

Energy expenditure during sleep, sleep deprivation and sleep following sleep deprivation in adult humans

Christopher M. Jung¹, Edward L. Melanson², Emily J. Frydendall¹, Leigh Perreault², Robert H. Eckel² and Kenneth P. Wright^{1,2}

¹*Sleep and Chronobiology Laboratory, Department of Integrative Physiology, Centre for Neuroscience, University of Colorado, Boulder, CO 80309-0354, USA*

²*Division of Endocrinology, Metabolism, and Diabetes, University of Denver-School of Medicine, Aurora, CO 80045, USA*

Non-technical summary One of the proposed functions of sleep is to conserve energy. We determined the amount of energy conserved by sleep in humans, how much more energy is expended when missing a night of sleep, and how much energy is conserved during recovery sleep. Findings support the hypothesis that a function of sleep is to conserve energy in humans. Sleep deprivation increased energy expenditure indicating that maintaining wakefulness under bed-rest conditions is energetically costly. Recovery sleep after sleep deprivation reduced energy use compared to baseline sleep suggesting that human metabolic physiology has the capacity to make adjustments to respond to the energetic cost of sleep deprivation. The finding that sleep deprivation increases energy expenditure should not be interpreted that sleep deprivation is a safe or effective strategy for weight loss as other studies have shown that chronic sleep deprivation is associated with impaired cognition and weight gain.

Abstract Sleep has been proposed to be a physiological adaptation to conserve energy, but little research has examined this proposed function of sleep in humans. We quantified effects of sleep, sleep deprivation and recovery sleep on whole-body total daily energy expenditure (EE) and on EE during the habitual day and nighttime. We also determined effects of sleep stage during baseline and recovery sleep on EE. Seven healthy participants aged 22 ± 5 years (mean \pm s.d.) maintained ~ 8 h per night sleep schedules for 1 week before the study and consumed a weight-maintenance diet for 3 days prior to and during the laboratory protocol. Following a habituation night, subjects lived in a whole-room indirect calorimeter for 3 days. The first 24 h served as baseline – 16 h wakefulness, 8 h scheduled sleep – and this was followed by 40 h sleep deprivation and 8 h scheduled recovery sleep. Findings show that, compared to baseline, 24 h EE was significantly increased by $\sim 7\%$ during the first 24 h of sleep deprivation and was significantly decreased by $\sim 5\%$ during recovery, which included hours awake 25–40 and 8 h recovery sleep. During the night time, EE was significantly increased by $\sim 32\%$ on the sleep deprivation night and significantly decreased by $\sim 4\%$ during recovery sleep compared to baseline. Small differences in EE were observed among sleep stages, but wakefulness during the sleep episode was associated with increased energy expenditure. These findings provide support for the hypothesis that sleep conserves energy and that sleep deprivation increases total daily EE in humans.

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Corresponding author Kenneth P. Wright Jr: Sleep and Chronobiology Laboratory, Department of Integrative Physiology, 1725 Pleasant Street, Clare Small 114, University of Colorado, Boulder, CO 80309-0354, USA.
Email: kenneth.wright@colorado.edu

Abbreviations BMI, body mass index; CTTC, Clinical Translational Research Centre; DEXA, dual energy X-ray absorptiometry; EE, energy expenditure; RQ, respiratory quotient; PSG, polysomnographic; SWS, slow-wave sleep; REM, rapid eye movement; WASO, wakefulness after sleep onset; WPSO, wakefulness prior to sleep onset.

Introduction

One of the proposed functions of sleep is to conserve energy (Berger & Phillips, 1995). Energy expenditure (EE) is hypothesized to be lower during sleep *versus* wakefulness to reduce total daily energy needs. In support of this theory, sleeping metabolic rate has been reported to be lower than resting metabolic rate during wakefulness with estimated reductions in EE of 7 to 69% among different mammalian species (Toutain *et al.* 1977; White *et al.* 1985; Wiersma *et al.* 2005; Revell & Dunbar, 2007). In humans, it is well established that EE is lower following the onset of sleep and during the scheduled sleep episode when compared to pre-sleep wakefulness (Kreider *et al.* 1958; Robin *et al.* 1958; Buskirk *et al.* 1960; White *et al.* 1985; Fraser *et al.* 1989; Bonnet *et al.* 1991); however, the total daily energy conserved by sleep has yet to be quantified in humans. Therefore, the primary aim of the current study was to quantify for the first time the energy conserved during sleep, or conversely, the metabolic cost of missing one night of sleep in humans. Specifically, we compared total daily EE during a habitual day consisting of 16 h wakefulness and 8 h sleep to EE during 24 h of total sleep deprivation and hypothesized that sleep deprivation would significantly increase total daily EE. We also quantified for the first time the energy conserved during recovery sleep following total sleep deprivation. We hypothesized that during the habitual nighttime, sleep would significantly reduce EE compared to sleep deprivation and that recovery sleep would significantly decrease EE compared to a habitual night of sleep.

Significant differences in EE have been reported between sleep stages in some (Breibbia & Altshuler, 1965; Fontvieille *et al.* 1994) but not all studies (Webb & Hiestand, 1975; Haskell *et al.* 1981; White *et al.* 1985; Palca *et al.* 1986). Of those reporting differences in EE between sleep stages, one consistent finding was lower EE during deep slow-wave sleep (SWS). Therefore, a secondary aim of the current study was to examine the effects of sleep stage on EE during baseline and recovery sleep. We hypothesized that EE would vary between sleep stages and that EE would be lowest during SWS on the recovery night. As an exploratory aim, we examined the effects of sleep and sleep deprivation on substrate utilization.

Methods

Ethical approval

Study procedures were approved by the Scientific Advisory and Review Committee of the Colorado Clinical and Translational Sciences Institute, the Colorado Multiple Institutional Review Board, and by the Investigational Review Board at the University of Colorado Boulder. Written informed consent was obtained from subjects.

The protocol was in accordance with the latest revision of the *Declaration of Helsinki*.

Subject characteristics

We studied seven subjects (5 males, 2 females) aged 22.4 ± 4.8 years (mean \pm s.d.) with a BMI of 22.9 ± 2.4 kg m⁻² (mean \pm s.d.) and per cent body fat of $27.2 \pm 7.2\%$ (mean \pm s.d.) as determined by dual-energy X-ray absorptiometry (DEXA; DXA, Model DPX-IQ Lunar Radiation Corporation, Madison, WI, USA). Subjects were determined healthy by physicians at the Clinical and Translational Research Centre (CTRC) based on physical exam, blood chemistries, 12-lead clinical electrocardiography, medical and psychiatric history. Furthermore, detailed health and sleep and circadian rhythm disorder history status was assessed at the Sleep and Chronobiology Laboratory and a polysomnographic (PSG) sleep disorder screening night verified subjects were free of sleep disorders. Exclusion criteria were any current or chronic medical or psychiatric conditions; shift work or dwelling below the Denver altitude (1600 m) in the year prior; travel across more than one time zone in the 3 weeks prior to the laboratory procedures; BMI outside the normal range of 18.5 to 24.9; recent self-reported weight loss; or physically active lifestyle, defined as greater than 1 h of structured exercise per week. Physically inactive subjects were studied to control for the effects of detraining during the sedentary laboratory procedures on energy expenditure. Furthermore, exercise was proscribed 2 days prior to the laboratory protocol to control for short-term effects of exercise on energy expenditure.

Subjects were instructed to refrain from consuming caffeine and alcohol for 3 days prior to the laboratory protocol to control for withdrawal and acute effects of these drugs on our primary outcome measures. Subjects self-reported they were medication free and urine toxicology verified subjects were drug free upon admission to the study. Female subjects were free of oral contraceptives and were studied during the week of menses (early follicular phase), or the first week post-menses during the follicular phase of the menstrual cycle to control for differences in sleep (Ito *et al.* 1993), thermoregulatory physiology (Wright & Badia, 1999), and energy expenditure that may be related to changes in reproductive hormones (Davidsen *et al.* 2007).

Pre-study control – ambulatory wakefulness, sleep recordings and energy intake

One week prior to the laboratory protocol, subjects were instructed to maintain a consistent ~ 8 h per night sleep schedule. Compliance with this schedule was verified by call-in times to a time-stamped voice recorder of when subjects went to bed and awakened from sleep, daily

sleep diaries and wrist actigraphy recordings (Actiwatch-L, Phillips Respironics, Bend, OR, USA). These ambulatory recording procedures ensured that subjects were not sleep deprived prior to the laboratory visit. Three days prior to the laboratory visit, energy intake was controlled by providing subjects with an isocaloric diet designed by the CTRC nutritionist.

Experimental procedures

Subjects were admitted to a research suite on the CTRC ~6 h prior to their habitual bedtime (Fig. 1). Protocol events such as meals, bathroom breaks, bed and wake times and free time were scheduled according to the subjects' habitual bedtime as determined by the sleep-wakefulness times during the week prior to entry into the laboratory (e.g. bedtime was assigned a relative clock hour of 24.00 h although actual bedtimes were determined by each subject's habitual sleep-wakefulness schedule). This procedure permitted subjects to sleep at their habitual circadian phase. A modified constant routine (Duffy & Wright, 2005) was employed to control for the influence of environmental and behavioural factors on our primary outcome measures. Specifically, during scheduled wakefulness, subjects were studied in a semi-recumbent posture with the head of the bed raised to ~35 deg, ambient temperature was maintained in the thermoneutral range (22.3–22.9; $22.5 \pm 0.02^\circ\text{C}$ (range; mean \pm S.D.)), and artificial lighting was maintained at dim levels (~1.5 lux in the angle of gaze, <3 lux ambient; <8 lux maximum; IL-1400 photometer, International Light, Newburyport, MA, USA) to control for acute effects of light on temperature and endocrine physiology (Czeisler & Wright, 1999). Wakefulness and compliance with constant routine procedures were verified via continuous monitoring by research staff. If a subject showed signs of sleepiness, the subject was called by name and asked to change their activity (e.g. stop watching a movie or reading and engage in conversation). When not directly engaging subjects, continuous monitoring of EEG activity by staff ensured wakefulness.

Day 1 of the laboratory visit included an 8 h sleep opportunity to habituate subjects to the physiological recordings as well as to serve as a sleep disorders screen (Fig. 1). Day 2 served as baseline – scheduled 16 h wakefulness followed by an 8 h sleep opportunity. Days 3–4 consisted of 40 h total sleep deprivation followed by an 8 h recovery sleep episode (Sleep deprivation – 1 to 24 h awake; Recovery – 25 to 40 h awake and 8 h recovery sleep).

Energy expenditure and substrate utilization assessment

Energy expenditure and respiratory quotient (RQ) were determined in 1 min intervals from oxygen consumption

and carbon dioxide production measured in a whole-room indirect calorimeter (Melanson *et al.* 2002). Gas concentrations were determined from the flow rate and the differences in CO₂ and O₂ concentrations between entering and exiting air by using Hartman and Braun (Frankfurt, Germany) CO₂ (Uras 3G) and O₂ (Magnox 4G) analysers. The analysers were calibrated daily using calibration gasses of known concentration. The accuracy and precision of the system is tested monthly using propane combustion tests. The expected volume of O₂ and CO₂ is determined based on expected production of 2.55 and 1.53 l of O₂ and CO₂, respectively, per gram of propane burned (Withers, 2001). The average O₂ and CO₂ recoveries during the course of this study were $\geq 95.0\%$. We have previously determined that the coefficient of variation in 24 h EE was 5.8% (unpublished data, ELM). Urine was collected throughout the duration of the calorimetry stay and analysed for total nitrogen concentration (Skogerboe *et al.* 1990) to determine 24 h protein oxidation (Livesey & Elia, 1988). Energy expenditure and substrate oxidation (fat and carbohydrate) were calculated from oxygen consumption and the non-protein RQ based on the equations of Jequier *et al.* (1987).

In-laboratory energy intake

Energy content of the diet was designed to meet individual daily energy requirements as determined by DEXA measurements of fat-free mass and an activity factor (pre-study, 1.5; in-laboratory, 1.2). Dietitians prepared isocaloric meals that contained macronutrient contents of 30% fat, 50% carbohydrate and 20% protein; 200 mEq Na⁺, 100 mEq K⁺; 2500 ml fluids and no caffeine. Meal content and timing was exactly the same for each day of laboratory study (Fig. 1) to control for thermic effects of food across days. A single subject did not finish one dinner during the 25–40 h of total sleep deprivation on day 4, otherwise subjects consumed the diet provided.

Polysomnography

Polysomnographic recordings were obtained with Siesta System digital sleep recorders (Compumedics USA Ltd, Charlotte, NC, USA). Electroencephalographic recordings were obtained from F3–A2, C3–A2, C4–A1 and O1–A2 according to the international 10–20 system. Sleep was scored in 30 s epochs according to standard guidelines from brain region C3–A2 or C4–A1 (Rechtschaffen & Kales, 1968). Sleep onset was defined as the first three continuous 30 s epochs of sleep (Wright *et al.* 1995).

Data analysis

Energy expenditure, substrate utilization and RQ were averaged for each 24 h day: Baseline (hours awake 1–16 and 8 h scheduled sleep), Sleep deprivation (hours awake 1–24) and Recovery (hours awake 25–40 and 8 h scheduled recovery sleep). Energy expenditure was also averaged for each scheduled wakefulness and sleep episode; and for each hour across the day. Data were aligned to habitual wake time, thus controlling for influence of circadian phase on EE within each individual (Spengler *et al.* 2000). Energy expenditure data during scheduled sleep episodes were also examined by wakefulness–sleep stage. Wakefulness–sleep stage and EE data were offset by 2 min to account for the lag time of response of the whole-room indirect calorimeter relative to the EEG recordings (Fontvieille *et al.* 1994). Average EE was calculated for the following stages: wakefulness prior to sleep onset (WPSO), wakefulness after sleep onset (WASO), stage 1 sleep, stage 2 sleep, slow-wave sleep (SWS; stages 3 and 4 sleep combined), and rapid eye movement sleep (REM). Individual differences in sleep stage duration, as well as the fact that sleep is scored in 30 s epochs and EE is estimated in 60 s epochs, required that we bin EE sleep stage data as follows: EE that corresponded to Stage 2 and SWS were averaged for episodes of ≥ 15 continuous minutes of the specific sleep stage, with the exception of one subject who had a maximum of 10.5 min of continuous SWS; EE that corresponded to REM sleep were averaged for episodes of ≥ 9.5 continuous minutes of REM, with the exception of one subject who had a maximum of 5 min of continuous REM. Stage 1 sleep, WPSO and WASO are short-duration transitional stages, therefore the average EE for episodes of ≥ 1 min of stage 1 sleep, and the average EE for episodes ≥ 30 s of WPSO and

WASO were calculated. Unavoidably, WPSO and WASO episodes contained some sleep.

Statistical analysis

Non-parametric Wilcoxon matched pairs *t* tests were used to test for differences in total daily EE across days, scheduled wakefulness and sleep EE, and for 24 h RQ and substrate utilization. Repeated-measure ANOVAs were used to test for differences between average hourly EE and day of study (time of day \times day interaction). Differences in sleep stage duration by sleep episode (scheduled baseline *versus* recovery sleep episode) were determined using *t* tests. Repeated-measure ANOVAs were also used to determine differences in EE between stages of sleep and wakefulness and between baseline and recovery sleep episodes (sleep–wakefulness stage \times sleep episode interaction). For repeated-measure ANOVA analyses, Huynh–Feldt correction factors were used to correct for violations of homogeneity of variance and modified Bonferroni corrections were used to correct for the number of planned comparisons (Keppel, 1991).

Results

Effects of sleep, sleep deprivation and recovery sleep on energy expenditure

Figure 2 shows average hourly EE (kJ min^{-1}) for each day of study. Energy expenditure was significantly higher during scheduled wakefulness *versus* sleep during the habitual nighttime (relative clock hours 24.00 to 08.00 h), and EE was higher following each scheduled meal during the habitual daytime (day \times time of day interaction $F = (40, 240) 10.68$; $P < 0.0001$). Twenty-four hour EE (kJ day^{-1} ; Fig. 3A) was significantly higher during sleep deprivation compared to baseline and recovery days. On average, 24 h EE was $\sim 562 \pm 8.61$ kJ ($\sim 134 \pm 2.06$ kcals) or $\sim 7\%$ higher for sleep deprivation compared to baseline and $\sim 955 \pm 97$ kJ ($\sim 228 \pm 23$ kcals) or $\sim 12\%$ higher for sleep deprivation compared to recovery days (Fig. 3A). Furthermore, 24 h EE was on average $\sim 403 \pm 106$ kJ ($\sim 96 \pm 25$ kcals) or $\sim 5\%$ lower during recovery *versus* baseline days (Fig. 3A).

Figure 3B shows that the average 16 h EE (kJ min^{-1}) during the habitual daytime was similar regardless of sleep deprivation, whereas the average 8 h nighttime EE was significantly higher during sleep deprivation compared to baseline and recovery sleep episodes (Fig. 3C). Figure 3C also shows that the average 8 h nighttime EE was significantly lower during recovery *versus* baseline sleep. Specifically, 8 h nighttime EE was on average $\sim 673 \pm 10.4$ kJ ($\sim 161 \pm$ kcals) or $\sim 32\%$ higher during nighttime sleep deprivation and on average

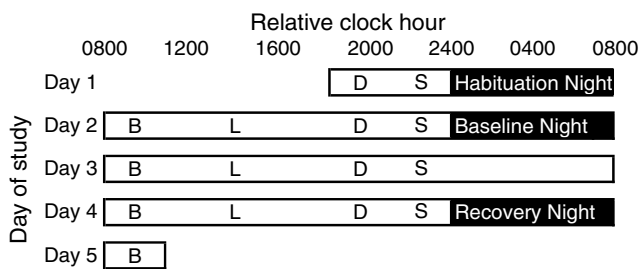


Figure 1. Study protocol

Black boxes represent scheduled sleep opportunities and white boxes represent scheduled wakefulness. Breakfast, lunch, dinner and a snack are denoted by B, L, D and S, respectively. Relative clock hour is on the abscissa and day of study is on the ordinate. Day 1 consisted of a habituation and sleep disorders screening night. Day 2 (baseline) consisted of 16 h of wakefulness and 8 h baseline sleep opportunity. Day 3 (sleep deprivation) consisted of 24 h of sleep deprivation. Day 4 (recovery) consisted of the remaining hours awake 25–40 h of sleep deprivation and 8 h recovery sleep. Energy expenditure was measured during days 2, 3 and 4.

~84 ± 3.1 kJ (~28 ± 1.9 kcals) or ~4% lower during nighttime recovery sleep when compared to the scheduled baseline sleep episode. Additionally, energy expenditure increased above baseline sleep levels in all subjects during the sleep deprivation night and decreased below baseline sleep levels in all but one subject during the recovery sleep night (Supplementary online material Fig. S1). There was no significant correlation between the magnitudes of change from baseline between sleep deprivation and recovery nights ($r = -0.02$, $P = 0.97$).

No statistical differences for average RQ and protein, fat and carbohydrate oxidation were observed between 24 h days (Supplementary online material Table S1).

Sleep-wakefulness stage and energy expenditure

Table 1 shows that sleep onset latency was significantly shorter and per cent of Stage 1, per cent time awake, and the number of arousals were significantly lower, whereas per cent SWS was significantly higher during the recovery compared to baseline sleep episode. The per cent of

stage REM, stage 2 and duration of arousals were not significantly different between baseline and recovery sleep episodes. We also found that arousals were more likely to occur from REM and stage 2 sleep on baseline and recovery nights (Supplementary online material Fig. S2).

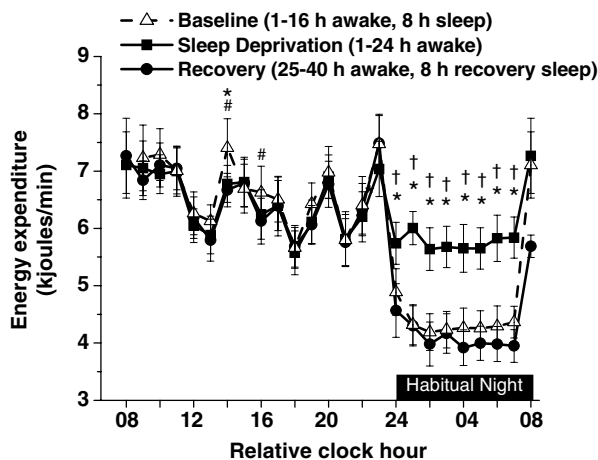


Figure 2. Energy expenditure for hourly averages for the three 24 h days

Data are plotted for relative clock hours with subjects' habitual wake time arbitrarily assigned a value of 08.00 h. The black bar represents the habitual night when sleep was scheduled on baseline and recovery nights and during which sleep deprivation occurred. Relative clock hours 08.00 and 24.00 h represent habitual wake and bedtimes, respectively. Relative clock hour 24.00 h includes data binned from 24.00 to 00.59 h and thus is the first hour of the scheduled sleep episode. Relative clock hour 08.00 h consists of data binned from 08.00–08.59 h, and thus is the first hour of the scheduled wake episode. Peaks of EE during the habitual daytime are associated with the thermic effects of food. * represent significant differences ($P < 0.05$) between baseline and sleep deprivation (1–24 h awake). # represents significant differences ($P < 0.05$) between baseline and recovery (25–40 h awake/8 h recovery sleep). † represents significant differences ($P < 0.05$) between sleep deprivation (1–24 h awake) and recovery (25–40 h awake/8 h recovery sleep). Error bars represent s.e.m.

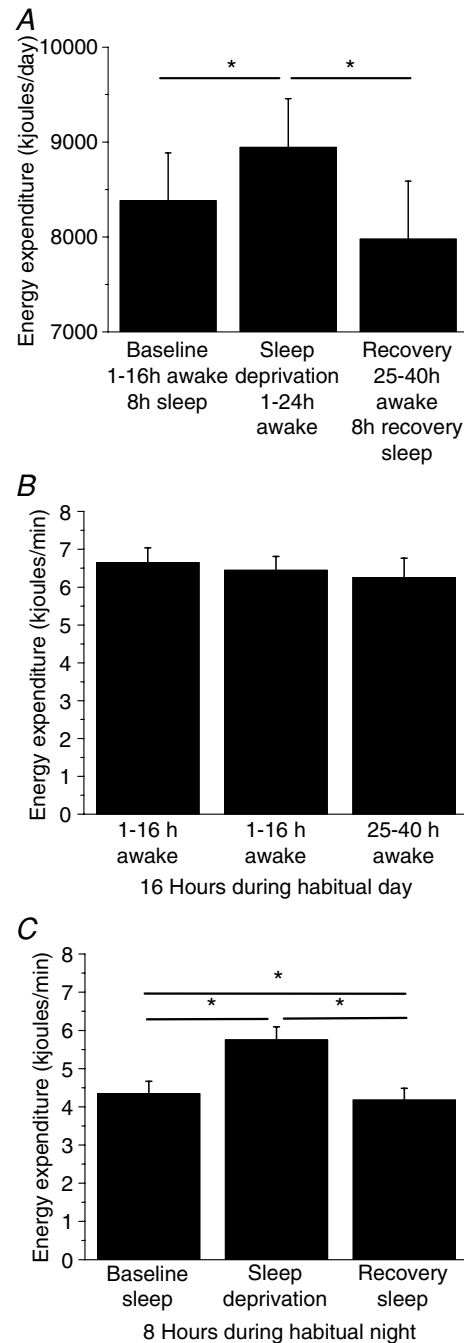


Figure 3. Total daily energy expenditure and energy expenditure associated with habitual wake and sleep episodes A, total daily EE in kJ day^{-1} for each day of the study. Energy expenditure in kJ min^{-1} during the 16 h habitual wake episode (B) and the 8 h habitual sleep episode (C). Lines represent significant differences between data at endpoints of the line. * $P < 0.05$. Error bars represent s.e.m.

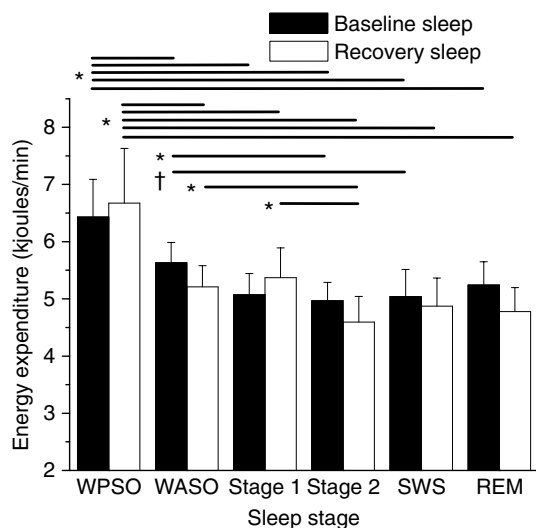
Table 1. Polysomnographically (PSG) recorded sleep

Measure	Baseline sleep episode	Recovery sleep episode
% of recording time		
Stage 1	3.4 ± 0.8	1.7 ± 0.4*
Stage 2	54.4 ± 1.6	49.9 ± 3.3
SWS	18.5 ± 1.3	29.6 ± 2.6*
REM sleep	18.7 ± 1.4	17.6 ± 1.9
Wakefulness	4.7 ± 1.0	2.0 ± 0.2*
Average number of arousals	14.0 ± 1.7	10.6 ± 2.2*
Average duration of arousals (min)	0.69 ± 0.1	0.67 ± 0.1
Sleep onset latency (min)	13.4 ± 3.9	3.5 ± 0.8*

Sleep architecture (mean ± s.e.m) in per cent of the recording episode for sleep stages ($n = 5$), number and duration of arousals ($n = 5$) and sleep onset latency ($n = 7$) for the baseline and recovery nights. Wakefulness is the sum of WPSO and WASO. The sleep architecture analysis included 5 subjects because of PSG recording problems for 2 subjects. Note that percentages are rounded. *Significant dependent t test ($P < 0.05$) between sleep episodes.

Figure 4 shows the EE associated with sleep and wakefulness stages during baseline and recovery sleep episodes. A significant main effect of stage ($F = (5, 25) 11.16$; $P < 0.00001$) and planned comparisons revealed that average EE was significantly higher for WPSO compared to any sleep stage and to WASO during baseline and recovery sleep episodes. In addition, average EE was significantly higher for WASO compared to stage 2

sleep during baseline and recovery episodes. Furthermore, average EE was significantly higher for stage 1 compared to stage 2 sleep during the recovery episode. There was a non-significant trend of higher EE for WASO compared to SWS during the baseline episode ($P = 0.053$). Lastly, there were no significant differences in energy expenditure for a specific sleep stage between the baseline and recovery sleep episodes for sleep stage.

**Figure 4. Energy expenditure during wakefulness and sleep stages**

The EE associated with WPSO was significantly greater ($P < 0.05$) than any stage of sleep and WASO during the baseline (black) and recovery (white) nights. The EE associated with WASO was significantly different to stage 2 during the baseline and recovery nights. The EE associated with stage 1 was significantly different to stage 2 during the recovery night. The EE associated WASO had a non-significant trend for being different to SWS during the baseline night. Lines represent significant differences between stages at endpoints of the line. $N = 6$. Error bars represent s.e.m. * $P < 0.05$ between sleep stages within nights. † $P = 0.053$

Discussion

Sleep reduces EE and energy conservation is a hypothesized function of sleep. We quantified for the first time (1) the energy conserved by 8 h of sleep following 16 h of habitual wakefulness, and the energy conserved by 8 h of recovery sleep following one night of total sleep deprivation when sleep occurred at the habitual circadian phase; and (2) the metabolic cost of sleep deprivation assessed by 24 h EE in humans. We found that EE was higher during sleep deprivation compared to sleep and that EE was lower during an 8 h recovery sleep episode when compared to a habitual 8 h sleep episode. Sleep stage had little effect on EE with the exception of a small but significant difference in EE between stage 1 and stage 2 sleep during the recovery sleep episode. Wakefulness affected EE more than sleep stage with higher EE during WPSO than any sleep stage. Furthermore, EE during WASO was higher than EE during stage 2 sleep during baseline and recovery episodes.

Metabolic cost of sleep deprivation and the energy savings associated with sleep

Missing one night of sleep had a metabolic cost of $\sim 562 \pm 8.6$ kJ ($\sim 134 \pm 2.1$ kcal) over 24 h, which equates to a $\sim 7\%$ higher 24 h EE compared to a habitual day with an 8 h scheduled sleep episode. Thus, the metabolic cost

of staying up all night, or conversely, the total daily energy savings associated with sleep, is similar to the energy content of two slices of bread or ~ 225 ml of reduced fat 2% milk. Considered another way, the energetic cost of missing one night of sleep is similar to the energetic cost of a 68 kg adult walking ~ 3 km at a moderate pace. This amount of energy savings by sleep in humans appears small, yet if one considers that the amount of positive energy storage needed to explain the obesity epidemic is ~ 209 kJ day⁻¹ (~ 50 kcal day⁻¹) (Hill *et al.* 2003), the $\sim 562 \pm 8.6$ kJ (~ 134 kcal) energy savings we observed during sleep is physiological meaningful. Without sleep, humans would need a higher energy intake per day to meet total daily energy requirements. Our quantification of the 24 h metabolic cost of sleep deprivation was determined under controlled constant routine bed-rest conditions. It is likely that the metabolic cost of sleep deprivation in free-living individuals would have been even greater due to activity-associated energy demands (e.g. ambulation).

In rats, total daily EE was reported to be 50% higher during the first 24 h of total sleep deprivation compared to baseline (Everson *et al.* 1989b). In humans, we observed that total daily EE was $\sim 7\%$ higher compared to baseline suggesting that there may be species differences in the metabolic response to sleep loss. Related, methods used for sleep deprivation were likely to be more metabolically challenging for prior studies of rats than in our study of humans (e.g. involuntary disk-over-water method and *ad libitum* food intake for rats *vs.* voluntary sleep deprivation in a thermoneutral bed-rest environment with an isocaloric diet in humans). Under disk-over-water conditions, total sleep deprivation is reported to increase *ad libitum* food intake in rats (Everson *et al.* 1989a) whereas it is unknown if total sleep deprivation increases *ad libitum* food intake in humans. However, energy intake has been reported to increase after a night of partial sleep deprivation (Brondel *et al.* 2010). It would be hypothesized that total sleep deprivation would increase food intake in humans as sleep deprivation has been reported to reduce levels of the satiety hormone leptin (Mullington *et al.* 2003) and to increase levels of the orexogenic hormone ghrelin and hunger ratings (Schmid *et al.* 2008). As noted, energy intake was controlled in the current study so that subjects consumed the energy needed to maintain energy balance under non-sleep-deprived conditions. We designed our study to examine the influence of sleep and sleep deprivation *per se* on EE. Thus, our control over activity and food intake does not permit us to make strong comments about how total daily EE and energy balance may change during uncontrolled conditions, something that should be examined in future studies.

Increases in 24 h EE during sleep deprivation were largely due to increases in EE during the habitual night. The observed decrease in EE during sleep supports a proposed function of sleep-energy conservation. Findings

from prior studies indicated lower EE during sleep compared to wakefulness immediately prior to sleep (Kreider *et al.* 1958; Robin *et al.* 1958; Buskirk *et al.* 1960; White *et al.* 1985; Fraser *et al.* 1989; Bonnet *et al.* 1991). Methods used in prior studies did not allow distinction between decreases in EE due to time within the sleep episode and/or circadian phase, as no prior study compared EE during continuous wakefulness *versus* sleep across the habitual night. In the current study, we found that there was a 32% decrease in EE (~ 673 kJ (~ 161 kcal)) during sleep *versus* wakefulness during the 8 h habitual night. Thus, our findings demonstrate a relatively large sleep-dependent decrease in EE when controlling for time within the sleep episode and circadian phase within individuals.

Influence of recovery sleep on total daily EE and EE during the sleep episode

We found that 24 h EE was $\sim 403 \pm 106$ kJ ($\sim 96 \pm 25$ kcal) or $\sim 5\%$ lower during the recovery day compared to the baseline day. Thus, the 7% increase in 24 h EE on the sleep deprivation day was nearly offset by the energy saved during the recovery day, resulting in a net cost of 2% across the 48 h examined. It is likely that had we let subjects sleep *ad libitum* following sleep deprivation they would have slept longer (Dijk & Edgar, 1999), perhaps completely offsetting the entire metabolic cost of sleep deprivation. The latter suggests that under controlled feeding conditions needed to maintain weight, human metabolic physiology has the capacity to make adjustments to respond to the energetic cost of sleep deprivation and maintain energy balance across days. When we examined EE during the scheduled 8 h sleep episode, we found that EE was ~ 84 kJ (~ 20 kcal) or $\sim 4\%$ lower during recovery than baseline sleep. Changes in many physiological processes, including reduced arousals, might contribute to the lower EE found during recovery than baseline sleep.

Energy expenditure and sleep architecture

We found that EE levels were higher for stage 1 sleep, a transitional stage between wakefulness and sleep, than for stage 2 during the recovery sleep episode and that EE levels were higher during WPSO than EE during all sleep stages during both baseline and recovery sleep episodes. We also found that EE levels were higher during WASO, brief arousals from sleep, than for stage 2 sleep during both baseline and recovery sleep episodes. Since sleep stage data are traditionally scored in 30 s epochs and EE data are averaged every minute, some of the EE associated with WASO included EE that was associated with sleep. Therefore, the EE associated with WASO in the current study might be an underestimate of the EE

associated with brief awakenings. Regardless, we found the EE during WASO to be significantly higher than stage 2 sleep during the baseline and recovery nights. Overall, differences between sleep stages were relatively small whereas differences between wakefulness and sleep were more robust.

It is well established that sleep deprivation decreases the number of arousals and amount of WASO during recovery *versus* baseline sleep (De Gennaro *et al.* 2001; Curcio *et al.* 2003), which is consistent with the current findings, and thus, these changes might contribute to the lower EE we observed during recovery sleep. Since EE is higher during wakefulness than sleep, a reduction in sleep onset latency and the number of arousals during the scheduled sleep episode might be a primary mechanism of lower EE during recovery compared to baseline sleep in the current study. Additional support for the latter comes from findings of higher EE during tone fragmented sleep compared to a non-disturbed baseline night (Bonnet *et al.* 1991). Taken together, findings from Bonnet *et al.* (1991) and the current study suggest that factors that disrupt sleep such as environmental (e.g. noisy intensive care unit/bedroom), behavioural (e.g. consumption of caffeine) or pathophysiological (e.g. insomnia and sleep apnoea) might result in higher EE at night because of increased wakefulness and not a higher 'sleeping' energy expenditure *per se*. The latter hypotheses should be examined in future studies.

Findings from studies showing small differences in EE among sleep stages have generally indicated that EE was lowest during SWS compared to other stages of sleep (Brebbia & Altshuler, 1965; Fontvieille *et al.* 1994); however, as noted, significant differences in EE among sleep stages are not found in all studies (Webb & Hiestand, 1975; Haskell *et al.* 1981; White *et al.* 1985; Palca *et al.* 1986). It should be noted that prior findings of lower EE during slow-wave sleep compared to other sleep stages are limited by the fact that relatively short 5 min samples of EE were examined and that the EE levels were averaged across sleep stages that were 'contaminated' by other sleep and wakefulness stages in addition to the primary stage of interest (Brebbia & Altshuler, 1965; Fontvieille *et al.* 1994). Thus, it is possible that arousals from sleep could have influenced the EE results of such analyses. Indeed, we found that arousals from sleep were more likely to occur from stage 2 and REM sleep (Supplementary online material, Fig. S2), which could contribute to the reported higher EE during stage 2 and/or REM sleep compared to SWS in prior studies.

Energy conservation as a function of sleep in humans

As noted, our findings provide experimental support for the hypothesis that sleep conserves energy in humans and that the amount of energy conserved during

sleep represents a physiologically meaningful amount of whole-body total daily energy expenditure. Why, however doesn't a night of sleep save more than ~562 kJ (~134 kcal) of total daily EE in humans? It is possible that the energy saved during sleep is the net result of decreases in the energetic cost of some basic life functions contributing to resting metabolic rate and a repartitioning of some of the energy saved for use in sleep-dependent physiological processes. For example, metabolically costly processes of respiration (Trinder *et al.* 1992), heart rate (Shinar *et al.* 2006), gut motility (Kumar *et al.* 1990) and muscle activity (Shinar *et al.* 2006) are reduced during sleep and some of the resulting energy saved may be redistributed to other metabolically costly processes that are proposed as sleep functions (e.g. sleep-dependent hormone synthesis and release (Sassin *et al.* 1969), increases in immune function (Everson, 1993; Palmblad *et al.* 1976; Bergmann *et al.* 1996), replenishment of cerebral glycogen stores (Benington & Heller, 1995) and synaptic plasticity (Cirelli *et al.* 2005)). Thus, based on our findings and findings from the existing literature, we propose that one of the functions of sleep in humans is to conserve energy and that some of the energy saved is redistributed to support other critical sleep-dependent physiological processes.

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Author contributions

Experiments were performed at the Clinical and Translational Research Centre at the University of Colorado. All authors contributed to the following parts: (1) Conception and design of the experiment; (2) Collection, analysis and/or interpretation of data; (3) Drafting the article or revising it critically for important intellectual content. All authors approved the final version.

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Author's present address

C. M. Jung: Department of Biology, University of Alaska Anchorage, Anchorage, AK 99508, USA