Impact of insufficient sleep on total daily energy expenditure, food intake, and weight gain

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Insufficient sleep is associated with obesity, yet little is known about how repeated nights of insufficient sleep influence energy expenditure and balance. We studied 16 adults in a 14- to 15-d-long inpatient study and quantified effects of 5 d of insufficient sleep, equivalent to a work week, on energy expenditure and energy intake compared with adequate sleep. We found that insufficient sleep increased total daily energy expenditure by ∼5%; however, energy intake—especially at night after dinner—was in excess of energy needed to maintain energy balance. Insufficient sleep led to 0.82 ± 0.47 kg (±SD) weight gain despite changes in hunger and satiety hormones ghrelin and leptin, and peptide YY, which signaled excess energy stores. Insufficient sleep delayed circadian melatonin phase and also led to an earlier circadian phase of wake time. Sex differences showed women, not men, maintained weight during adequate sleep, whereas insufficient sleep reduced dietary restraint and led to weight gain in women. Our findings suggest that increased food intake during insufficient sleep is a physiological adaptation to provide energy needed to sustain additional wakefulness; yet when food is easily accessible, intake surpasses that needed. We also found that transitioning from an insufficient to adequate/recovery sleep schedule decreased energy intake, especially of fats and carbohydrates, and led to −0.03 ± 0.50 kg weight loss. These findings provide evidence that sleep plays a key role in energy metabolism. Importantly, they demonstrate physiological and behavioral mechanisms by which insufficient sleep may contribute to overweight and obesity.

calorimetry | misalignment | dysregulated eating | deprivation | restriction

More than 1.4 billion adults, 150 million school-aged children, and 43 million preschool children are estimated to be overweight or obese worldwide (1–3), substantially raising risk for cardiovascular diseases (4) hyperlipidemia (5), diabetes (5, 6), osteoarthritis (6), sleep apnea (7), depression (8), and cancer (9). Excessive food consumption and inadequate physical activity are primary factors contributing to the obesity epidemic. When daily energy intake is in excess of energy expenditure (EE) a state of positive energy balance occurs. Over weeks, months, or years, a small cumulative impact of sustained positive energy balance results in weight gain and obesity (10). Alongside the rise in obesity there has been a decline in the number of individuals who report obtaining the recommended 7–9 h of sleep, with many obtaining less than 6 h per night (11). Insufficient sleep is a risk factor of weight gain and obesity (11–13), yet how insufficient sleep contributes to this risk is unclear. Sleep influences energy metabolism (14, 15), and one function of sleep is to conserve energy (16). Proposed mechanisms that associate insufficient sleep and higher body mass index (BMI) include changes in satiety and hunger hormones altering food intake and changes in EE (17). Insufficient sleep is associated with decreases in the satiety hormone leptin, increases in the hunger-stimulating hormone ghrelin, and increases in appetite when food intake is controlled (18, 19). It has also been hypothesized that chronic insufficient sleep reduces EE, leading to weight gain (17). Understanding mechanisms by which insufficient sleep contributes to weight gain and obesity has public health relevance for education on importance of adequate sleep for health and has therapeutic implications for discovery of novel strategies to prevent weight gain and assist with weight loss and weight maintenance programs. Therefore, a primary aim of the current study was to quantify the energy cost of insufficient sleep and associated changes in food intake. Here, we report results from a 2-wk-long Clinical Translational Research Center (CTRC) study at the University of Colorado Hospital that used whole room calorimetry to measure 24-h EE and measured ad libitum food intake to assess both sides of the energy balance equation. We also examined how insufficient sleep affected consumption and oxidation of macronutrients. Lastly, we examined satiety and hunger hormones released by adipose tissue (leptin), stomach (ghrelin), and small intestine [peptide YY (PYY)—PYY reduces food intake], feelings of hunger and physical exhaustion, light exposure, and circadian phase. We hypothesized that insufficient sleep would increase total daily EE and alter satiety and hunger hormones [reduce leptin (18, 19) and PYY and increase ghrelin (18, 19)], resulting in increased hunger and food intake. Furthermore, we expected food intake would be more than necessary to meet increased energy demands of wakefulness during sleep loss, thus leading to positive energy balance and storage of carbohydrates and fats. We hypothesized that transitioning from sleep loss to an adequate sleep schedule would reduce EE and food intake.

Results

Sleep, Light Exposure, and Circadian Phase. Average bed and wake times and circadian melatonin onset and offset times are shown in Fig. 1. After baseline (BL), half the participants were provided a 5-h per night sleep opportunity for 5 d (5-h sleep loss condition), whereas the other half remained on a 9-h per night sleep opportunity for 5 d (9-h adequate sleep control condition) with ad libitum food intake (Fig. S1). Participants then crossed over to the other condition for 5 d, counterbalanced with equal numbers of men and women starting with 5 h or 9 h first. As designed, participants slept similar amounts in BL, 460.7 ± 29.0

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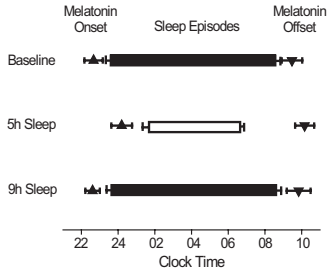

Fig. 1. Sleep and circadian timing. Average timing of sleep episodes (boxes), melatonin onset (black upward triangles), and melatonin offset (black downward triangles). Error bars are SEM. *P* values are calculated by mixed model ANOVAs. Melatonin onset significantly delayed in the 5-h condition ($P < 0.01$ versus BL and 9 h), whereas melatonin offset was similar for conditions ($P = 0.77$). Durations between melatonin onset and bedtime and between melatonin onset and melatonin offset were similar for conditions (both $P > 0.39$), whereas duration between melatonin offset and wake time was significantly longer in the 5-h condition ($P < 0.001$ versus BL and 9 h).

(±SD) and 9 h, 461.5 ± 42.6 min conditions, and slept less in the 5-h condition, 280.0 ± 10.1 min as determined by polysomnography. As participants did not sleep for all of each sleep opportunity, the difference in sleep time between 9-h and 5-h conditions was ∼3 h, equivalent to ∼39% reduction in sleep duration.

Average light exposure during scheduled wakefulness was similar for the BL, 9-h, and 5-h conditions (230 ± 122, 247 ± 101, and 229 ± 102 lx, respectively; $P = 0.47$ for condition; note 1 lx equals light from a candle 1 m away from the eye). Average lux levels during the 4 h of additional wakefulness at the end of the day in the 5-h condition were 91 ± 63 lx. Circadian melatonin phase and phase relationships to scheduled sleep and wake times were similar for BL and 9-h conditions, whereas circadian melatonin onset phase significantly delayed by ∼1.5 h and the duration between wake time and circadian melatonin offset phase was significantly longer in the 5-h condition (Fig. 1).

Total Daily and Hourly EE, Food Consumption, Macronutrient Disappearance and Balance, Energy Balance, and Weight Gain. Participants' total daily EE was ∼9% higher during the 5-h condition compared with BL and ∼5% higher during 5-h versus 9-h conditions ($P < 0.01$; Fig. 2*A*). Fig. 2*B* shows that regardless of condition order, 24-h EE was higher during the 5-h versus 9-h condition. Furthermore, hourly EE was higher during wakefulness versus scheduled sleep regardless of condition (Fig. 3).

At BL, the average daily caloric need was estimated at 2,204 ± 353 kcal. Participants consumed more calories than needed to maintain weight when food was available ad libitum and 24-h food intake was ∼6% greater during the 5-h than 9-h condition ($P < 0.05$; Fig. 2*C*). Table 1 shows participants consumed and used more carbohydrates in the 5-h condition, yet there were no significant differences in carbohydrate balance. Fig. 4 shows that participants consumed a smaller breakfast but consumed 42% more calories as after dinner snacks during sleep loss, which contained more carbohydrates, protein, and fiber (Table 1). Furthermore, during sleep loss, more calories were consumed at night after dinner than calories consumed for any individual meal. Calories consumed as lunch, dinner, and predinner snacks were similar between conditions (all $P > 0.46$). Food intake was influenced by condition order such that participants maintained elevated food intake after transitioning from the 9-h to 5-h condition (Fig. 2*D*) and increased their consumption of carbohydrates from 360.2 ± 106.9 g in 9 h to 390.6 ± 114.1 g in the 5-h condition ($P < 0.05$). In contrast, participants reduced their food intake after transitioning from the 5-h to 9-h condition (Fig. 2*D*), especially consumption of fats, 118.7 ± 32.9 g in 5 h to 106.9 ± 44.3 g in 9 h ($P < 0.05$) and carbohydrates, 398.2 ± 131.7 g in 5 h to 352.9 ± 118.2 g in 9 h ($P < 0.001$).

Overeating led to positive energy balance (Fig. 2*E*) and weight gain (Fig. 2*G*) in both sleep conditions. Although energy balance was not statistically different between conditions, participants on average gained more weight in the 5-h versus 9-h condition (Fig. 2*G*). Participants maintained a state of greater positive energy balance when they transitioned from the 9-h to the 5-h condition (Fig. 2*F*), whereas participants were in a state of lower positive energy balance after they transitioned from the 5-h to 9-h condition (Fig. 2*F*). Related, participants who started in the 9-h condition gained weight (not significant from zero baseline, $P = 0.17$) and subsequently gained additional weight (significant from zero baseline, $P < 0.001$) after they transitioned to the 5-h condition (Fig. 2*H*); whereas participants who started in the 5-h condition initially gained weight (significant from zero baseline, $P < 0.01$) and subsequently lost a small amount of weight (Fig. 2*H*; not significant from zero baseline, $P = 0.88$) after they transitioned to the 9-h condition.

Satiety and Hunger Hormones. Average 24-h leptin levels increased from 5.5 ± 5.2 ng/mL at BL by ∼22% to 6.7 ± 5.1 ng/mL in the 5-h condition ($P < 0.05$); leptin levels were intermediate in the 9-h condition at 5.9 ± 4.7 ng/mL [9-h nonsignificant difference from BL ($P = 0.16$) and 5 h ($P = 0.095$)]. Average 24-h ghrelin levels significantly decreased from 794.6 ± 233.8 pg/mL at BL by ∼30% to 660.2 ± 235.4 pg/mL in 5-h ($P < 0.001$) and by ∼21% to 655.6 ± 229.3 pg/mL in 9-h ($P < 0.01$) conditions (no difference between 5 h and 9 h, $P = 0.81$). Average 24-h PYY levels significantly increased from 100.5 ± 35.1 pg/mL at BL by ∼32% to 136.1 ± 44.8 pg/mL in 5-h ($P < 0.01$) and by ∼35% 133.2 ± 48.8 pg/mL in 9-h ($P < 0.001$) conditions (no difference between 5 h and 9 h, $P = 0.68$). Hourly hormone data are shown in Fig. S2.

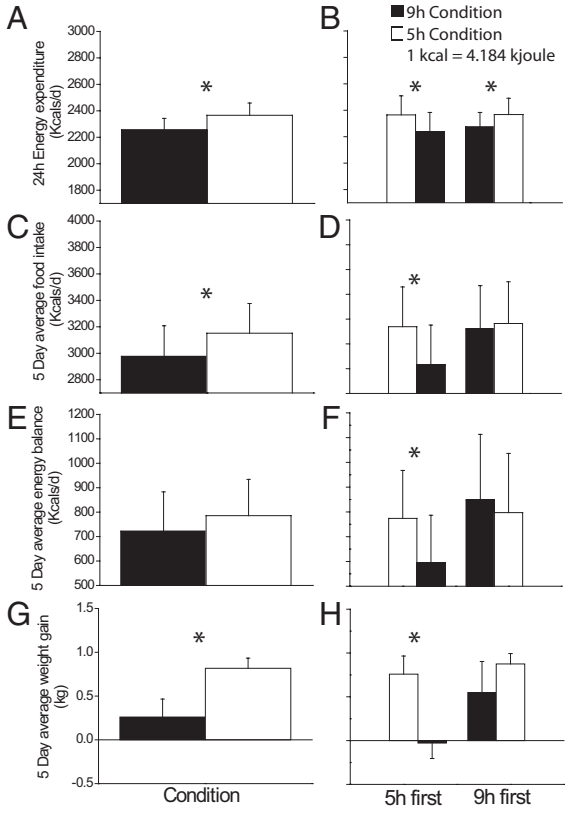

Fig. 2. Effect of sleep loss on energy expenditure, intake, balance, and weight gain. *P* values calculated by mixed model ANOVAs for condition (*Left*, $n = 16$, two-tailed) and planned comparisons for condition by order (*Right*, $n = 8$ each order, one-tailed dependent *t* tests). Error bars are SEM. *Significant difference between 5-h and 9-h conditions ($P < 0.05$).

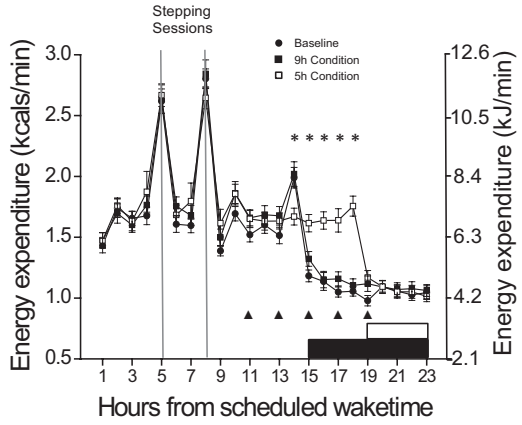

Fig. 3. Hourly energy expenditure in the calorimetry room. Energy expenditure expressed as kilocalories per minute on the *Left* axis and kilojoules per minute on the *Right* axis relative to scheduled wake time. Gray lines represent low-intensity stepping sessions. Error bars are SEM. *P* values are calculated by dependent *t* test with modified Bonferonni correction $P < 0.0159$. *Significant difference between the 5-h condition and baseline and 9-h conditions; ▲ represents significant difference between the baseline and 5-h and 9-h conditions. In addition to significant effects noted, there was a significant difference between baseline and 9-h conditions at hours awake 9.

Hunger and Physical Exhaustion Scales. Hunger decreased from 44.7 ± 21.4 points at baseline by 39% and 37% to 27.1 ± 9.9 and 28.3 ± 12.2 points during the 5-h ($P < 0.01$) and 9-h ($P < 0.01$) conditions, respectively (no difference between 5 h and 9 h, $P = 0.51$). Physical exhaustion increased to 54.9 ± 18.9 points during the 5-h condition by 30% and 19% compared with 42.1 ± 15.5 and 46.0 ± 19.1 points during the BL and 9-h condition, respectively (both $P < 0.001$ versus 5 h; no difference between BL and 9 h, $P = 0.19$). Order effects for scales are shown in Fig. S3.

Sex Differences. Total sleep time, circadian phase shift, and circadian phase relationships did not differ by sex (all $P > 0.37$). Overall, men expended more energy (2,575.6 ± 64.6 kcal/d men versus 2,045.2 ± 56.6 kcal/d women), consumed more calories (3,850.8 ± 118.9 versus 2,277.4 ± 92.4 kcal/d), were in greater positive energy balance (1,275.2 ± 80.2 versus 232.2 ± 74.2 kcal/d), and gained more weight (0.95 ± 0.14 versus 0.13 ± 0.16 kg) than women during ad libitum food availability regardless of sleep opportunity (all sex differences $P < 0.0015$). Hunger significantly decreased in men from baseline to 9-h and 5-h conditions (both $P < 0.01$), whereas hunger did not change in women from baseline to either condition (both $P > 0.69$) (Fig. S3). Compared with baseline, men consumed ∼68% and ∼62% more in the 5-h and 9-h conditions than needed to maintain weight, whereas women consumed ∼19% and ∼10% more than necessary to maintain weight in the 5-h and 9-h conditions, respectively. Men gained weight in the 5-h (1.11 ± 0.09 kg, $P < 0.05$ from zero baseline) and 9-h (0.78 ± 0.25 kg, $P < 0.05$ from zero baseline) (no condition differences in weight gain for men, $P = 0.30$) conditions, whereas women gained weight in the 5-h condition (0.52 ± 0.16 kg; $P < 0.05$ from zero baseline) and lost a small amount of weight in the 9-h condition (−0.26 ± 0.20 kg; not significant from zero baseline $P = 0.23$) (condition differences in weight gain for women $P < 0.05$; sex differences for weight gain within conditions both $P < 0.01$).

Discussion

Insufficient sleep is considered an independent risk factor for weight gain and obesity. We show that 5 d of insufficient sleep increases energy needs, but that sleep loss also increases food intake such that intake is in excess of energy needed leading to weight gain. Food intake, especially of carbohydrates, was high despite appropriate responses of satiety and hunger hormones that signaled food intake was in excess. During sleep loss, participants ate smaller breakfasts but ate more over the day, especially carbohydrates, proteins, and fiber at night after dinner. Changes in circadian phase and the circadian timing of awakening may have contributed to the altered eating patterns during insufficient sleep. Specifically, participants may have eaten smaller breakfasts because they awakened at an earlier circadian phase when the internal circadian clock was promoting sleep; i.e., wake time occurred during the biological night when melatonin levels were still high. Furthermore, a delay in melatonin onset—the beginning of the biological night—may have led to a circadian drive for more food intake at night. Transitioning from sleep loss to an adequate/recovery sleep schedule led to reduced food intake, especially fewer fats and carbohydrates, and to weight loss. Sex differences are in agreement with previous research that women have more dietary restraint than men during ad libitum food intake, selecting a diet that more closely matches their daily caloric needs (20). We uniquely show,

Table 1. Total daily macronutrient intake, disappearance, and balance

Measure	9-h condition ($n = 16$)	5-h condition ($n = 16$)	*P* value
Macronutrient intake			
Carbohydrate, g	356.5 (109.0)	394.4 (119.1)	<0.001
Fat, g	119.6 (48.0)	123.4 (39.8)	0.32
Protein, g	123.3 (39.7)	122.3 (106.6)	0.82
Macronutrient disappearance			
Carbohydrate, g	298.0 (103.7)	319.2 (26.7)	<0.05
Fat, g	66.1 (24.6)	72.5 (30.9)	0.32
Protein, g	87.0 (30.2)	81.9 (25.14)	0.13
Macronutrient balance			
Carbohydrate, g	38.8 (52.4)	54.2 (57.6)	0.23
Fat, g	53.5 (58.0)	50.9 (56.1)	0.63
Protein, g	36.2 (16.8)	40.3 (19.2)	0.28
Macronutrient intake of calories consumed after dinner			
Carbohydrate, g	75.2 (43.6)	118.4 (60.0)	0.001
Fat, g	28.1 (20.6)	33.8 (15.9)	0.13
Protein, g	14.8 (9.6)	21.8 (11.1)	<0.001
Fiber, g	3.2 (1.6)	5.4 (1.9)	<0.001

n, number of participants. Values in parentheses are SD. Comparison of condition effects for 9-h and 5-h sleep opportunities. *P* values are two-tailed calculated by mixed model ANOVAs for main effect of condition.

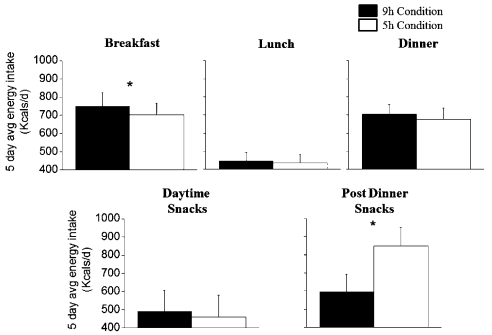

Fig. 4. Energy intake of meals. Energy intake for 9-h and 5-h sleep conditions during ad libitum food availability expressed in kilocalories. Error bars are SEM. *P* values are calculated by mixed model ANOVAs for main effect of condition ($n = 16$). *Significant difference between 5 h and 9 h ($P < 0.05$).

however, that insufficient sleep appears to reduce dietary restraint in women, increasing their risk for weight gain.

Energy Expenditure and Energy Intake During Sleep Loss and Adequate Sleep Schedules. We observed that 5 d of insufficient sleep, equivalent to a work week, increases total daily EE by a physiologically meaningful amount. The average increase of ∼5% (∼111 kcal/d or ∼464 kJ/d) in 24-h EE observed during sleep loss compared with 9-h control is similar to the energy cost of a 70-kg adult performing water aerobics for ∼24 min. Increased total daily EE during sleep loss was predominantly driven by the energy cost of additional wakefulness. This physiologically meaningful difference was not detected in prior research (21, 22). Although factors such as study design and population studied may contribute to this discrepancy, methodological differences associated with the measurement of EE likely explain the majority of the difference in findings. Compared with the whole room calorimetry precision of (0.5–2%), the doubly labeled water technique used in prior research (21, 22) provides less sensitive and precise (∼6–8%) estimates of EE (23). Our finding that 5 d of sleep loss increases EE is unique, but consistent with prior research from our investigative team on the energetic costs of total sleep deprivation (16). Previously, we observed one night of total sleep deprivation under controlled bed rest conditions increased 24-h EE by ∼7% (∼134 kcal/d or ∼562 kJ/d) (16). Taken together, these findings indicate that total sleep deprivation or insufficient sleep both increase daily EE, thus providing further support that one function of sleep in humans is to conserve a small but physiologically meaningful amount of energy. Chronically, if increased energy demands during sleep loss were not met with increased food intake, weight loss would ensue. Thus, insufficient sleep per se may not directly lead to weight gain and findings from nonhuman models support the latter. Specifically, sleep-restricted rodents lost weight even though they ate more (24) and rats with sleep disturbance because of ventrolateral preoptic area of the hypothalamus lesions (25) gained less weight even though they ate normal amounts of food. Although EE was not directly measured in the latter rodent studies, the findings are consistent with the physiological principal that energy needs are higher during sleep loss. Our findings also suggest that negative energy balance and weight loss would ensue over time in studies of sleep loss that provide energy balance diets designed to maintain weight at baseline. This may help to explain why leptin levels are lower and ghrelin levels are higher in prior sleep loss studies that controlled food intake (18, 19). As discussed previously, sleep loss is not a safe or effective means of losing weight (16) and our current findings of dysregulated food intake and weight gain in humans during sleep loss expounds this point.

Our findings indicate an important contributor to weight gain during sleep loss in humans is dysregulated eating behavior. Total daily food intake, especially of carbohydrates, was greater during sleep loss beyond that necessary to meet increased energy needs thus leading to weight gain. In addition, nighttime consumption of postdinner carbohydrate, protein, and fiber calories was 42% higher during sleep loss. Sleep loss has been shown by others to increase consumption of carbohydrate-rich after dinner snacks, but not overall daily intake (21). Thus, nighttime eating after dinner appears to consistently increase during sleep loss, although macronutrients consumed differs between studies, likely reflecting differences in snack options or populations studied (e.g., lean participants in current study versus overweight participants studied in ref. 21). We also found participants ate smaller breakfasts during sleep loss. Our findings add to the growing body of evidence from epidemiological (26) and nonhuman models (27, 28) that indicate that overeating at night may contribute to weight gain.

We show insufficient sleep leads to a delay in circadian timing and thus a change in the circadian timing of meals, especially breakfast. Sleep and circadian systems are highly integrated and sleep loss as a consequence of circadian misalignment is well documented (29, 30). Our finding showing that circadian misalignment may result from maintaining insufficient sleep is unique and indicates that altered circadian timing may contribute to negative health outcomes associated with short sleep schedules. How the circadian timing of meal intake influences metabolic physiology cannot be determined in the current ad libitum protocol. Detailed evaluation of circadian misalignment in future studies of sleep loss is warranted, especially because curtailing sleep by advancing only bed or wake times could have different effects on circadian timing, food intake, and energy metabolism.

Satiety and Hunger Hormones. Findings from prior studies suggest that changes in satiety and hunger hormones during sleep loss, when food intake is controlled, initiate increases in hunger that would augment food intake (18, 19). Our findings indicate however that mechanisms by which sleep loss contributes to weight gain are likely to be more complex as overeating occurred despite increases in leptin and PYY and decreases in ghrelin that signaled food intake was in excess (31–33). Although altered by overeating, leptin, ghrelin, and PYY were still in the range observed in healthy lean individuals. Differences in eating behavior occurred in the 5-h and 9-h conditions despite similar patterns of circulating hormones, and this may be indicative of decreased responsivity to gut fullness and satiety hormones during sleep loss. Our findings showing increased food intake despite changes in hormones that promote satiety/reduce hunger are consistent with findings from studies of clock mutant mice (34) and sleep-restricted ad libitum fed humans (21). The controlled CTRC study limited the duration of sleep loss and thus it is possible that given a longer time course of overeating, participants would have responded to changes in satiety and hunger hormones (35). Changes in other hormones not examined may also promote food intake during sleep loss (e.g., cholecystokinin, glucagon-like peptide-1). Furthermore, why overeating during ad libitum food availability occurred in the 9-h condition is unclear, but perhaps not unexpected based on the availability and palatability of food provided (36), and comparisons of other feeding models during adequate versus insufficient sleep are needed.

Physical Exhaustion Ratings. It is unknown whether higher physical exhaustion observed during sleep loss in our study will translate to lower physical activity levels and more positive energy balance in the social–behavioral environment, as suggested by other laboratory findings (37, 38). As sleep loss induces significant safety impairments in cognitive performance equivalent to alcohol intoxication, we do not believe that experimentally induced sleep loss outside of a controlled laboratory environment is safe.

Effects of Sleep History in an Ad Libitum Feeding Environment. Being awake longer permits a greater opportunity to eat. However, we found that overeating was not simply due to more time to eat, as our counterbalanced-crossover design showed that sleep history influenced overeating. Specifically, participants continued to

overeat a similar amount and gained weight after transitioning from the 9-h to 5-h condition. Conversely, fat and carbohydrate intake was significantly reduced and a small amount of weight loss ensued after transitioning from the 5-h to 9-h condition.

How Does Sleep Loss Promote Weight Gain? Increased food intake during sleep loss appears to be a physiological adaptation to provide the body with the energy needed to sustain extended wakefulness. However, when exposed to the modern obesogenic environment of readily accessible food, weight gain occurs because food intake is more than necessary to offset the energy cost of sleep loss. This weight gain would be exacerbated if physical exhaustion from sleep loss leads to reduced physical activity in the work–home environment. Changes in peripheral satiety and hunger hormones do not explain the overeating we observed. Thus, a central mediated drive to increase food intake to meet the energy demands of sleep loss may have contributed to overfeeding. For example, orexin/hypocretin levels increase during sleep loss (39) and orexin/hypocretin neurons are an important component of sleep–wakefulness and feeding neural systems (40, 41). It is also possible that sleep loss alters brain mechanisms involved in nonhomeostatic food intake (e.g., mood, comfort, reduced eating restraint). As discussed earlier, sleep loss also appears to consistently increase food intake at night. This, plus changes in circadian timing implicate time of day or circadian metabolic pathways in sleep-loss–induced weight gain.

Mounting evidence, including findings from the current study, suggests that public health interventions should include sleep education programs as part of strategies to prevent weight gain. Furthermore, our finding that obtaining an adequate sleep duration reduced overeating and consumption of fats and carbohydrates, combined with findings of reduced fat loss during a caloric restriction regimen when obtaining insufficient sleep (42) indicates clinical trials are needed to determine whether sleep is a modifiable risk factor that can assist weight loss and maintenance programs to improve dietary habits and metabolic health.

Methods

Subjects. Sixteen healthy participants (eight women) aged 22.4 ± 4.8 y (mean ± SD) with self-reported habitual sleep schedules of 8.26 h ± 0.69 h, BMI 22.9 ± 2.4 kg/m^2 and percent body fat 21.8 ± 8.3% as determined by dual energy X-ray absorptiometry (DEXA) (DPX-IQ; Lunar) were studied. Study procedures were approved by the Scientific Advisory and Review Committee of the Colorado Clinical and Translational Sciences Institute, by the Colorado Multiple Institutional Review Board (IRB), and by the University of Colorado, Boulder IRB. Written informed consent was obtained from participants who then underwent health screening including: medical, psychological and sleep history, semistructured clinical psychiatric interview, physical examination, complete blood cell count and comprehensive metabolic panel, urine toxicology, 12-lead electrocardiogram, and polysomnographic sleep disorders screen. Based on these tests, participants were deemed free of medical and psychological disorders. Inclusion criteria were: 18–35 y old; BMI 18.5–24.9 kg/m^2; habitual sleep time >7 and <9.25 h; low–moderate caffeine (<500 mg/d); alcohol use (average fewer than two standard drinks per day per week and five or fewer drinks per day); no drug dependence; and nonsmokers. Low physically active participants were studied to control for detraining during sedentary laboratory procedures on EE. Also see *SI Methods*. Exclusion criteria were: current or chronic medical/psychiatric conditions; pregnancy; shift work or dwelling below Denver altitude (1,600 m) the year prior; travel across more than one time zone 3 wk before CTRC study; maximal lifetime BMI >27.5 kg/m^2; recent self-reported weight loss; and abnormal eating patterns identified by dietitian interview and three-item eating questionnaire (43). Participants self-reported being medication free and urine toxicology for illicit drugs verified drug-free status at screening and CTRC study. All participants who met inclusion criteria and started CTRC procedures completed the protocol.

Study Protocol. One week before study, participants discontinued caffeine use and maintained consistent ~9-h-per-night sleep schedules. Compliance was verified by daily time-stamped call-ins of bed and wake times, sleep diaries, and wrist activity and light-exposure recordings (Actiwatch-L; Phillips Respironics). These procedures ensured participants were not sleep restricted before the CTRC protocol. Three days before the study, participants were provided a diet that met their predicted individual daily caloric needs (DXA or resting metabolic rate with a 1.5 activity factor). The CTRC Nutrition Core prepared meals with daily macronutrient ratios of 30% fat, 55% carbohydrate, and 15% protein reflecting average US daily intake. Participants were instructed to eat all food provided and nothing else except water and exercise was proscribed to ensure they entered the CTRC in energy balance. The CTRC protocol began with a 3-d BL segment of 9-h-per-night sleep opportunities at the participant's habitual bedtime, as determined by prestudy monitoring. This procedure permitted participants to initially sleep at their habitual entrained circadian phase. Sleep was restricted by delaying bedtime and advancing wake time each by 2 h. A 5-h sleep opportunity was chosen because: (*i*) on average it does not reduce deep slow wave sleep as does more severe sleep restriction, (*ii*) it is a level of sleep restriction that occurs across a 5-d work week in many occupations (e.g., military and security operations, emergency responders, and shift workers), and (*iii*) it is a level of sleep restriction that is consistent with that used to examine the influence of sleep loss on metabolism (18, 19, 21, 42). We chose a 9-h sleep opportunity for our control condition to ensure individuals were provided with a sufficient opportunity for sleep. Weight maintenance diets continued for BL days. During ad libitum feeding of the 5-h and 9-h conditions, the CTRC Nutrition Core prepared meals (~1,500 kcal each for breakfast, lunch, dinner, and ~200 kcal each for snack one and snack two at ~2.17 h, 6 h, 10 h, 12 h, and 14 h from scheduled wake time, respectively) designed to provide participants ~130–150% more calories than BL. Additional snack choices were freely available during scheduled wakefulness of the 5-h and 9-h conditions (Table S1). Participants ate as much of scheduled meals and snacks as desired during the 5-h and 9-h conditions. Participants performed 20-min low-intensity stepping sessions twice per day to mimic daily physical activity outside the CTRC. The specially designed sleep research suite permitted exposure of participants to indoor lighting and sunlight through the window during scheduled wakefulness and darkness during scheduled sleep (0 lx achieved by a lockable blackout shade with tracks to prevent light leakage). We chose this procedure to approximate changes in light exposure patterns that occur during insufficient sleep schedules in the home–work–social environment. During calorimeter room days, participants were maintained in dim lighting during scheduled wakefulness (<8 lx maximum) to permit assessment of melatonin levels.

Measures. A whole room calorimeter quantified changes in EE and macronutrient disappearance (16) on the last BL day (day 3) and last day of each sleep condition (days 8 and 13; Fig. S1). EE and respiratory quotient (RQ) were assessed from oxygen (O_2) consumption and carbon dioxide (CO_2) production (16, 44). Gas concentrations were determined from differences in CO_2 and O_2 between entering and exiting air with a fuel-cell–based dual channel O_2 analyzer (FC-2 Oxzilla; Sable Systems International) and two infrared CO_2 analyzers (CA-10 CO_2 analyzers; Sable Systems International) (45). Accuracy and precision of the system is tested monthly using propane combustion tests and average O_2 and CO_2 recoveries during this study were ≥98.0%. Protein disappearance was calculated based on urine total nitrogen (46). EE, carbohydrate, and fat disappearance were calculated from O_2 consumption and RQ (47). Food intake was determined by the CTRC Nutrition Core using ProNutra software (48). We used a 5-d average for food intake for each condition to most accurately represent global changes in food intake that occurred during each condition. Morning body weight was recorded with participants wearing identical clothing. Ghrelin, leptin, PYY, and melatonin were assessed from hourly blood samples during calorimetry room days via an indwelling venous catheter with heparinized saline drip and 12-foot extension tubing through the calorimetry room porthole. This permitted blood sampling without entering the room during scheduled wakefulness and sleep. Visual analog scales were used to assess hunger and physical exhaustion ratings (0 = not hungry at all and 100 = as hungry as I've ever felt; 0 = energetic and 100 = physically exhausted) starting 1.5 h after scheduled wake time and every 2 h thereafter during scheduled wakefulness. Sleep recordings were obtained (Siesta; Compumedics) on day 1 (sleep disorders screen) and the last 2 d of BL, 5-h and 9-h segments of the protocol. Recordings consisted of monopolar EEGs referenced to contralateral mastoids (C3xA2, C4xA1, O1xA2, and F3xA2), right and left electrooculograms, chin electromyogram, electrocardiogram, and respiration. Scheduled wakefulness was verified by research staff via continuous monitoring and with the addition of EEG on calorimetry days.

Data Analyses. EE was calculated hourly and for total daily EE. Macronutrient oxidation was calculated for each 24-h day. Total daily food intake and the caloric intake for meals, as well as scheduled and unscheduled snacks pre- and postdinner time, were calculated. Energy and macronutrient balance was

calculated as the difference between the 5-d average food intake for each condition and total daily EE and macronutrient oxidation measured in the room calorimeter. Carbohydrate balance was calculated factoring fiber intake. Hormones were analyzed as a 24-h mean and hourly. Total sleep time was averaged for sleep recordings the last 2 d of each condition. Circadian phase was determined for the dim-light melatonin onset (DLMO 25%) and dim-light melatonin offset (DLMOff 25%) and phase relationships with bed and wake times and each other were calculated (49, 50). Average outcomes were analyzed with mixed model ANOVAs with condition and condition order as fixed factors and subject as a random factor, also with and without sex as a fixed factor using Statistica (version 10.0; Statsoft). Analyses of sex differences were not planned and are considered exploratory. Hourly outcomes for EE and hormones were analyzed with condition and hours from scheduled wake time as fixed factors and modified Bonferroni correction factors for multiple comparisons. Single sample *t* tests were used to compare changes in weight from a zero baseline. Analyses focused on condition differences with two-tailed tests. Assessment of order effects were of interest as they permitted examination of prior sleep history on ad libitum food intake and energy metabolism (i.e., continuous adequate 9-h sleep opportunities followed by 5-d sleep restriction and 5-d sleep restriction followed by 5-d, 9-h adequate/recovery sleep opportunities). Planned comparisons for condition by order effects were performed using one-tailed dependent *t* tests to test directional hypotheses for primary outcome measures: 24-h EE, food intake, energy balance, and carbohydrate and fat intake, all predicted to be higher during the 5-h condition.

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