and colleagues<sup>28</sup> examined differences in sleep, eating, and weight between "normal

Submitted for publication January, 2013

Submitted in final revised form April, 2013

Accepted for publication April, 2013

Address correspondence to: Andrea Spaeth, MA, Department of Psychology, University of Pennsylvania, 1020 Blockley Hall, 423 Guardian Drive, Philadelphia, PA 19104; Tel: (215) 898-0474; Fax: (215) 573-6410; E-mail: [aspaeth@sas.upenn.edu](mailto:aspaeth@sas.upenn.edu)

sleepers” (sleep midpoint < 05:30) and “late sleepers” (sleep midpoint > 05:30) and found that late sleepers exhibited a shorter sleep duration, consumed more calories at dinner and after 20:00, consumed more fast food and full-calorie soda, and had a higher BMI compared to normal sleepers. In a group of healthy inpatients, individuals who ate during late-night/early morning (23:00-05:00) consumed more calories per day and gained more weight than non-nighttime eaters.<sup>29</sup> In an outpatient weight-loss effectiveness study, participants who were late eaters (lunch after 15:00) lost less total weight and displayed slower weight loss than early eaters (lunch before 15:00).<sup>30</sup> Animal studies have also shown a relationship between meal timing and weight gain: Circadian Locomotor Output Cycles Kaput (CLOCK) mutant mice exhibited an attenuated diurnal feeding rhythm and were hyperphagic and obese.<sup>31,32</sup> Moreover, mice exposed to light at night consumed more food during the light phase and had increased body mass compared with mice in a standard light/dark cycle, despite equivalent levels of caloric intake and total daily activity.<sup>33</sup>

The aforementioned lines of evidence suggest that sleep loss potentiates weight gain; however, few controlled experiments have manipulated sleep duration and objectively measured weight gain and *ad libitum* caloric intake. To address this deficiency, we experimentally tested the hypothesis that SR produces weight gain in a large sample of diverse healthy adults using a control condition. We also explored how SR affects possible contributors to weight gain and tested the hypotheses that SR increases daily caloric intake, increases meal frequency, and delays meal timing.

## METHODS

The studies were approved by the Institutional Review Board of the University of Pennsylvania and all subjects were compensated for their participation.

### Subjects and Protocol

Two-hundred twenty-five healthy individuals, aged 22-50 y, were recruited in response to study advertisements. They reported habitual nightly sleep durations between 6.5 h and 8.5 h, habitual bedtimes between 22:00 and 00:00, and habitual morning awakenings between 06:00 and 09:00. They had no evidence of habitual napping, no sleep disturbances (i.e., no complaints of insomnia, daytime sleepiness, or other sleep-wake disturbances), and an absence of extreme morningness or extreme eveningness, as assessed by questionnaire.<sup>34</sup> They were free of acute and chronic medical and psychological conditions, as established by interviews, clinical history, questionnaires, physical examinations, and blood (including a fasting blood glucose test) and urine tests. Subjects were monitored at home with actigraphy, sleep-wake diaries, and time-stamped call-ins to assess bedtime and wake time during the week prior to the in-laboratory phase and the week after the laboratory phase.

Subjects were nonsmokers and had a BMI ranging between 19-30. They did not participate in shift work, transmeridian travel, or irregular sleep/wake routines in the 60 days prior to the study. Sleep disorders were excluded by a night of laboratory polysomnography and oximetry measurements. Subjects were not permitted to use caffeine, alcohol, tobacco, and medications (except oral contraceptives) in the week before the laboratory experiment, as verified by blood and urine screenings.

Subjects participated in one of five protocols in the Sleep and Chronobiology Laboratory at the Hospital of the University of Pennsylvania. Subjects were studied for 12, 14, or 18 consecutive days continuously with daily clinical checks of vital signs and symptoms by nurses (with an independent physician on call). Subjects were randomized as a group ( $n = 4$  to 5 per group) to either the SR or control condition. In all five protocols, the SR condition consisted of two initial baseline nights of 10 h or 12 h TIB per night (22:00-08:00/10:00) followed by 5 nights of sleep restricted to 4 h TIB per night (04:00-08:00). A subset of subjects experienced 2 nights of recovery sleep (12 h TIB, 22:00-10:00) following sleep restriction. SR consisting of 4 h TIB for 5 consecutive nights was selected because this degree of sleep loss produces cumulative neurobehavioral deficits in most healthy adults<sup>35-39</sup> and is within the range of sleep loss that occurs as a result of lifestyle factors.<sup>1,2,40,41</sup>

The protocol days for the SR condition are labeled as follows throughout the manuscript: baseline (BL, the day following the first night of baseline sleep with a 22:00 bedtime); extended wakefulness (EW, the day following the second night of baseline sleep with a 04:00 bedtime); sleep restriction days 1-4 (SR1-4, days following SR with a 04:00 bedtime); sleep restriction day 5 (SR5, the fifth day following sleep restriction with a 22:00 bedtime) and recovery days 1-2 (R1-2, days following recovery sleep with a 22:00 bedtime). The control condition involved the same procedures as the SR condition in each protocol, except that subjects were allowed 10 h TIB every night (22:00-08:00) during the in-laboratory stay.

During the in-laboratory phase of the study, subjects were not permitted to leave the laboratory. In both the SR and control conditions, subjects were ambulatory but were not allowed to exercise. Subjects were permitted to watch television, read, play video or board games, and perform other sedentary activities between test bouts (which were completed while sitting at a computer).

Subjects wore a wrist actigraph throughout the in-laboratory protocol. On certain protocol days, subjects wore ambulatory electroencephalography (EEG) and electrocardiography (ECG) recording equipment for 24 h intervals. The light levels in the laboratory were held constant at < 50 lux during scheduled wakefulness and < 1 lux during scheduled sleep periods. Ambient temperature was maintained between 22°-24°C. Subjects were behaviorally monitored by trained staff continuously throughout the protocol to ensure adherence.

## Procedure and Measurements

### Body Weight

Body weight was measured in  $N = 225$  subjects ( $n = 198$  sleep-restricted subjects and  $n = 27$  control subjects). Of the control subjects (age  $31.9 \pm 8.4$  y; BMI  $25.0 \pm 3.1$  [mean  $\pm$  standard deviation]),  $n = 12$  (44%) were female and  $n = 17$  (63%) were African American. Of the sleep-restricted subjects (age  $31.3 \pm 7.9$  y; BMI  $24.8 \pm 3.3$ ),  $n = 89$  (45%) were female and  $n = 116$  (59%) were African American. During a physical examination 6-7 days prior to the in-laboratory phase of the study, and upon admittance to and discharge from the in-laboratory protocol, nurses measured each subject's height and weight (while subjects wore minimal clothing and no shoes) at the Clinical and Translational Research

Center (CTRC) at the Hospital of the University of Pennsylvania (HUP) using the same calibrated scale. All subjects were weighed during the physical examination between 10:00-12:00. The majority of subjects ( $n = 183$ , 81%) were weighed between 13:00-15:00 during admittance and discharge from the in-laboratory phase of the study. Of the remaining subjects,  $n = 26$  (12%) were weighed between 09:00-12:00 during admittance and discharge, and  $n = 16$  (7%) were weighed between 14:00-16:00 during admittance and discharge. In all cases, subjects were not fasted during the weigh-in days and they had access to a restroom for optional voiding before being weighed.

### Caloric Intake

In order to determine contributors to weight gain, caloric intake was measured in a subset of subjects ( $n = 31$  sleep-restricted subjects: 52% female, 65% African American, age  $34.4 \pm 9.2$  y, BMI  $25.2 \pm 3.7$  and  $n = 6$  control subjects: 33% female, 67% African American, age  $34.0 \pm 9.8$  y, BMI  $25.7 \pm 3.1$ ). All sleep-restricted subjects experienced 2 nights of baseline sleep followed by 5 nights of sleep restriction. Nineteen of the 31 sleep-restricted subjects experienced 2 nights of recovery sleep following SR. Control subjects experienced 10 h TIB per night for each night of the protocol.

### Food/Drink Timing and Availability

Subjects selected their meals/snacks by choosing from various menu options, selecting additional food/drink available in the kitchen within the laboratory suite (which included a refrigerator, microwave, and toaster oven) and by making requests to the monitors and study coordinator. In order to ensure that subjects were provided sufficient time to eat each day, three 30- to 45-min opportunities were specified in the protocol during days with a 22:00 bedtime (09:00, 12:35, and 18:30) and one additional 30-min opportunity to eat was specified in the protocol during days with a 04:00 bedtime (00:30). In addition to these specified meal times, subjects were also allowed to consume food/drink at any time during the protocol other than when they were completing neurobehavioral tests. During a typical day, in addition to the meal times specified in the protocol, subjects could consume food/drink from 09:45-10:00, 11:05-12:00, 13:10-14:00, 14:30-16:00, 16:30-16:45, 17:30-18:00, 19:20-20:00, 20:30-22:00, 22:30-00:00, 01:15-02:00, and 02:30-03:50. Subjects were never told that they had to eat/drink and they were instructed to eat/drink whenever they wanted as long as it did not interfere with testing times. Subjects were also instructed that they could eat what they ordered or could select from other foods available in the laboratory kitchen and that they should eat as much (or as little) as they preferred. Subjects retrieved their own food/drink from the kitchen inside the laboratory suite whenever they wanted to eat/drink and could eat at a table in the common area or privately in their bedrooms.

### Food/Drink Measurement

All food was weighed and recorded prior to being provided to subjects. To enhance the measurement accuracy of each food's weight, food was provided in individual containers (for example, a dinner consisting of chicken, peas, and rice was provided in three separate containers). Each day, a detailed description of the items and the amount consumed and intake

time was recorded by trained monitors. Additionally, any food/drink that was left over after each meal was weighed and recorded. The intake data were entered into The Food Processor SQL program (ESHA Research, Salem, OR), a validated<sup>42</sup> professional nutrition analysis software and database program that provides components of food/drink intake including calories and macronutrients.

### Data Analysis

Between-subjects analyses of variance (ANOVAs) (with study entry BMI, age, race, and gender as covariates) compared weight changes between control subjects and sleep-restricted subjects. Between-subjects ANOVAs (with study entry BMI and age as covariates) compared weight changes between gender and race groups. Repeated-measures ANOVAs compared caloric intake, macronutrients, and meal timing across protocol days. Only 19 sleep-restricted subjects were included in the analyses examining caloric intake during days following recovery sleep. *Post hoc* comparisons were performed with paired *t*-tests using the False Discovery Rate<sup>43</sup> to account for multiple comparisons in order to examine differences between BL, SR, and R days. Effect sizes were calculated using Cohen's  $d$ <sup>44</sup> (small,  $d = 0.2$ ; medium,  $d = 0.5$ ; large,  $d = 0.8$ ). Correlation analysis between weight gain and caloric intake was performed using Spearman's  $\rho$ .

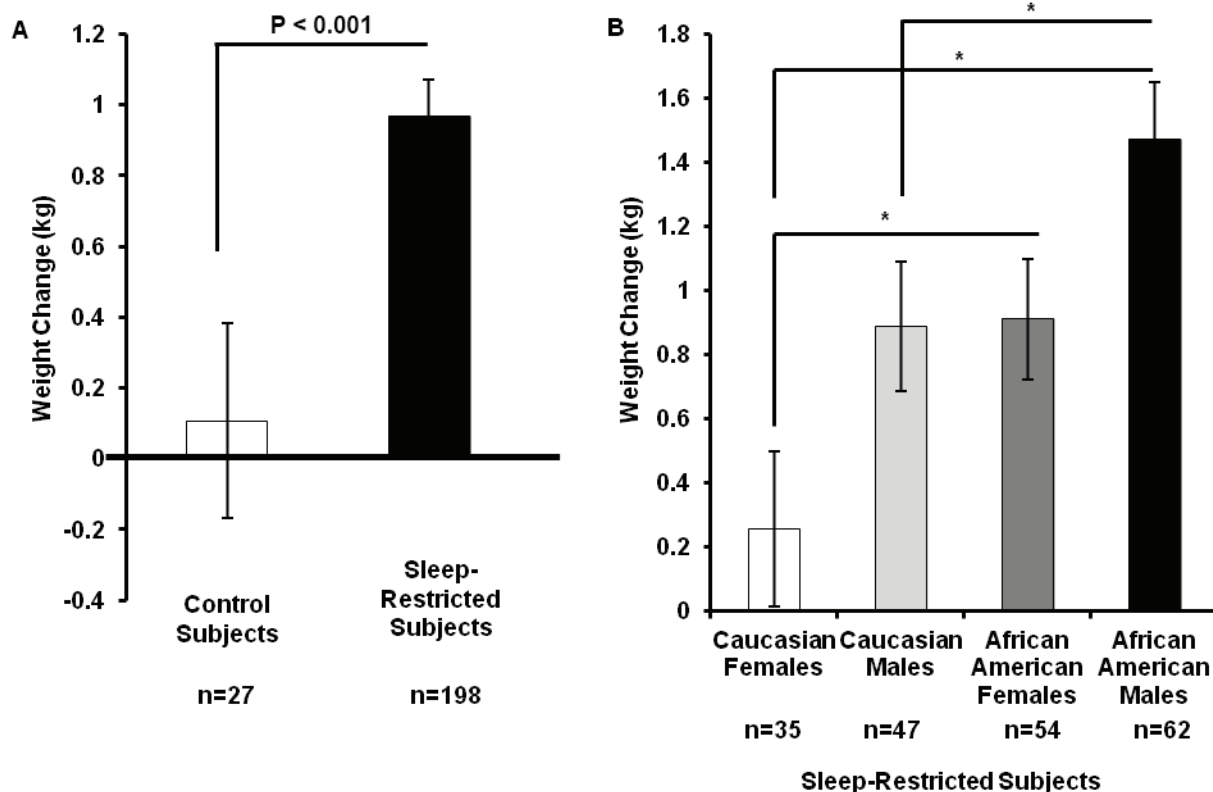
## RESULTS

### Weight Change

To examine if subjects were weight-stable at the start of the in-laboratory phase of the study, each subject's weight during admittance was compared with his/her weight during the physical examination (approximately a 1 week interval). The change in weight was not significantly different between control subjects ( $-0.04 \pm 0.82$  kg [mean  $\pm$  standard deviation]) and sleep-restricted subjects ( $0.09 \pm 0.95$  kg;  $P > 0.4$ ) and neither group's change in weight was different from zero ( $P_s > 0.20$ ). During the in-laboratory protocol, sleep-restricted subjects ( $0.97 \pm 1.43$  kg) gained significantly more weight than control subjects ( $0.11 \pm 1.85$  kg;  $F(1, 223) = 7.52$ ,  $P = 0.007$ ,  $d = 0.51$ ; Figure 1A). The change in weight during the protocol was not different from zero ( $P > 0.71$ ) for control subjects but was significantly different from zero for sleep-restricted subjects ( $P < 0.001$ ). The same pattern was observed when using weight change as a percentage of admittance body weight and BMI change as dependent variables. Sleep-restricted subjects gained a larger percentage of admittance body weight ( $1.4 \pm 2.0\%$ ;  $F(1, 223) = 7.40$ ,  $P < 0.007$ ) and exhibited a greater increase in BMI ( $0.33 \pm 0.49$ ;  $F(1, 223) = 8.42$ ,  $P < 0.004$ ) than control subjects (percentage of admittance weight change:  $0.2 \pm 2.6\%$ ; BMI change:  $0.03 \pm 0.63$ ). Sleep-restricted subjects whose caloric intake was monitored ( $n = 31$ ) gained  $0.52 \pm 1.60$  kg during the protocol and control subjects whose caloric intake was monitored ( $n = 6$ ) lost  $0.53 \pm 1.16$  kg during the protocol.

Among sleep-restricted subjects there were significant main effects for gender and race; males gained more weight than females ( $F(1, 192) = 8.29$ ,  $P = 0.004$ ,  $d = 0.37$ ) and African Americans gained more weight than Caucasians ( $F(1, 192) = 9.10$ ,  $P = 0.003$ ,  $d = 0.38$ ). African American





**Figure 1**—Effect of sleep loss on weight gain. (A) Subjects were healthy adults aged 22–50 y with a body mass index ranging between 19–30. Sleep-restricted subjects gained significantly more weight than control subjects ( $d = 0.51$ ). (B) Among sleep-restricted subjects, African Americans gained more weight than Caucasians ( $d = 0.37$ ) and males gained more weight than females ( $d = 0.38$ ). Data expressed as mean  $\pm$  standard error of the mean, \* $P < 0.05$ .

males showed the most weight gain, Caucasian females showed the least weight gain, and Caucasian males and African American females showed intermediate weight gain (*post hoc* analyses illustrated in Figure 1B). There were no sex or race differences in weight change in control subjects ( $P_s > 0.10$ ). The same pattern was observed when using weight change as a percentage of admittance body weight and BMI change as dependent variables. Among sleep-restricted subjects, African Americans gained a larger percentage of admittance body weight ( $1.7 \pm 2.2\%$ ;  $F(1, 223) = 9.85$ ,  $P = 0.002$ ) and exhibited a greater increase in BMI ( $0.40 \pm 0.52$ ;  $F(1, 223) = 9.18$ ,  $P = 0.003$ ) than Caucasians (percentage of admittance weight change:  $0.94 \pm 1.8\%$ ; BMI change:  $0.22 \pm 0.42$ ) and males gained a larger percentage of admittance body weight ( $1.6 \pm 2.0\%$ ;  $F(1, 223) = 5.38$ ,  $P = 0.02$ ) and exhibited a greater increase in BMI ( $0.38 \pm 0.50$ ;  $F(1, 223) = 4.96$ ,  $P = 0.03$ ) than females (percentage of admittance weight change:  $1.11 \pm 1.96\%$ ; BMI change:  $0.26 \pm 0.47$ ).

### Caloric Intake

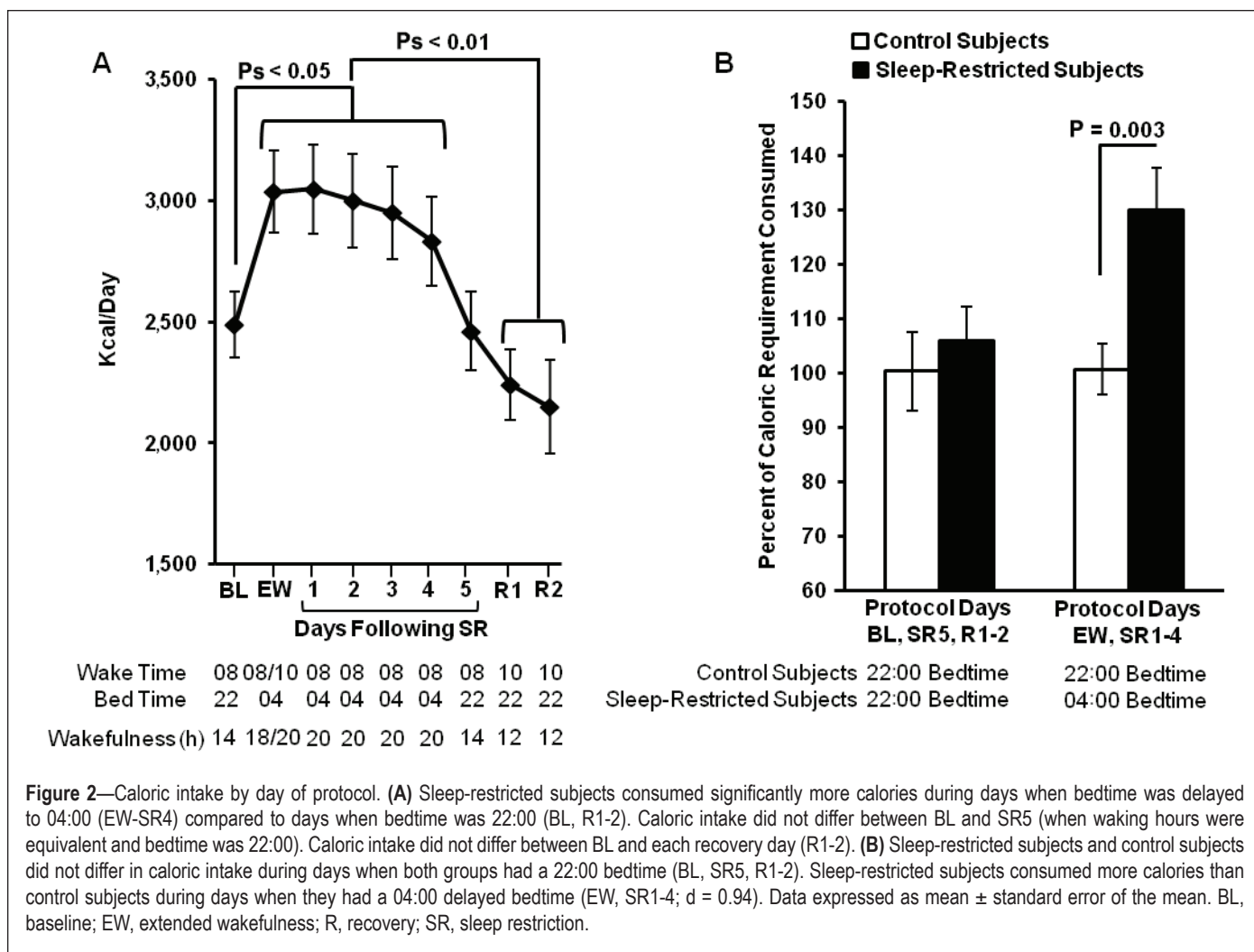
In control subjects, caloric intake did not vary significantly across protocol days ( $P = 0.09$ ). By contrast, in sleep-restricted subjects, caloric intake varied significantly across BL and SR days ( $F(6, 180) = 7.49$ ,  $P < 0.001$ ) and across BL, SR, and R days ( $F(8, 144) = 6.79$ ,  $P < 0.001$ ). Subjects consumed more calories during days when bedtime was delayed until 04:00 (EW, SR1–4; Figure 2A) compared to BL (*post hoc* analyses,  $P_s < 0.05$ ) and recovery days (*post hoc* analyses,  $P_s < 0.01$ ). On days when

bedtime and hours spent awake were comparable (BL and SR5), caloric intake did not significantly differ ( $P = 0.79$ ).

In order to compare caloric intake between sleep-restricted subjects and control subjects as well as to examine the relationship between caloric intake and weight change, caloric intake was calculated as a percentage: actual daily caloric intake / estimated daily caloric intake required for weight maintenance. Each subject's daily caloric intake required for weight maintenance was estimated using the Harris-Benedict equation<sup>45</sup> for basal metabolic rate [(men =  $66.4730 + (13.7516 * \text{weight (kg)}) + (5.0033 * \text{height (cm)}) - (6.755 * \text{age (y)})$ ); women =  $655.0955 + (9.5634 * \text{weight (kg)}) + (1.850 * \text{height (cm)}) - (4.676 * \text{age (y)})$ ] multiplied by 1.4, which corresponds to a sedentary lifestyle representative of a laboratory study in which activity is limited.<sup>46</sup> Average caloric intake was not significantly different between control and sleep-restricted subjects during days with a 22:00 bedtime (BL, SR5, R1–2;  $P = 0.58$ ). However, sleep-restricted subjects consumed significantly more calories than control subjects during days when they had a delayed bedtime (EW, SR1–4;  $F(1, 31.03) = 3.26$ ,  $d = 0.94$ ,  $P = 0.003$ ; see Figure 2B). In sleep-restricted subjects, average caloric intake during days with a delayed bedtime (EW-SR4) was significantly positively correlated with weight change (Spearman's  $\rho = 0.64$ ,  $P < 0.001$ ).

### Macronutrients

In sleep-restricted subjects, the number of grams consumed from each nutrient varied significantly across BL and SR days (protein:  $F(6, 180) = 5.74$ ,  $P < 0.001$ ; carbohydrates:



F (6, 180) = 6.78,  $P < 0.001$ ); fat: F (6, 180) = 4.70,  $P < 0.001$ ) and across BL, SR, and R days (protein: F (8, 144) = 6.18,  $P < 0.001$ ; carbohydrates: F (8, 144) = 5.23,  $P < 0.001$ ); fat: F (8, 144) = 5.17,  $P < 0.001$ ; Table 1). Consistent with increases in total caloric intake, sleep-restricted subjects consumed more grams of each nutrient during the first four delayed bedtime days (EW, SR 1-3) compared to baseline (*post hoc* analyses,  $P_s < 0.05$ ) whereas on the fourth day following sleep restriction (SR4), when overall caloric intake remained greater than BL intake, only fat consumption was significantly greater than BL ( $P < 0.05$ ; Table 1). Macronutrient consumption was not significantly different between BL and SR5 protocol days ( $P_s > 0.40$ ). Macronutrient consumption during each recovery day was not significantly different from BL or SR5 intake ( $P_s > 0.10$ ) but was lower than intake during delayed bedtime days (EW, SR1-4; *post hoc* analyses,  $P_s < 0.05$ ; Table 1).

To control for changes in total caloric intake across protocol days, the percentage of daily caloric intake derived from protein, carbohydrates, and fat were also calculated and compared (Table 1). There were no significant differences in the percentage of calories from protein, carbohydrates, or fat across all protocol days.

### Meal Patterns

The US Department of Labor considers 30 min sufficient for a 'meal period'<sup>747</sup>; therefore, meals were considered as discrete

episodes if there was a minimum of 30 min between intake bouts. The total number of meals varied across BL and SR days (F (6, 180) = 16.41,  $P < 0.001$ ) and across BL, SR, and R days (F (8, 144) = 12.45,  $P < 0.001$ ; Table 1). Compared with baseline, subjects consumed more meals during days when bedtime was delayed (EW, SR1-4; *post hoc* analyses,  $P_s < 0.01$ ). The number of meals consumed during the fifth day following sleep restriction (SR5) did not differ from those consumed during BL ( $P_s > 0.10$ ). Compared with each R day, subjects consumed more meals during days when bedtime was delayed (EW, SR1-4; *post hoc* analyses,  $P_s < 0.01$ ). The number of meals consumed during each R day did not differ from the number of meals consumed during BL and SR5 ( $P_s > 0.30$ ).

When examining average meal size, overall ANOVAs comparing meal size across BL and SR days (F (6, 180) = 3.16,  $P = 0.006$ ) and across BL, SR, and R days (F (8, 144) = 2.86,  $P < 0.06$ ) were significant (Table 1). However, *post hoc* analyses comparing EW, and SR1-5 days to BL and *post hoc* analyses comparing BL, EW, and SR1-5 days to each R day were not significant ( $P_s > 0.05$ ; Table 1).

### Meal Timing

Daily caloric intake was calculated for three time intervals: 08:00-14:59, 15:00-21:59 and 22:00-03:59 for BL and SR days. The first two time intervals were created by dividing the common

**Table 1**—Mean  $\pm$  standard deviation macronutrient content and meal patterns of caloric intake by protocol day

	Macronutrients and meal patterns								
	Total calories	Protein		Carbohydrates		Fats		Meal number	Meal size (calories)
		Grams	%	Grams	%	Grams	%		
BL	2,489.4 $\pm$ 759.2	85.2 $\pm$ 25.5	14.0	368.5 $\pm$ 118.8	59.2	79.9 $\pm$ 33.5	28.5	3.8 $\pm$ 0.9	644.1 $\pm$ 192.2
EW	3,036.2 $\pm$ 949.9 <sup>a,b</sup>	111.3 $\pm$ 34.2 <sup>a,b</sup>	15.2	434.6 $\pm$ 145.0 <sup>a,b</sup>	57.3	102.3 $\pm$ 38.1 <sup>a,b</sup>	29.8	5.2 $\pm$ 0.9 <sup>a,b</sup>	583.0 $\pm$ 207.6
SR1	3,047.3 $\pm$ 1,018.6 <sup>a,b</sup>	101.1 $\pm$ 37.4 <sup>a,b</sup>	13.3	446.4 $\pm$ 155.8 <sup>a,b</sup>	58.7	103.0 $\pm$ 42.0 <sup>a,b</sup>	30.1	4.6 $\pm$ 1.1 <sup>a,b</sup>	670.9 $\pm$ 236.0
SR2	2,999.3 $\pm$ 1,083.8 <sup>a,b</sup>	101.2 $\pm$ 39.5 <sup>a,b</sup>	13.6	432.1 $\pm$ 161.3 <sup>a,b</sup>	57.8	104.4 $\pm$ 44.5 <sup>a,b</sup>	31.2	5.3 $\pm$ 1.7 <sup>a,b</sup>	578.1 $\pm$ 209.4
SR3	2,949.9 $\pm$ 1,068.8 <sup>a,b</sup>	101.2 $\pm$ 39.8 <sup>a,b</sup>	13.9	436.7 $\pm$ 166.7 <sup>a,b</sup>	59.2	95.3 $\pm$ 46.0 <sup>a,b</sup>	28.9	5.2 $\pm$ 1.3 <sup>a,b</sup>	573.9 $\pm$ 183.3
SR4	2,833.0 $\pm$ 1,016.5 <sup>a,b</sup>	95.3 $\pm$ 43.4 <sup>b</sup>	13.4	402.4 $\pm$ 141.5 <sup>b</sup>	57.4	100.0 $\pm$ 43.9 <sup>a,b</sup>	31.3	5.0 $\pm$ 1.5 <sup>a,b</sup>	575.8 $\pm$ 224.7
SR5	2,462.3 $\pm$ 894.9	84.0 $\pm$ 33.8	13.8	357.5 $\pm$ 131.6	58.7	82.66 $\pm$ 39.1	29.5	3.6 $\pm$ 0.8	685.2 $\pm$ 296.2
R1	2,241.4 $\pm$ 628.4	69.0 $\pm$ 25.5	12.6	356.0 $\pm$ 97.7	63.8	66.4 $\pm$ 28.8	26.2	3.6 $\pm$ 0.8	624.4 $\pm$ 154.6
R2	2,149.3 $\pm$ 839.0	73.0 $\pm$ 33.0	13.6	327.9 $\pm$ 138.1	61.2	65.4 $\pm$ 31.7	27.2	3.8 $\pm$ 1.1	576.6 $\pm$ 206.1

% is representative of total daily caloric intake. <sup>a</sup>Significantly different from BL; Ps < 0.05. <sup>b</sup>Significantly different from each Recovery Day (R1-2); Ps < 0.05. BL, baseline; EW, extended wakefulness; R, recovery; SR, sleep restriction.

**Table 2**—Mean  $\pm$  standard deviation timing of caloric intake by protocol day

	Meal timing						
	Total calories	08:00-14:59		15:00-21:59		22:00-03:59	
		Calories	%	Calories	%	Calories	%
BL	2,489.4 $\pm$ 759.2	1,475.3 $\pm$ 428.8	60.5	1,014.1 $\pm$ 470.1	39.4	—	—
EW	3,036.2 $\pm$ 949.9 <sup>a</sup>	1,481.4 $\pm$ 517.4	48.8 <sup>a</sup>	887.8 $\pm$ 357.2	29.2 <sup>a</sup>	666.9 $\pm$ 263.1	22.0
SR1	3,047.3 $\pm$ 1,018.6 <sup>a</sup>	1,450.9 $\pm$ 469.0	48.6 <sup>a</sup>	1,140.6 $\pm$ 452.2	37.8	455.7 $\pm$ 380.2 <sup>b</sup>	13.6 <sup>c</sup>
SR2	2,999.3 $\pm$ 1,083.8 <sup>a</sup>	1,374.4 $\pm$ 519.8	46.4 <sup>a</sup>	1,139.1 $\pm$ 453.5	39.0	485.8 $\pm$ 386.5	14.7 <sup>c</sup>
SR3	2,949.9 $\pm$ 1,068.8 <sup>a</sup>	1,329.8 $\pm$ 463.1	46.7 <sup>a</sup>	1,075.2 $\pm$ 608.4	35.6	544.9 $\pm$ 326.8	17.7
SR4	2,833.0 $\pm$ 1,016.5 <sup>a</sup>	1,307.6 $\pm$ 487.0	47.6 <sup>a</sup>	914.1 $\pm$ 437.3	32.2 <sup>a</sup>	611.3 $\pm$ 392.3	20.2
SR5	2,462.3 $\pm$ 894.9	1,445.0 $\pm$ 552.9	59.6	1,017.3 $\pm$ 473.5	40.4	—	—

% is representative of total daily caloric intake. <sup>a</sup>Significantly different from BL; Ps < 0.05. <sup>b</sup>Significantly different from EW; Ps < 0.05. <sup>c</sup>Significantly different from EW and SR4; Ps < 0.05. BL, baseline; EW, extended wakefulness; SR, sleep restriction.

waking hours across BL and SR protocol days into two equal 7-h intervals. The third time interval equaled the 6 h of wakefulness that occurred during delayed bedtime days (EW, SR1-SR4) but not during the baseline and SR5 protocol days. Recovery days were not included in these analyses due to a delayed wake time (10:00) that differed from the other protocol days.

Total caloric intake during 08:00-14:59 was lower during days following SR (SR1-5) compared to days following BL sleep (BL and EW;  $F(1, 30) = 4.23$ ,  $P = 0.047$ ; Figure 3A); however, calories consumed during 15:00-21:59 did not significantly differ between conditions ( $P = 0.096$ ; Figure 3A). Caloric intake during 22:00-03:59 varied across days ( $F(4, 120) = 3.48$ ,  $P = 0.01$ ); this overall difference was due to a significant reduction in calories consumed between the first and second nights with a delayed bedtime (EW and SR1; *post hoc* analyses,  $P < 0.05$ , Table 2). Across all nights with a delayed bedtime, subjects chose to consume calories during each hour of the late-night interval as follows: 22:00-22:59:  $n = 19$  (61%), 23:00-23:59:  $n = 13$  (42%), 00:00-00:59:  $n = 25$  (81%), 01:00-01:59:  $n = 23$  (74%), 02:00-02:59:  $n = 25$  (81%), and 03:00-03:59:  $n = 13$  (42%); thus, intake was not limited to only the specified meal time (00:30), but occurred throughout the late-night

interval. Notably, a majority of subjects voluntarily chose to consume calories during the late-night interval on each night: EW:  $n = 31$  (100%), SR1:  $n = 26$  (84%), SR2:  $n = 28$  (90%), SR3:  $n = 29$  (94%), SR4:  $n = 31$  (100%).

The percentage of daily caloric intake during each of the three time intervals was calculated to control for total caloric intake changes across protocol days. The percentage of calories consumed during the first two time intervals differed significantly across BL and SR days (08:00-14:59:  $F(6, 180) = 11.21$ ,  $P < 0.001$ ; 15:00-21:59:  $F(6, 180) = 4.53$ ,  $P < 0.001$ ; Table 2). Subjects consumed a significantly lower percentage of calories from 08:00-14:59 during delayed bedtime days compared to the day following baseline sleep (*post hoc* analyses,  $P_s < 0.05$ ), and a lower percentage of calories from 15:00-21:59 during EW and SR4 days compared to the BL day (*post hoc* analyses  $P_s < 0.05$ ). The percentage of calories consumed during the late-night time interval varied across SR days (22:00-03:59:  $F(4, 120) = 6.27$ ,  $P < 0.001$ ; Table 2). The percentage of calories consumed from 22:00-03:59 was greater during the first and fifth night of SR (EW and SR4) compared to the second and third nights of SR (SR1 and 2; *post hoc* analyses,  $P_s < 0.05$ , Table 2).

## Macronutrients

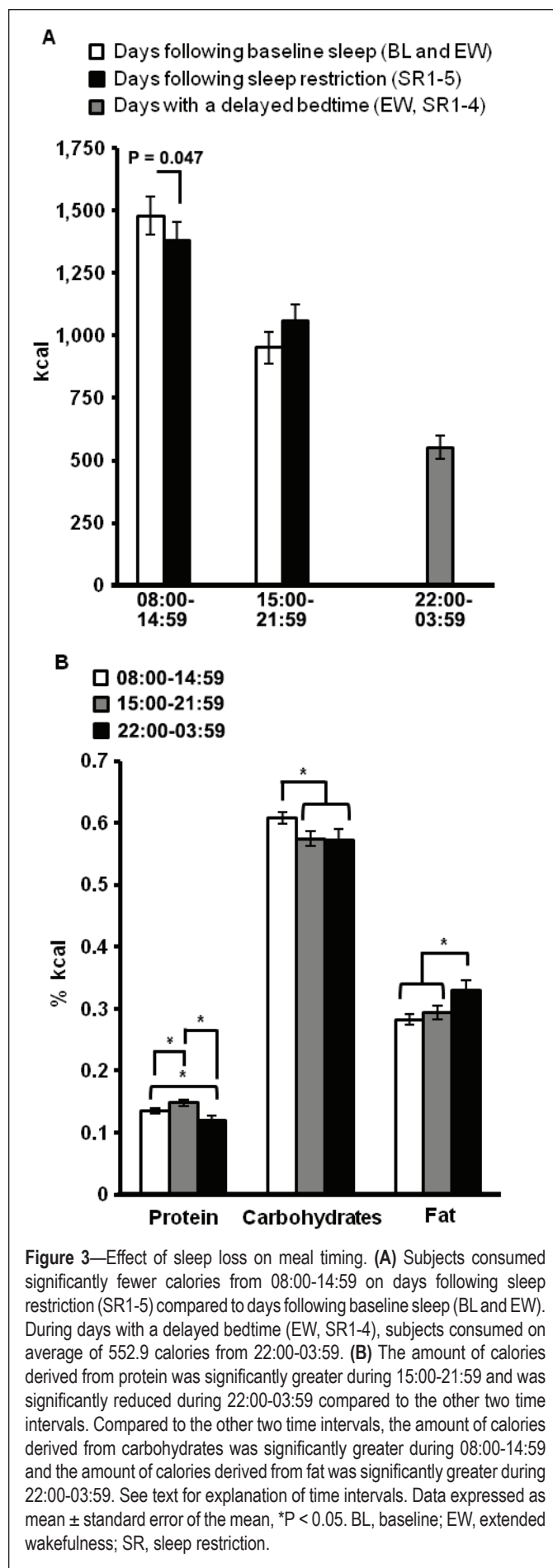
The number of grams and the percentage of calories derived from protein, carbohydrate, and fat during each time interval were calculated and compared across protocol days. There were no significant differences in the macronutrient content (grams or percentage of calories) consumed during each time interval across protocol days ( $P_s > 0.05$ ). The macronutrient content during each time interval was averaged across all days and also compared. The macronutrient content of each time interval differed significantly (protein:  $F(2, 60) = 8.12, P = 0.001$ ; carbohydrates:  $F(2, 60) = 3.48, P = 0.04$ ; fat:  $F(2, 60) = 7.29, P = 0.001$ ; Figure 3B). The amount of calories derived from protein was significantly greater during 15:00-21:59 and was significantly reduced during 22:00-03:59 compared to the other two time intervals ( $P_s < 0.05$ ). Compared to the other two time intervals, the amount of calories derived from carbohydrates was significantly greater during 08:00-14:59 ( $P_s < 0.05$ ) and the amount of calories derived from fat was significantly greater during 22:00-03:59 ( $P_s < 0.05$ ).

## DISCUSSION

In the largest sample of healthy adults studied to date under controlled laboratory conditions, sleep-restricted subjects gained more weight than control subjects. Among sleep-restricted subjects, African Americans gained more weight than Caucasians and males gained more weight than females. Among sleep-restricted subjects, caloric intake during days with a delayed bedtime was positively associated with weight gain. Sleep-restricted subjects consumed an excessive amount of calories beyond daily caloric requirements during days with a delayed bedtime compared with control subjects who consumed an adequate amount of calories during corresponding days. Thus, increases in caloric intake in sleep-restricted subjects were not due to novelty of the laboratory setting or other environmental factors.

In sleep-restricted subjects, daily caloric intake was increased during days when their bedtime was delayed until 04:00 (EW, SR1-4) compared to days when their bedtime was 22:00 (BL, SR5, R1-2) and this increase was associated with greater intake of all three macronutrients and greater meal frequency. Compared to days following BL sleep (BL and EW), the amount of calories consumed from 08:00-14:59 was reduced (by 96.8 calories), the amount of calories consumed from 15:00-21:59 was not significantly changed, and 552.9 additional calories were consumed from 22:00-03:59 during sleep restriction. Thus, the overall increase in caloric intake on days with a delayed bedtime was exclusively due to intake during the late-night period of additional wakefulness.

Our experimental weight gain findings support the relationship between short sleep duration and increased BMI observed in epidemiological studies<sup>16-19</sup> and those studies indicating that males may be more susceptible to weight gain resulting from sleep loss.<sup>20,21</sup> Sleep-restricted African Americans were particularly vulnerable to weight gain—this finding is important considering African Americans are more likely to habitually sleep less than 6 h per night.<sup>2,48</sup> We are currently examining the behavioral and physiological mechanisms underlying differences in weight gain following sleep restriction between males and females and between African Americans and Caucasians.





Consistent with previous studies examining *ad libitum* food access during sleep restriction,<sup>15,22</sup> our subjects increased caloric intake during days with a delayed bedtime. This caloric intake increase occurred during the EW day that did not follow sleep restriction but consisted of a 20-h day with a 04:00 bedtime, and notably did not occur during the SR5 day that followed sleep restriction but consisted of only 14 h of wakefulness and a 22:00 bedtime. The increase in caloric intake on EW but not on SR5 suggests that a delayed bedtime and/or hours of wakefulness may be better predictors of caloric intake than sleep duration the preceding night. Future studies are needed to determine the amount of additional calories burned with a delayed bedtime to compare increased caloric intake and the increased energy expenditure required from extended wakefulness. Jung and colleagues<sup>49</sup> measured energy expenditure in a total sleep deprivation paradigm and found that approximately 134 additional calories were needed for an 8-h extended wake time; however, their subjects were confined to bed rest, so this finding likely is an underestimation of energy requirements under normal activity conditions. The positive correlation between weight gain and caloric intake during sleep restriction in our study suggests that subjects consumed more calories than necessary to compensate for the additional energy requirement of extended wakefulness.

In the current study, meal times were specified in the protocol to ensure that subjects had adequate time to eat; however, subjects were told they could eat/drink whenever they were not testing. Subjects were never presented with food/drink or told that they had to eat at a specific time; rather, food and drinks were always available for them to retrieve from the laboratory kitchen. Based on this *ad libitum* design, we were able to examine meal patterns (the number of meals subjects consumed throughout the day and the size of each meal they consumed) as well as meal timing (when subjects chose to consume calories). We observed an increase in the number of meals consumed during days with a delayed bedtime without a change in average meal size. This is an important finding because meal patterns are indicative of physiological mechanisms underlying caloric intake; the factors that control meal onset (meal number) are distinct from those that control meal termination (meal size).<sup>50</sup> Processes that promote meal termination and limit meal size include gastrointestinal signals such as gastric distention and cholecystokinin.<sup>50</sup> Postprandial signals (which affect the interval to the next meal) and meal initiation signals (which influence the start of meals) regulate meal number.<sup>50</sup> Based on our findings, it is more likely that sleep restriction and a delayed bedtime affected postprandial and meal initiation signals rather than satiation signals. For example, ghrelin, a meal initiation signal, increases meal number without affecting the size of meals and studies have shown that ghrelin levels are increased during SR.<sup>12</sup> Future studies should focus on how ghrelin is modulated by extended wakefulness/sleep loss and examine other postprandial signals such as hypothalamic dopamine<sup>51</sup> and amylin.<sup>52</sup>

Contrary to previous findings from a 14-day SR protocol,<sup>16</sup> we did not observe an increase in carbohydrate intake during days with a delayed bedtime. The proportion of calories derived from protein, carbohydrates, and fat were consistent across all protocol days. Therefore, subjects did not overconsume a specific macronutrient at the expense of the other two macro-

nutrients during sleep restriction. Our study only consisted of 5 nights of SR; therefore, we may have observed changes in macronutrient intake with a longer SR protocol. On protocol day SR4, subjects consumed significantly more grams of fat compared to the baseline day whereas grams of protein and carbohydrates consumed were not different between these 2 days. This increase in fat consumption is consistent with a SR experiment in adults which found an increase in fat consumption<sup>22</sup> and a study showing that adolescents who were short sleepers (less than 8 h per night) consumed more fat compared to their peers who slept 8 h or more per night.<sup>24</sup>

Recent research has highlighted the critical contribution of meal timing to weight regulation.<sup>26</sup> We observed a shift in the timing of caloric intake during days with a delayed bedtime. Subjects consumed additional calories during the late-night period when they remained awake and then consumed fewer calories the morning following SR. Thus, the proportion of calories consumed was altered such that subjects consumed the majority of calories in early evening/late-night hours rather than in morning/early afternoon hours. Previous experiments have shown that mice gained more weight when consuming calories during a period when they were normally asleep compared to mice who were fed on a normal schedule, even when the same amount of calories were consumed.<sup>33</sup> Therefore, future studies should vary schedules of SR in humans to determine whether bedtime affects the timing of caloric intake and weight gain. In addition, studies examining brain activation and the neuroendocrine mechanisms underlying the relationship between sleep duration and energy balance, should focus on this late-night period, when additional calories are consumed.

We also observed an increase in the proportion of calories from fat during late-night hours; this increase may be particularly contributory to weight gain. Baron and colleagues found that the percentage of fat consumed after 22:00 was associated with greater total caloric intake and a higher BMI among individuals.<sup>53</sup> In a laboratory controlled study, patients with night eating syndrome exhibited a delay in carbohydrate and fat intake compared to healthy control subjects<sup>54</sup> and epidemiological studies have shown that patients with night eating syndrome are at greater risk for obesity<sup>55,56</sup> and weight gain.<sup>29,57</sup> Recent studies examining brain activation in the morning following sleep loss showed that neuronal activity in response to food stimuli was greater after restricted sleep compared to after habitual sleep<sup>58</sup> and that total sleep deprivation was associated with increased activation of the right anterior cingulate cortex, an area involved in reward and anticipation, in response to food images.<sup>59</sup> Future studies focusing on sleep loss and brain activation should examine subjects during the late-night period of extended wakefulness as this is the time when neuronal activity related to reward may be associated with increased fat consumption.

### Limitations

Our study has several limitations. First, energy expenditure is an important factor that might contribute to weight gain. Subjects in our study were not allowed to exercise during the protocol; therefore, activity levels were limited. Because caloric intake was *ad libitum*, subjects did not fast during the protocol and therefore we could not assess resting metabolic rate, which may be affected by sleep loss. Second, although caloric intake



was *ad libitum*, subjects were only allowed to consume food and drink provided by hospital and laboratory staff; foods that contained caffeine (including chocolate) were prohibited. In addition, although there were approximately 10 opportunities to eat during a typical protocol day, subjects were not allowed to eat/drink during neurobehavioral testing that occurred throughout the day. Therefore, subjects may have desired to eat certain foods that were unavailable to them or may have wanted to eat during certain times when they were not allowed to do so due to testing; both factors may have reduced total caloric intake and subsequent weight gain. Third, it should be noted that timing of caloric intake and voiding varied across subjects prior to weight measurements. Fourth, our subjects were healthy, were between the ages of 22-50 y, and had BMIs between the range of 19-30. The results may therefore not generalize to other groups, including obese individuals, adolescents or the elderly. Finally, the sample size of subjects with caloric intake information was too small to make comparisons between race and gender—thus, we cannot determine whether caloric intake underlies the race and gender weight gain differences.

## CONCLUSIONS

Previous epidemiological studies indicate a relationship between short sleep duration and weight gain. The current study examined behavioral mediators of this relationship by objectively measuring weight, caloric intake, and meal timing in controlled laboratory protocols involving 5 nights of sleep restricted to 4 h TIB per night. Sleep-restricted subjects gained more weight compared to controls and showed significant gender and race differences in weight gain. Chronically sleep-restricted subjects with late bedtimes may be more susceptible to weight gain and obesity due to overall greater caloric intake as well as increased consumption during late-night hours. Such caloric intake during late-night hours may be particularly contributory to weight gain as these calories appear to be greater in fat compared to calories consumed during morning, afternoon, and evening hours.

## ACKNOWLEDGMENTS

The authors thank the subjects who participated in the experiments and the faculty and staff of the Division of Sleep and Chronobiology who helped acquire the data. Work for this study was performed at the Division of Sleep and Chronobiology, Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA. This research was supported by NIH grants R01 NR004281 (to Dr. Dinges) and F31 AG044102 (to Ms. Spaeth); the Department of the Navy, Office of Naval Research Award No. N00014-11-1-0361 (to Dr. Goel); Clinical and Translational Research Center (CTRC) grant UL1TR000003; and National Space Biomedical Research Institute through NASA award NCC 9-58 (to Dr. Dinges).

## DISCLOSURE STATEMENT

This was not an industry supported study. Dr. Goel has received compensation for serving as a consultant on NASA and NSBRI grants, for serving as a NIH study section member, and for lectures delivered at the University of Pittsburgh Medical Center, Drexel University College of Medicine, the World Federation of Sleep Research & Sleep Medicine Societies meeting,

and the Society for Light Treatment and Biological Rhythms meeting. Dr. Dinges is compensated for serving on a scientific advisory council for Mars, Inc. Dr. Dinges is compensated by the Associated Professional Sleep Societies, LLC, for serving as Editor in Chief of *SLEEP* and Dr. Goel is an Associate Editor for *SLEEP*. Dr. Goel and Dr. Dinges recuse themselves from all decisions related to *SLEEP* manuscripts on which they have a conflict of interest. Ms. Spaeth has indicated no financial conflicts of interest.

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