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Repetitive exposure to shortened sleep leads to blunted sleep-associated blood pressure dipping

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Abstract

Blood pressure (BP) dips at night during sleep in healthy individuals but in disturbed sleep, dipping is blunted. However, the impact of chronic insufficient sleep duration, with limited intermittent recovery sleep, on BP dipping is not known. The objective of this study was to examine, in a controlled experimental model, the influence of chronic sleep restriction on BP patterns at night and during the day. In a highly controlled 22-day in-hospital protocol, 45 healthy participants (age 32 ± 2 yrs.; BMI 24 ± 1 kg/m²; 22 men and 23 women) were randomly assigned to one of two conditions: 1) repeated sleep restriction; (4h of sleep/night from 0300–0700 for 3 nights followed by recovery sleep of 8h, repeated 4 times in succession), or 2) a sleep control group (8h/night from 2300–0700). Beat-to-beat BP and polysomnography were recorded and revealed that sleep-associated diastolic blood pressure (DBP) dipping was significantly blunted during all 4 blocks of sleep restriction ($p=0.002$). Further, DBP was significantly increased for the whole day during the 1st, 2nd and 4th block of sleep restriction (all $p<0.01$), and systolic blood pressure (SBP) was significantly increased for the whole day during the 1st block of sleep restriction. In conclusion, repeated exposure to significantly shortened sleep blunts sleep-associated BP dipping, despite intermittent catch-up sleep. Individuals frequently experiencing insufficient sleep may be at increased risk for hypertension due to repetitive blunting of sleep-associated BP dipping, and resultant elevations in average circadian BP.

Keywords

sleep deprivation; autonomic nervous system; blood pressure; heart rate; dipping; diurnal; circadian; sodium excretion

INTRODUCTION

Several lines of evidence suggest that insufficient sleep contributes to the development of cardiovascular disease (CVD) risk factors and stroke [29]. Longitudinal studies including at

least 5 years of follow-up have reported significant associations between short sleep and elevated BP [13, 16], and experimental studies have reported elevated BP following both acute total sleep deprivation [6, 21] and partial sleep restriction [30].

Early studies using intra-arterial ambulatory blood pressure (BP) monitoring found that nocturnal BP significantly decreases during sleep [18] and surges in response to morning awakening [10]. A recent systematic review for the U.S. Preventive Services Task Force suggested that ambulatory BP measurement (noninvasively measured across day and night) is a better predictor of long-term cardiovascular outcomes than office BP and is a reference standard for evaluating/screening for high BP in adults [23]. The average BP decline from wake to nocturnal BP is 10%–20%, which is known as normal dipping. Reduction in nocturnal BP dipping is a stronger predictor of cardiovascular adverse events than daytime BP, even after adjustment for other covariates [14]. Furthermore, poor sleep can blunt BP dipping [25], implicating sleep as a mechanism in BP homeostasis. However, there are no studies which have investigated the effects of chronic short sleep, free of sleep disorders, on BP.

Due to busy schedules it is not unusual to cut back on sleep during the week and to catch up on weekends, or days off [1]. Whether or not such “recovery” sleep on the weekend can compensate for the adverse effects of short sleep on BP dipping, is unknown. The purpose of this study was to examine the influence of repeated blocks of sleep restriction on BP patterns at night and during the day. Blocks of sleep restriction consisted of 3 consecutive nights of short sleep followed by one recovery night of 8 hours of sleep opportunity. We repeated this schedule pattern 4 times, producing 4 blocks of repeated exposure to sleep restriction. This model mimics the real life sleep schedule of many people, with short sleep duration for consecutive nights followed by insufficient recovery sleep, before the pattern is repeated. We hypothesized that sleep plays an important role in BP regulation, and predicted that sleep-associated nocturnal BP dipping would be blunted during sleep restriction and would fail to adapt to repetitive blocks of restricted sleep.

METHODS

Participants

This study was approved by the Beth Israel Deaconess Medical Center Institutional Review Board, and all participants provided informed consent. Forty-five medically screened, healthy individuals (22 men and 23 women) between the ages of 21 and 53 participated, and 43 completed. One male withdrew after study start because it was discovered that he was wearing a nicotine patch, one female withdrew due to illness.

Participants underwent a complete medical history and physical screening, including blood chemistry. This screening was done to rule out participants with psychiatric, neurological, pain-related, and immune disorders, diabetes mellitus, chronic renal disease, significant allergy, and cardiovascular disease. Overnight sleep studies were performed to rule out sleep disorders (respiratory disturbance index of >5 events/hour on polysomnographic sleep study, leg movements with arousal >10/hour) before being enrolled for the in-hospital phase of the

protocol. Subjects were excluded from the study if they showed signs of acute or chronic disease.

All female subjects reported regular menstrual cycles without significant discomfort during pre-menses/menses. Use of regular medications with the exception of birth-control was exclusionary. Two weeks of actigraphic data along with sleep diaries were collected to ensure that the subjects had a usual daily sleep duration between 7–9 hours, sleep efficiency > 80%, and habitual sleep periods beginning within one and one half hours of 2300h (the scheduled normal bed time during the study).

Experimental Design

The 22-day protocol (Figure 1) was carried out in the Clinical Research Center (CRC). Following 2 days of adaptation and one day of baseline recording with 8h sleep opportunity from 2300–0700 hours; participants were randomly assigned to an experimental group involving 4 blocks of sleep restriction or to an 8 hour/night sleep control group. In the sleep restriction group, participants slept 4h/night from 0300–0700 for 3 consecutive nights, and then were permitted a night of 8h recovery sleep. This pattern was repeated 4 times; and when completed there were two additional nights of 8h sleep scheduled. Participants remained in bed in semi-supine position with dimmed light (<20 lux) between 2300–0300 during sleep restriction, no food or water was allowed, with the aim to minimize differences between conditions, except for sleep opportunity. Each participant was accompanied by a research assistant who helped maintain their wakefulness and social interaction, as well as ensure data quality and protocol compliance. During the sleep deprivation hours between 2300–0300 in the SR group, subjects lost the ability to maintain wakefulness for only very short times (1–5 minutes total, per 1 hour block), and this amount did not change across the 4 cycles (data not shown). The subjects' usual activities were talking, reading, writing, watching TV/movies, playing video/board games, etc. during their 22-day stay. In the sleep control group, sleep was permitted between 2300–0700 throughout the 22-day stay.

On the morning following the first two nights of restricted sleep, participants were instrumented with beat-to-beat BP and polysomnography and the equipment was removed the next morning after at least 30 minutes of wakefulness, resulting in up to approximately 24 hours of continuous beat-to-beat BP recordings. Weighed diets (designed to maintain participant's body weight, controlled for fats, carbohydrates, sodium and potassium) were provided at standard times (breakfast at 0730, lunch at 1230, and supper at 1830) along with a beverage. Additional water intake was provided in hourly aliquots based on weight-adjusted norms, and adjusted in the first two adaptation days to accommodate individual preference. Fluid intake and output were measured and tracked. Room temperature was maintained at participant's preferred level during the day, and dropped by 2°C at night. Outside of days when participants were instrumented for physiological recordings (recording days), they went on hourly walks to maintain their daily physical activity levels. In addition, 3 times per week they used the hospital fitness center.

Measurements

Actigraph and Sleep Diary—An Actiwatch (Actiwatch 2, Respironics Inc., Murrysville, PA) and a sleep diary were given to the participant after initial screening. Fourteen days of sleep data were collected to evaluate participants' habitual bedtimes and sleep times according to inclusion criteria.

Subjective Ratings—During wake time participants rated their subjective sleepiness and a few other feeling-state parameters such as appetitive hunger and thirst, every 2h on computerized visual analogue scales. In the sleep restriction group participants continued to rate their subjective sleepiness and other states, every 2h during the sleep deprivation period (2300-0300), as well.

Beat-to-beat BP—The arterial waveform in a finger of the non-dominant hand was obtained beat-to-beat by digital photoplethysmography (Portapres system, Finapres Medical Systems, Amsterdam, Netherlands); this non-invasive method was chosen to minimize sleep disturbance. Two small finger cuffs were applied to the non-dominant index and middle finger (or to the ring finger depending on individual preference.) These cuffs inflated and deflated continuously to measure beat-to-beat BP. The alteration between the cuffs was set at 30min or 15min depending on the subjects' tolerance. A research technician attended the recordings, and calibrations to brachial BP were done in the morning and in the evening. In the present study, Portapres recordings started between 7–10 AM on a recording day and ended between 7:30–8:30 AM on the next morning. Portapres measures have been used extensively to measure 24 hour BP variations [7, 22].

Polysomnographic recording—Sleep was recorded using the Embla N7000 system (Medcare US, Buffalo) on the screening night to ensure that participants were free of sleep disorders (sleep apnea, and restless legs syndrome). The Embla N7000 system was also used to collect sleep data on recording days during the study period (see Figure 1), and on an additional final night of sleep before leaving the study (data not shown). Sleep and wake periods were recorded and manually scored for sleep, according to standardized procedures [2]. ECG electrodes were placed beneath each clavicle.

Urinary Sodium Excretion—Urine samples were collected during the night period (2300-0700) on heavy recording days. The total urine volumes for night periods were recorded by the nurses. Urine sodium concentrations were measured by ion selective electrode in a Cobas 6000 chemistry analyzer from Roche Diagnostics (Indianapolis, IN). Measurements were performed by a CLIA-certified clinical laboratory; inter-assay coefficient of variation was 2.7%. For each participant, the sodium excretion value (mmol) was calculated as the concentration of sodium in the urine (mmol/L) multiplied by the urinary volume.

Data Analysis

Beat-to-beat BP—Beat-to-beat BP signals acquired by the Portapres system were fed directly into the Embla system, where the data were transformed to European Data Format, and exported to LabChart (LabChart 7, ADInstruments Co.) for off-line analysis. Beat-to-

beat BP recordings up to 24h were successfully obtained from 43 participants. Eight participants were missing data on one day, 5 participants were missing data on two days and 1 participant was missing data on 3 days' recordings (due to malfunctioning devices), this reflects approximately 8% missing data. Due to varied BP start time in the morning, 20h BP data is presented from 1100-0700. Data for each participant were first averaged for each hour, and then the hourly average data entered into a mixed model analysis. Data are presented as estimated mixed model average systolic blood pressure (SBP) and diastolic blood pressure (DBP).

Beat-to-beat Heart Rate—Heart rate (HR) was acquired on the Embla N7000 system, data were transformed to the European data format, and imported to LabChart for offline analysis. Seven participants had one day (out of 6 heavy recording days), or <3%, of missing HR data due to technical problems.

Nocturnal dip—For direct comparison, nocturnal BP dipping was calculated using the first 4 hours of the sleep period (i.e. 2300-0300 for the 8h sleep and 0300-0700 for the 4h sleep condition). The percent change in first 4h sleep BP was calculated as $[100 \times (\text{wake BP} - \text{sleep BP}) / \text{wake BP}]$, the wake time data were analyzed from 1100-2300 (12h). Nocturnal dipping data was analyzed from 43 participants.

Statistical Analysis—All data were analyzed statistically using software SPSS (IBM SPSS 22.0; IBM Corp, Armonk, NY) and SAS (SAS 9.4, SAS Institute Inc., Cary, NC, USA). We used mixed linear models to estimate the effects of repeated sleep restriction on BP and HR parameters. Fixed factors included: 1) condition (sleep restriction vs. sleep control), 2) blocks (Baseline (BL), 1-4 blocks of sleep restriction or sleep control, Recovery (Rec)), 3) time (wake and sleep or hourly bins), 4) interaction between condition and blocks, and 5) interaction between blocks and time (wake and sleep or hourly bins, when sleep restriction and sleep control groups were analyzed separately). For daily nutrition data, the fixed factors included condition (sleep restriction vs. sleep control), day (day 2 to day 20), and interaction between condition and day. Subject was treated as a random factor. Pairwise comparison within the mixed linear models was used to estimate at which time-points values differed between blocks and their own baseline, in each group. An independent t-test was used to compare demographic data between groups (sleep restriction vs. sleep control) at baseline. Results are expressed as means $\pm$ SE, and means (or delta values) were estimated from the mixed model, when used. Effects were analyzed and considered significant $P \leq 0.05$ (2-tailed). We also considered the result as a statistical trend when $P \leq 0.1$ (2-tailed).

RESULTS

Demographics

Forty-three healthy participants (21 men and 22 women between the ages of 21-53; average age 31 ± 2), completed the study and were included in the analyses. Body mass index (Kg/m^2) averaged 24 ± 1 for both groups, BP and HR were not different between sleep restriction and sleep control groups (all, $p \geq 0.20$). Participants in both groups had similar average habitual sleep duration (7.8h for both groups) and sleep efficiency, or percent of

time spent asleep after sleep began and before final awakening in the morning (83% and 85% for restricted and control groups, respectively) estimated by actigraph and sleep log, before entering the study.

Intake and Output Measures

During the 22 day stay, energy intake did not differ between sleep restriction and sleep control (condition $\times$ day interaction, $p=0.827$). Body weight did not change and daily water and sodium intake were well maintained throughout the study (Table 1, condition $\times$ block interaction, $P=0.767$ for water, and $P=0.124$ for sodium). In contrast, there was a condition by night interaction for urinary sodium excretion, showing higher values during the sleep restricted nights compared with control (Table 1, condition $\times$ block interaction, $P=0.052$), due to a trend of increased sodium excretion in the 3rd ($p=0.069$) block and significantly increase in the 4th ($p=0.039$) block. The changes in night time urinary sodium excretion were not correlated to daytime nor nighttime BP changes (data not shown). There were no differences between the sleep restriction and sleep control groups in terms of daily consumed protein, fats, carbohydrates (presented in both grams and percentages), nor daily potassium or sodium.

Hemodynamic Parameters

BP Dipping—Figure 2 shows nocturnal sleep-associated BP dipping. The top panel summarizes the percent dipping for SBP (left) and DBP (right), and indicates the blocks with significant blunting. SBP and DBP wake (hatched bars) and sleep (solid bars) periods are shown from baseline through the blocks of sleep restriction and recovery sleep (middle panels); and on the days for the sleep control condition (bottom panels). There was a significant interaction effect (blocks $\times$ time) for DBP in the sleep restriction group ($p=0.002$); and a trend for SBP ($p=0.090$). DBP dipping was significantly attenuated during sleep restriction blocks compared with baseline, for every block of sleep restriction ($p<0.05$ for each block compared with baseline). In the sleep control group, dipping was unchanged throughout the study (block $\times$ time interaction, $P=0.18$).

Daily Averages—Figure 3 depicts the average circadian SBP, DBP and HR changes associated with sleep conditions. There was a significant interaction (condition $\times$ block, $P<0.001$) for SBP, showing an overall elevation in sleep restriction compared with the control sleep condition. This elevation over BL in SBP was seen in the first block of sleep restriction, and decreased below BL during recovery sleep (indicated by asterisks in Figure 3, left panel). DBP (Figure 3, middle panel) also showed a condition by block interaction ($p=0.001$). In the sleep restriction group, DBP was significantly increased over BL during the first, second, and fourth blocks of restriction (indicated by asterisks in Figure 3, middle panel). And similarly, HR (Figure 3, right panel) showed a significant interaction (condition $\times$ block, $p<0.001$) elevated over BL in the first block, whereas in the control condition, HR stayed significantly lower than it had been at BL, throughout the study days, for the remainder of the protocol.

Figure 4 depicts the hourly averaged DBP during baseline, 4 blocks and recovery in the sleep restriction group. There was a significant interaction effect (between block and time of

the day, $P=0.022$) in the sleep restriction group. In sleep restriction, DBP maintained wake period levels during 4h of sleep deprivation at night (between 2300-0300) compared to baseline and recovery. SBP showed similar changes (data not shown, block $\times$ time of the day interaction, $P=0.006$).

Sleep Electrophysiology

As expected, total sleep time was significantly decreased (condition $\times$ block interaction, $P<0.001$) by the sleep restriction protocol, and sleep efficiency was increased (condition $\times$ block interaction, $P=0.022$). There was no change in deep slow wave sleep (N3 minutes), despite sleep restriction (condition $\times$ block interaction, $p=0.243$), but there was a reduction in other stages of sleep, and of wakefulness during sleep (Table 1).

Despite a substantial amount of sleep loss, wakefulness was well maintained during the vigil hours between 2300-0300 in the sleep restriction group. Participants lost the ability to maintain wakefulness, and lapsed into 30 second epochs of sleep, for only very short times (1–5 minutes total, per 1 hour block), and this amount did not change across the 4 blocks (data not shown).

Subjective Estimations of Appetitive and Feeling States

Subjective sleepiness ratings during the sleep deprivation nighttime period were close to double the daytime ratings (Table 1). Daytime subjective sleepiness ratings (excluding nocturnal periods) significantly increased throughout the 4 blocks in the sleep restriction group, but not sleep control (condition $\times$ block interaction, $P=0.006$). Subjective thirst and self-reported appetite for salty food as assessed during the first test of the morning following heavy recording days did not show any changes throughout the protocol in either group (data not shown).

DISCUSSION

This highly controlled physiological study on the effects of prolonged exposure to insufficient sleep with only occasional opportunities to catch up on lost hours, resulted in two important findings concerning the role of sleep in autonomic and cardiovascular regulation in healthy adults. Firstly, chronic, repetitive sleep restriction to 4 hours in the latter part of the night blunts the BP dipping that occurs during sleep, without signs of adaptation over time. Secondly, shortened sleep affects 24h BP through relative elevations in sleep-associated values, without affecting daytime pressures. These findings suggest that one mechanism whereby insufficient sleep duration may lead to increased risk for cardiovascular diseases is by blunting BP dipping.

Observational studies have examined the association between poor sleep and BP dipping, and reported a significant correlation between lower sleep efficiency and blunted BP dipping [19, 20, 27]. In the current study, electrophysiologically defined sleep quality was excellent during restricted sleep, yet BP dipping was blunted. Sleep stages themselves are known to modulate BP. Direct recordings from human muscle sympathetic nerves have shown a pronounced decrease in firing from wake to slow wave sleep, accompanied by lowered BP and HR [28]. This is in contrast with rapid eye movement (REM) sleep, where BP and HR

are closer to levels seen in waking, and sympathetic nerve activity is at its daily high[28]. The fact that this study found reduced sleep-associated BP dipping, in spite of increased sleep efficiency, slow wave sleep (N3)% and REM% during sleep restriction, supports the hypothesis that sleep is an important mechanism of BP control.

As participants were closely monitored throughout the protocol, there was minimal lapsing into sleep during the deprivation periods. The only measurement that was differentially affected during the night, including subjective indices, was sodium excretion. While increased sodium excretion has been reported in total sleep deprivation studies of 24 hours of continuous wakefulness[8, 15], this is the first to show this increase in chronic repeating sleep restriction, and it is of note that this change became significant only after repeated blocks of restricted sleep challenge.

Plasma renin activity is known to increase in non-REM, particularly slow wave sleep, and decrease in REM sleep[4, 26], and patients with fragmented sleep due to sleep apnea have reduced BP dipping, increased nocturnal urinary output and urinary sodium excretion, increased atrial natriuretic peptide release and decreased renin-angiotensin-aldosterone activity[11, 17]. While a sleep-renal connection has been established, this is the first study to show that repetitive exposure to insufficient sleep affects sodium excretion. Since we controlled the sodium intake throughout the study, the increased sodium excretion may indicate measurable drops in total body sodium in response to repetitive sleep restriction. Further research is required to elucidate the relative involvement of sympathetic, atrial natriuretic peptide, and renin-angiotensin-aldosterone mechanisms.

The sustained blunted BP dipping reached significance in DBP and showed a trend in SBP, indicating a differential effect of repeated sleep restriction on total peripheral resistance and cardiac output. Previous studies reported endothelial dysfunction in response to sleep deprivation. Specifically, acute total sleep deprivation (i.e. 40h) caused endothelial dysfunction by decreasing cutaneous vascular conductance even before the increase in sympathetic activity and SBP [24], and further, eight days of partial sleep deprivation (i.e., 5.1 hours/night) impaired flow mediated dilation [5]. Thus, it can be speculated that both endothelial dysfunction and increased sympathetic activity induced vasoconstriction would increase total peripheral resistance (primarily affecting DBP) and manifest before the increase in SBP, in this model of repeated exposure to sleep restriction.

Limitations

There are three limitations to the current study that warrant discussion. One is the timing of the sleep period. The circadian placement of the short sleep period, during the latter half of the night when circadian influences favor REM sleep [3], resulted in higher amounts of REM sleep during the first 4 hours of sleep, in the restricted condition. Although slow wave sleep, which is known to facilitate nocturnal BP drop [28], was maintained in the sleep restricted condition, we cannot generalize to other possible time placements of the 4 hour sleep period. Further research is required in order to determine whether permitting sleep between 2300-0300 for instance, instead of 0300-0700 as was done in the current study, would affect BP dipping in the same way.

Another limitation is the age of the subjects. The participants were adults in their early 30s, on average, an age when diastolic hypertension may emerge as a risk factor for subsequent development of conjoint SBP and DBP hypertension [12]. It is not clear how older adults would respond to exposures to repetitive sleep restriction.

Thirdly, the problem associated with using Portapres is that the absolute values collected from arteries in the digits may not closely correspond to the arterial BP measured from the upper arm. However, our emphasis is on within-subject changes in response to manipulations of sleep schedule. For each participant stay, we used the same cuffs to minimize technical bias, wherever feasible. The Portapres produces less noise and tactile stimuli than ambulatory arm measurement devices [9], and was chosen for its minimal sleep disruption. The larger measurement sample size collected from Portapres also provided more accurate estimation of overall BP compared to the limited sample size from an ambulatory BP monitor.

Perspective

This study is the first to investigate sleep-associated BP dipping in the context of repeated exposure to significantly shortened sleep in healthy participants with good quality sleep. The results of this study show that duration of sleep is important for regulating BP dipping and thereby, average 24h BP. Results of this study show that sleep-associated BP dipping does not adapt to insufficient sleep taken in the latter half of the normal sleep period time.

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Figure 1.

Protocol Summary. Gray bars indicate the scheduled sleep periods, and hatched bars with vertical lines represent the wake and sleep periods with intensive physiological monitoring (polysomnography, single channel ECG and beat-to-beat blood pressure recordings).

Following three nights of 8h sleep, subjects were randomly assigned to sleep restriction group (4h group) or sleep control group (8h group). In the 4h group, subjects slept 4 hours (0300–0700) for three consecutive nights, followed by one night of 8h sleep, the block repeated 4 times, with an additional two nights of 8h sleep at the end. In the 8h group, subjects were permitted to sleep normally (2300–0700), throughout the study.

Figure 2.

Systolic (SBP; left) and diastolic blood pressure (DBP; right) dipping in sleep restriction group (top panels). The BP dipping data plotted on the top panels were calculated from the means of BP summarized in the bar graphs in the middle panels. *Significantly different ($P < 0.05$) from baseline in the restriction group. Bar graph: wake (1100–2300) BP (hatched bars) and first 4 hours of sleep BP (solid bars) at baseline (BL), 1st block of interventions to 4th block and Recovery (Rec) in sleep restriction group (middle panels) and sleep control group (lower panels). The first 4h of sleep SBP and DBP data were included (2300–0300 for control and 0300–0700 for the sleep restricted condition). Mixed model analysis found a

significant interaction (block $\times$ time, $P=0.002$) effect in DBP, and a trend in SBP (block $\times$ time, $P=0.09$).

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Figure 3.

Changes (delta) in daily average (20 hours) systolic blood pressure (SBP, left panel); diastolic arterial pressure (DBP, middle panel); and heart rate (HR, right panel), in 4 blocks of sleep control/restriction and recovery (Rec) compared to baseline (BL). Mixed model analyses found significant interactions for each of these models ($p < 0.01$); Individual block data are compared to BL and significance ($p < 0.05$) indicated in the figure (*).

Figure 4.

Hourly averaged diastolic blood pressure (DBP) in sleep restricted participants. For each hourly bin, the corresponding time across the day showing on the x-axis, represents the time immediately after the end of that hour collection, for example, the bin plotted at 23 on x-axis, represents the DBP data collected from 2200–2259h. Blue bar represents the sleep period in 8h BL and Rec sleep opportunities (from 2300–0700), whereas red bar represents the sleep period in 4h sleep opportunities (from 0300–0700). Colored lines indicate diurnal DBP profile for BL, Blocks 1–4 and Rec.

Table 1

Daily water and Sodium intake, nighttime urinary sodium excretion, subjective sleepiness and sleep parameters.

Variable	Control (N=22; 11 women)						Restriction (N=21; 11 women)						%Interaction P-Value
	BL	1 st	2 nd	3 rd	4 th	Rec	BL	1 st	2 nd	3 rd	4 th	Rec	
Water Intake (24h), mL	2456±109	2428±109	2391±109	2396±109	2377±109	2409±109	2501±111	2462±111	2513±111	2500±111	2460±111	2474±111	0.77
Sodium Intake (24h), mg	2462±179	2912±179	2519±179	2654±179	2676±179	2379±181	2440±183	2415±183	2391±183	2527±183	2626±186	2606±186	0.12
[§] Nighttime Sodium excretion, mmol	24±3	25±3	26±3	24±3	21±3	26±3	25±3	25±3	29±3	32±3 [‡]	30±3 [‡]	21±3	0.05
[¶] Daytime Sleepiness	20±4	22±4	21±4	19±4	17±4	15±4	17±4	31±4 [*]	35±4 [*]	33±4 [*]	32±4 [*]	22±4	0.01
[¶] Nighttime Sleepiness	--	--	--	--	--	--	--	66±6	71±6	59±7	61±6	--	0.32
TST, min	389±8	406±8 [*]	411±8 [*]	391±8	408±8 [*]	402±8	411±8	224±8 [*]	225±8 [*]	227±8 [*]	223±8 [*]	429±8 [*]	<0.01
SE, %	81±2	85±2 [*]	86±2 [*]	82±2	85±2 [*]	84±2	86±2	94±2 [*]	94±2 [*]	95±2 [*]	93±2 [*]	90±2 [*]	0.02
N1, min	35±2	37±2	32±2	34±2	32±2	34±2	41±2	11±2 [*]	12±2 [*]	9±2 [*]	12±2 [*]	34±2	<0.01
N2, min	201±7	210±7	218±7 [*]	203±7	210±7	206±7	207±7	85±7 [*]	86±7 [*]	86±7 [*]	92±7 [*]	215±7	<0.01
N3, min	72±5	71±5	72±5	72±5	73±5	69±5	84±5	77±5	76±5	78±5	74±5	84±5	0.24
REM, min	80±6	89±6	90±6	83±6	93±6 [*]	93±6 [*]	79±6	48±6 [*]	55±6 [*]	55±6 [*]	45±6 [*]	97±6 [*]	<0.01

* Significant difference (p<0.05) compared to baseline.

[‡] Significant difference (p<0.05) or

[‡] Trend (p<0.10) to significant difference, compared to sleep control group.

[§] Urinary sodium excretion during nighttime (2300-0700) on heavy recording days.

[¶] Subjective sleepiness (a.u.) during daytime and night time (2300-0300 in sleep restriction blocks).

[¶] Condition × block interaction p value obtained from mixed linear model.

TST, total sleep time; SE, sleep efficiency; N1, N2, N3, stage 1-3 in non-rapid eye movement sleep; REM, rapid eye movement sleep.