Acute sleep deprivation reduces energy expenditure in healthy men1–4

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ABSTRACT

Background: Epidemiologic evidence indicates that chronic sleep curtailment increases risk of developing obesity, but the mechanisms behind this relation are largely unknown.

Objective: We examined the influence of a single night of total sleep deprivation on morning energy expenditures and food intakes in healthy humans.

Design: According to a balanced crossover design, we examined 14 normal-weight male subjects on 2 occasions during a regular 24-h sleep-wake cycle (including 8 h of nocturnal sleep) and a 24-h period of continuous wakefulness. On the morning after regular sleep and total sleep deprivation, resting and postprandial energy expenditures were assessed by indirect calorimetry, and the free-choice food intake from an opulent buffet was tested in the late afternoon at the end of the experiment. Circulating concentrations of ghrelin, leptin, norepinephrine, cortisol, thyreotropin, glucose, and insulin were repeatedly measured over the entire 24-h session.

Results: In comparison with normal sleep, resting and postprandial energy expenditures assessed on the subsequent morning were significantly reduced after sleep deprivation by ~5% and 20%, respectively (P < 0.05 and P < 0.0001). Nocturnal wakefulness increased morning plasma ghrelin concentrations (P < 0.02) and nocturnal and daytime circulating concentrations of thyreotropin, cortisol, and norepinephrine (P < 0.05) as well as morning postprandial plasma glucose concentrations (P < 0.05). Changes in food intakes were variable, and no differences between wake and sleep conditions were detected.

Conclusion: Our findings show that one night of sleep deprivation acutely reduces energy expenditure in healthy men, which suggests that sleep contributes to the acute regulation of daytime energy expenditure in humans. Am J Clin Nutr 2011;93:1229–36.

INTRODUCTION

Epidemiologic data indicate that a decrease in nocturnal sleep duration is associated with an increased risk of developing obesity (1, 2). For instance, in the Nurses’ Health Study, women sleeping <5 h per night displayed the highest degree of body weight, whereas a sleep duration of 7–8 h was associated with the lowest (but still normal) degree of body weight (2). A number of experimental sleep studies have hinted at several mechanisms by which chronically reduced sleep time may favor obesity in humans. Thus, a bedtime restriction to 4 h/night on 2 consecutive days as well as a single night of total sleep deprivation (TSD) have been shown to increase daytime plasma ghrelin concentrations in young men, especially in the early morning hours (3, 4). Ghrelin is mainly produced by the stomach and causes hyperphagia while decreasing the energy expenditure (5). Therefore, a ghrelin-driven shift in the energy balance to positive values (ie, an energy intake that exceeds the energy expenditure) could be hypothesized to cause weight gain under conditions of chronic sleep loss. However, conflicting experimental data suggested that the effect of sleep loss on energy homeostasis is more complex than previously assumed; recurrent partial sleep deprivation in young men increased the 24-h food intake and, to some extent, physical activity (6) and induced a preference for high-calorie snacks (7). In contrast, in experiments performed in our laboratory (8), 2 d of bedtime restriction in young men did not increase the food intake assessed in the laboratory but decreased physical activity measured under free-living conditions. Also, 14 d of partial sleep deprivation in middle-aged men and women did not result in significant reductions in energy expenditure (7).

Against this background, we aimed to elucidate the role of sleep loss for energy expenditures in a homogenous sample of healthy young men. We compared the effects of regular sleep and TSD on morning energy expenditures measured by indirect calorimetry (IC) before and after a standard breakfast. We also measured free-choice food intakes from a rich test buffet offered in the late afternoon.

SUBJECTS AND METHODS

Subjects

Fourteen healthy male subjects participated in the experiments [age (mean ± SEM): 22.6 ± 0.8 y; body mass index (in kg/m2): 4 From the Department of Neuroendocrinology, University of Lübeck, Lübeck, Germany (CB, MH, AL, CM, JB, and TL); the Interdisciplinary Obesity Center, Kantonsospital St Gallen, St Gallen, Switzerland (BS); the Department of Neuroscience, Uppsala University, Uppsala, Sweden (CB and HBS); and the Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen, Tübingen, Germany (JB). 2 The funding sources had no role in the design, conduct, and reporting of the study or in the decision to submit the manuscript for publication. 3 The study was funded by the Deutsche Forschungsgemeinschaft (SFB 654 “Plasticity and Sleep”), Germany, and the Swedish Research Council, Sweden. 4 Address correspondence to C Benedict, Department of Neuroendocrinology, Hs.50.1, University of Lübeck, Ratzeburger Allee 160, 23538 Lübeck, Germany. E-mail: benedict@kfg.uni-luebeck.de.

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23.9 ± 0.5; all nonsmokers]. An interview before the study assured that participants had a regular sleep-wake rhythm during the 6 wk before the experiments and were not on medication. Acute illness was excluded by a physical examination and routine laboratory testing. In the week before each experiment, subjects were instructed to go to bed between 2300 and 2330, to get up by 0700 on the next morning, and not to take any naps during the day. The presence of sleep disturbances was excluded by sleep monitoring in a separate adaptation night that also served to habituate subjects to the experimental setting. The study was approved by the ethics committee of the University of Lübeck, and the procedures followed were in accordance with the Helsinki Declaration. All subjects gave written informed consent and were paid for participation in the study (initial recruitment date: 3 March 2008).

**Study design and procedure**

According to a randomized and balanced crossover design, each subject participated in two 24-h conditions (sleep and TSD), each which comprised a baseline period (1800–2300) followed by a nighttime intervention period (2300–0700) in which subjects slept or stayed awake, and a postintervention period (0700–1800) (Figure 1). Both sessions were separated by ≥4 wk. To prevent possible anticipatory effects, subjects were unaware until 2300 about the actual study conditions and had received the general information that, in each session, sleep and nocturnal wakefulness, respectively, might be possible. Subjects arrived in the laboratory at 1630 (ie, 90 min before the baseline period started) and had abstained from eating and drinking calorie- or caffeine-containing beverages during the preceding 4.5 h. Body weights did not differ between sleep and TSD conditions (82.7 ± 2.2 compared with 83.0 ± 2.3 kg; P > 0.1). During the experiment proper that started at 1800, subjects rested in bed in a supine position until the next afternoon at 1300 of the postintervention period (ie, immediately after the morning energy-expenditure measurements were finished), when they changed to a sitting position until the end of the experiment. During each experimental session, subjects ate regular standard meals (ie, the energy intake was the same for each subject) as follows: 1) dinner (baseline period, 1930–2000; carbohydrates, 0.7 MJ; fat, 0.5 MJ; and protein, 0.5 MJ), 2) liquid test meal (postintervention period, 0830–0900; carbohydrates, 1.9 MJ; fat, 1.3 MJ; and protein, 0.6 MJ), and 3) lunch (postintervention period, 1330–1400; carbohydrates, 1.9 MJ; fat, 1.9 MJ; and protein, 0.7 MJ). To test the influence of sleep deprivation on food intakes, in the late afternoon (1730) of the postintervention period, a buffet of ~16.5 MJ was offered from which subjects could eat ad libitum for 30 min (Table 1). The buffet comprised a broad variety of foods to cover a range of possible food preferences and also to provide satisfying food portions. The subjects were not aware that their food intakes were measured afterward.

In the sleep condition, lights were turned off at 2300, and subjects were awakened between 0630 and 0700 when entering light sleep (stage 1 or 2). An electroencephalogram was recorded continuously with a Neurofax amplifier (Nihon Kohden GmbH, Rosbach, Germany; www.nihonkohden.de), and polysomnography was performed according to standard criteria (9). Sleep stages were determined offline by an experienced scorer blinded to the study hypothesis. To keep subjects awake in the TSD condition, they were allowed to spend their time with a selection of movies, games, and books, and they were continuously monitored by the experimenters. Also, lights were on in the TSD condition (~300 lux). In the morning after regular sleep or nocturnal wakefulness, energy expenditures were measured by IC before and after the consumption of the standard breakfast (see below), and

![Figure 1](image-url)  
**Figure 1.** Experimental protocol. In one condition, nocturnal sleep was permitted from 2300 (lights off) to 0700 (lights on); in the other condition, subjects (n = 14) remained awake throughout the whole experimental period. In the morning, the energy expenditure was measured by indirect calorimetry (gray bars) before and after ingestion of a liquid test meal (T). In addition to the test meal, subjects were provided with standardized meals including dinner (D) and lunch (L), and at the end of the session, the free-choice food intake (F) was measured. Syringe symbols denote blood samplings for the determination of plasma glucose and hormone concentrations. From 1800 on the baseline day to 1300 on the postintervention day, subjects rested in bed in a supine position. Thereafter, they remained in a sitting position until 1800.

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1 The afternoon test buffet was offered to subjects along with coffee or tea at 1730 on the day after sleep or total sleep deprivation, and 30-min ad libitum food intake from the buffet was assessed. All values were rounded. CH, carbohydrate; F, fat; P, protein.
Subjects were requested to rate their hunger on a visual analog scale. For repeated hormonal measures, an intravenous catheter was placed in the vena cephalica. To prevent clotting, approximately 500 mL saline solution was infused throughout the 24-h experimental period. During the night, blood sampling was performed from an adjacent room via long thin tubes without disturbing the subject’s sleep. Blood was sampled twice during the baseline period (1800 and 2100) and then every 1.5 h between 2400 and 0900 at 1-h-intervals after consumption of the liquid test meal (1000-1300) and finally at 1500 and 1800 of the postintervention period.

Measurements of energy expenditure

Based on pilot experiments including TSD, measurements of pre- and postprandial energy expenditures were restricted to the time interval between 0700 and 1300 to minimize risk of artifacts because of subjects dozing or falling asleep during assessments. Metabolic rates (energy expenditure expressed as kJ/min) were measured by IC with a ventilated-hood system (Deltatrac II, MBM-200 Metabolic Monitor; Datex-Engström, Achim-Uphusen, Germany). The IC device enabled the estimation of the energy expenditure by measuring respiratory gases. Before each use, the IC was calibrated with Quick Cale calibration gas (Datex-Engström) to 5% CO2 and 95% O2. The resting metabolic rate (RMR) was continuously measured in a ≤30-min period between 0745 and 0815 in the morning after the nighttime period. Previous studies have shown that the intraindividual variance in the resting energy expenditure is explained to the largest part by changes in the fat-free mass. Thus, the resting energy expenditure was adjusted for the fat-free mass (assessed in each experimental session by bioimpedance before the baseline period was started (BIA 2000-M; Data Input, Frankfurt, Germany) as previously described (10).

Between 0830 and 0900 of the postintervention period, subjects consumed 600 mL of a vanilla-flavored liquid test meal (Fresubin energy drink; Fresenius Kabi, Bad Homburg, Germany) at a dose of 20 mL liquid test meal/min (which totaled 3.8 MJ, 5.6 g protein/100 mL, 5.8 g fat/100 mL, and 18.8 g carbohydrate/100 mL). Subsequently, the postprandial increase in the energy expenditure (ie, the thermic effect of food) was assessed for the initial 20-min interval of each hour for a total of 4 h. In between measurements, subjects did not wear the hood and drank 150 mL water after each measurement. An inspection of electroencephalogram activity during measurements indicated that none of the subjects showed signs of sleep. To avoid chilling or overheating during the energy-expenditure measurements, subjects were covered, and the ambient temperature was held constant (at 23°C).

Core body temperature, heart rate, and trunk movements

A thermistor connected to an ambulatory data storage device (Minilogger, Minimitter Inc, Bend, OR) was applied for the 24-h monitoring of rectal core body temperature (CBT) (sampling at 0.5-min intervals). Subjects were also fitted with a combined heart rate and movement sensor (Actiheart; Cambridge Neurotechnology, Cambridge, United Kingdom) on their chests to measure movements along the body’s longitudinal axis and heart rates. Data obtained with the Actiheart device (Cambridge Neurotechnology) were collected in 1-min epochs. To adjust data to a common sampling rate of one sample per hour (as used for blood sampling), individual data of the CBT, heart rate, and trunk movements were averaged across 60-min intervals (eg, measurements between 2030–2130 resulted in one 2100 value).

Assays

Plasma glucose concentrations were measured in fluoride plasma (hexokinase method, Aeroset; Abbott Diagnostics, North Chicago, IL). For hormonal measurements, blood samples were centrifuged immediately, and the supernatant fluid was stored at −80°C. Concentrations of thyreotropin, cortisol, and insulin were measured with an Immulite analyzer (Siemens Medical Solutions Diagnostics, Los Angeles, CA). Ghrelin (Total; Linco Research, St Charles, MO) and leptin (Linco Research) were measured by radioimmunoasays. Norepinephrine concentrations were measured in plasma by standard HPLC. Analytic sensitivities of concentrations were as follows: thyreotropin, 0.004 μIU/mL; cortisol, 5.5 nmol/L; insulin, 13.9 pmol/L; leptin, 0.05 ng/mL; ghrelin, 0.093 ng/mL; and norepinephrine, 0.03 nmol/L. To convert values for blood glucose to milligrams per deciliter, values were multiplied by 18.02; to convert values for insulin to microunits per milliliter, values were multiplied by 0.144; to convert values for cortisol to micrograms per deciliter, values were multiplied by 0.0362; to convert values for norepinephrine to picograms per milliliter, values were multiplied by 169.2.

Statistical analyses

For statistical evaluation, SPSS version 17.0 (SPSS Inc, Chicago, IL) was used. Data are presented as means ± SEMs. Statistical analyses were based on analyses of variance (ANOVA) including the repeated-measures factors sleep/TSD (reflecting the condition) and time (reflecting the different time points of measurement). Significant ANOVA tests were followed by post hoc comparisons by using Student’s t test for paired data. A 2-sided P < 0.05 was considered significant.

RESULTS

Energy expenditure and late-afternoon food intake

RMR (fasting energy expenditure expressed as kilojoules per minute) was reduced after sleep deprivation compared with during sleep (5.5 ± 0.1 compared with 5.8 ± 0.2 kJ/min; P < 0.05 for the sleep/TSD main effect; Figure 2A). Also, the increase in the postprandial metabolic rate (PMR) was, on average, approximately 20% lower in the TSD than in the sleep condition (1.06 ± 0.06 compared with 1.32 ± 0.07 kJ/min; P < 0.0001), with this difference reaching significance in the first 2 postprandial measurements (Figure 2B).

Morning hunger ratings and late-afternoon food intake

In the morning after TSD (ie, at 0700), subjects reported significantly greater hunger on the visual analog scale than they did after sleep (5.7 ± 0.5 compared with 2.3 ± 0.5 cm; P < 0.0003). However, the free-choice food intake from the late afternoon buffet was not affected by TSD (TSD compared with
Glucose and hormonal measurements

None of the baseline hormonal and plasma glucose measurements (ie, between 1800 and 2100 on the baseline day) indicated any significant differences between conditions (P > 0.23 for all comparisons; Figure 3, A–G).

Ghrelin and leptin

Early nocturnal plasma ghrelin concentrations at 0130 were reduced during TSD compared with during early sleep (0.72 ± 0.06 compared with 0.80 ± 0.06 ng/mL; P < 0.04 for a comparison of values at 0130; P < 0.03 for the sleep/TSD × time interaction; Figure 3A). An opposing pattern emerged during the second night-half (ie, 0430–0730) when plasma ghrelin concentrations were, on average, 11.1 ± 4.2% higher when subjects were awake (P < 0.02; Figure 3A). Serum leptin concentrations did not differ between conditions (TSD compared with sleep, 24-h mean: 3.07 ± 0.35 compared with 3.05 ± 0.35 ng/mL; P > 0.42 for all comparisons; Figure 3B).

Glucose and insulin

The calculation of the area under the curve (using the trapezoidal rule) indicated lower night-time glucose concentrations in the TSD compared with sleep conditions (night-time period, 2400–0600: 30.6 ± 0.4 compared with 32.2 ± 0.3 nmol · L⁻¹ · h⁻¹; P < 0.001; Figure 3C) in the absence of nocturnal changes in insulin (P > 0.47 for all comparisons; Figure 3D). In regards to relative differences between conditions with sleep values set to 100% (area under the curve between 0900 and 1300 of the postintervention period), TSD also resulted in significantly higher plasma glucose concentrations after the consumption of the standard breakfast (108.1 ± 3.8%; P < 0.05; one-sample t test). Postprandial increases in serum insulin concentrations were not influenced by TSD.

Norepinephrine, cortisol, and thyreotropin

Twenty-four-hour concentrations of plasma norepinephrine were increased during TSD compared with during sleep (1.10 ± 0.09 compared with 0.97 ± 0.06 nmol/L; P < 0.01; Figure 3E). This difference was particularly pronounced during the night (TSD compared with sleep, 2400–0600: 0.82 ± 0.06 compared with 0.57 ± 0.04 nmol/L; P < 0.001), but norepinephrine concentrations remained enhanced after TSD in the morning hours when IC was measured (TSD compared with sleep, 0900–1300: 1.17 ± 0.12 compared with 0.98 ± 0.07 nmol/L; P < 0.02). Mean 24-h serum cortisol concentrations were higher in the TSD than in sleep conditions (236 ± 9 compared with 219 ± 7 nmol/L; P < 0.05 for the sleep/TSD main effect; P < 0.003 for the sleep/TSD × time interaction; Figure 3F). Twenty-four-hour concentrations of thyreotropin were also distinctly higher during TSD than during sleep (2.45 ± 0.25 compared with 1.84 ± 0.18 μIU/mL; P < 0.002 for the sleep/TSD main effect; P < 0.001 for the sleep/TSD × time interaction; Figure 3G).

CBT, heart rate, and trunk movements

Baseline values of the temperature, heart rate, and trunk movements did not differ between conditions (P > 0.21 for all comparisons; Figure 4A). However, during the night and shortly after awakening, CBT was significantly higher in the TSD than in the sleep condition (night-time period, 2400–0730: 36.8 ± 0.08°C compared with 36.6 ± 0.07°C; P < 0.02). Thereafter, this pattern reversed such that CBT was lower after TSD than after sleep (postintervention period, 0900–1800: 36.9 ± 0.04°C compared with 37.0 ± 0.04°C; P < 0.02). From 0900 to 1300, the averaged CBT (expressed as the difference to baseline values between 1800 and 2300 of the baseline day) was positively correlated to the postprandial energy expenditure (r = 0.43, P < 0.03; Pearson’s correlation analysis). During TSD, the 24-h

FIGURE 2. Sleep loss reduced the morning energy expenditure in humans. After a night of regular sleep (black bars) and a night of continuous wakefulness (white bars), metabolic rates were measured by indirect calorimetry in healthy young men under resting conditions (resting metabolic rate [RMR]) between 0745 and 0815 (A) and after the consumption of a liquid standard breakfast (600 mL of a vanilla-flavored energy drink that contained 3.8 MJ) [postprandial metabolic rate (PMR)] (B). The PMR was measured 4 times for a 20-min period between 0900 and 1300. PMR indicated the respiratory energy emitted as heat and was calculated as the increase in energy expenditure above the RMR. Repeated-measures ANOVA showed a significant interaction between sleep-wake and time (P < 0.03). Values are presented as means ± SEMs. *P < 0.05, **P < 0.01, and ***P < 0.001 for pairwise comparisons between conditions; n = 14.
mean heart rate was higher than during the regular sleep-wake cycle (68 ± 2 compared with 65 ± 2 beats/min; P < 0.02), with the largest differences between conditions emerging during the night-time period (TSD compared with sleep, 2400–0600: 64 ± 1 compared with 56 ± 2 beats/min; P < 0.001; Figure 4B). Overall, no significant differences in trunk movements were shown between conditions (wake compared with sleep, 24-h mean: 2.3 ± 0.5 compared with 2.6 ± 0.4 activity counts/min; P > 0.45 for all comparisons; Figure 4C). During IC, trunk movements were also comparable between TSD and sleep conditions (2.0 ± 0.4 compared with 2.3 ± 0.3 activity counts/min; P > 0.43 for all comparisons), which excluded confounding influences of physical activity on the observed differences in energy expenditure between conditions.

**Sleep recordings**

Sleep in the sleep condition was typical for laboratory conditions [total sleep time: 418 ± 8 min; wake: 11 ± 3 min; stage 1: 25 ± 4 min; stage 2: 242 ± 8 min; slow-wave sleep (SWS): 67 ± 6 min; rapid eye movement (REM) sleep: 72 ± 6 min]. The sleep-onset latency was 32 ± 8 min. SWS latency was 24 ± 4 min, and REM sleep latency was 97 ± 12 min.

**DISCUSSION**

We showed that one night of sleep loss induced a decrease in energy expenditure under resting and postprandial conditions during the subsequent daytime period. A drop in energy expenditure because of sleep loss may constitute a mechanism that,
Sleep loss has been consistently shown to induce marked neuroendocrine alterations, in particular increases in plasma ghrelin concentrations (3, 4, 11, 12). In humans, the administration of ghrelin stimulated food intake (13), and higher concentrations of the hormone were associated with lower levels of resting and postprandial energy expenditure (14). Accordingly, habitual short nocturnal sleep duration may promote weight gain by reducing the energy expenditure and increasing the food intake. In the current study, sleep loss increased hunger feelings in the following morning. However, in the afternoon, food intakes and macronutrient choices from the buffet were not significantly affected by TSD, which apparently deviated from previous findings that showed that acute sleep curtailment enhanced food intakes and also affected food preferences because sleep-deprived humans showed an increased consumption of calories from snacks (6, 7, 15). However, this discrepancy may be explained by the particular features of our procedures that yielded a relatively high calorie intake during the 24-h period of interest which may have masked differences in the afternoon. Likewise, such a potentially biasing influence of laboratory overeating has been previously observed (8).

Sleep loss was also suspected to increase the risk of developing type 2 diabetes (16). In line with previous findings of a decreased morning glucose tolerance after recurrent sleep curtailment (17), our subjects displayed higher postprandial plasma glucose values after nocturnal wakefulness compared with during sleep in the absence of changes in insulin concentrations, which suggested a reduced effectiveness of insulin-mediated glucose uptakes after sleep loss.

Our main result was a reduction in morning energy expenditures that emerged under fasting and postprandial conditions when subjects were sleep deprived. With consideration of the close relation between the metabolic rate and CBT (18), the reduction in energy expenditure in the morning after TSD may have reflected a homeostatic mechanism that compensated, at least in part, the increased metabolic demand because of nocturnal wakefulness. This assumption was indirectly buttressed by the fact that the physiologic decline in CBT that emerged after sleep onset was dampened when subjects stayed awake (19).

According to this scenario, it is possible that the 24-h energy expenditures were comparable between conditions because nocturnal and morning effects of wakefulness would have counterbalanced each other. However, prolonged periods of shortened sleep duration have been consistently reported to induce a sustained decrease in CBT by up to 0.5°C (20). This could have further contributed to decreases in energy expenditure as observed in the current study and, thereby, facilitated body weight gains in the long term (21), with the assumption that long-term energy intakes were not reduced to compensate for any reduction in energy expenditures.

At first glance, the sleep loss–induced reduction in energy expenditure appeared to diverge from recent observations of unchanged energy expenditures in middle-aged subjects submitted to a 14-d period of sleep restriction to 5.5 h/night (7). However, there were essential methodologic differences between both studies including, but not limited to, factors such as the difference in mean ages of volunteers (the previous compared with the current study: 39 compared with 22.5 y), sex distributions (number of men and women in the previous compared with current study: 6 men and 5 women compared with 14 men and 0 women), and differences in physical activity patterns (previous compared with current study: moving freely in the laboratory compared with bed rest). Furthermore, the reduction in energy expenditure in the morning after nocturnal wakefulness may have required greater sample sizes to
be replicated under more moderate conditions of recurrent bedtime restriction. The sleep-restriction protocol of the previous study primarily deprived the subjects of REM sleep (that dominates the second half of nocturnal sleep), whereas the time spent in deep SWS (that occurs mostly during the first night-half) remained unchanged (7). There is growing evidence that the contribution of sleep to the homeostatic regulation of metabolic functions is primarily mediated by SWS (22). Against this background, our data, in conjunction with previous observations (22), indirectly suggested that SWS in particular is critical for the level of daytime energy expenditure. Nevertheless, the effect of different sleep stages on energy expenditure remains to be thoroughly investigated by using, for instance, a SWS suppression protocol as previously published (22).

In confirmation of previous observations (23), the nocturnal wakefulness of subjects activated stress systems as indicated by the nocturnal increase in norepinephrine and cortisol concentrations and elevations of heart rates. However, these changes are known to be associated with an increased, rather than decreased, energy expenditure as shown in our experiments after sleep loss (24, 25). A possible explanation for this seemingly paradoxical pattern of effects is that the body’s sensitivity to catabolic signals is generally hampered by acute sleep loss. This explanation is also supported by previous observations of the reduced excitability of skeletal muscles by sympathetic stimulation after one night of sleep deprivation (26). Likewise, the sleep loss-induced increase in thyreotropin secretion, which is a hormone that is well known to enhance cellular energy expenditure (27), failed to compensate for the strong suppressing effect of acute sleep deprivation on morning energy expenditure. It is also known that prolonged partial sleep restriction can flatten circadian hormonal rhythms (3, 28). Against this background, it is tempting to speculate that habitual sleep loss facilitates weight gain by counteracting the orchestration of hormonal rhythms involved in the maintenance of energy balance (29, 30).

Limitations

The reduction in pre- and postprandial energy expenditures observed in the morning after total nocturnal sleep deprivation may not necessarily be shown under conditions of partial sleep deprivation [eg, as reported by Nedeltcheva et al (7)]. A high 24-h calorie consumption in both experimental conditions as well as the moderate statistical power associated with the relatively low sample size did not allow definitive conclusions about the effect of TSD on food intakes. Because calorimetric measurements were not conducted during the whole 24-h experimental period (eg, the nocturnal energy expenditure was not monitored), the current study did not allow for an extrapolation to 24-h energy expenditures and, therefore, no accurate estimation of energy balance (ie, the difference between the food intake and calorie need). Subjects stayed in bed in the current experiments to enable standardized measurements of the metabolic rate. Thus, exercise-related energy expenditure, which was previously observed to have been reduced after partial sleep deprivation (8), could not be measured in the current study.

Conclusions

Our results gathered in healthy young men show that sleep plays an immediate regulatory role for energy expenditures. Whether reductions in energy expenditures and CBTs induced by acute sleep deprivation pertain to long-term partial sleep deprivation and thus may constitute mechanisms linking a chronically short sleep duration with obesity (21, 31) need further investigation. Nevertheless, our findings demonstrated that the disruption of the sleep-wake cycle, as frequently occurs in shift workers, caused moderate but significant adaptive reductions in energy expenditures on the subsequent day.

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The authors’ responsibilities were as follows—CB, JB, and TL: designed the study; CB and TL: analyzed data; AL and CM: enrolled patients; CB, HBS, MH, BS, JB, and TL: contributed to writing the manuscript; and AL and CM: collected data and conducted experiments. All authors had full access to all data in the study and took responsibility for the integrity and accuracy of data analyses. None of the authors had a conflict of interest.

REFERENCES

16. Nedeltcheva AV, Kessler L, Imperial J, Penev PD. Exposure to recurrent sleep restriction in the setting of high caloric intake and
physical inactivity results in increased insulin resistance and reduced glucose tolerance. J Clin Endocrinol Metab 2009;94:3242–50.


