Sleep Efficiency and Nocturnal Hemodynamic Dipping in Young, Normotensive Adults

Running Head: Sleep Efficiency and ABPM

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ABSTRACT

Blunted dipping of nocturnal systolic arterial pressure (SAP) and heart rate (HR) are independent risk factors for hypertension and all-cause mortality. While several epidemiological studies report a significant association between short sleep duration and hypertension, associations between sleep efficiency and the nocturnal drop of SAP remain controversial. Moreover, relations between sleep efficiency and HR diurnal patterns have been overlooked. We hypothesized that low sleep efficiency (<85%) would be associated with blunted nocturnal SAP and HR dipping. Twenty-two normotensive subjects (13 men, 9 women; age 18-28 years) wore an actigraphy watch for 7 days and nights, and an ambulatory blood pressure monitor for 24 hours on a non-actigraph night. There were no differences in age, sex, body mass index, mean sleep time, number of awakenings, or 24-h blood pressure between the low (n=12) and high (n=10) sleep efficiency groups. However, the low sleep efficiency subjects demonstrated a blunted dip of nocturnal SAP (10 ± 1% vs. 14 ± 1%, P=.04) and HR (12 ± 3% vs. 21 ± 3%, P=.03) when compared to the high sleep efficiency group. The low sleep efficiency group also demonstrated a higher mean nocturnal HR (63 ± 2 vs. 55 ± 2 beats/min, P=.02). These findings support growing evidence that sleep efficiency, independent of total sleep time, may be an important cardiovascular risk factor.

Key Words: ambulatory blood pressure, fragmented sleep, hypertension, sleep deprivation, autonomic activity
INTRODUCTION

Blood pressure and heart rate both follow a diurnal pattern in which they increase during the day and decrease at night (37). The magnitude of blood pressure reduction at night varies among the population, and blunted nocturnal blood pressure dipping (i.e., a decrease <10%) is associated with increased risk of hypertension (48), heart failure (23), and mortality (14, 24, 46). While often overlooked, epidemiological studies also reported elevated heart rate to have prognostic value independent of blood pressure (15, 18, 19, 36). Moreover, blunted nocturnal heart rate dipping is associated with an increase in adverse cardiovascular events and all-cause mortality in both normotensive and hypertensive adults (4, 47).

Recent studies suggest that sleep quality, independent of sleep duration, may play an important role in blood pressure regulation. Sleep efficiency (sometimes referred to as sleep fragmentation) is a standard and objective index of sleep quality, and is defined as the time spent asleep divided by total time in bed. Sleep efficiency can be objectively quantified using noninvasive limb actigraphy (1, 5, 11, 26, 29, 34, 40, 42). A number of studies have examined the associations between sleep efficiency and 24-hour ambulatory blood pressure in both adults (21, 22, 27, 28, 31, 41, 43) and adolescents (2, 30, 32). While some studies report a significant correlation between reduced sleep efficiency and a blunted nocturnal systolic arterial pressure (SAP) dip (2, 28, 31, 41), others report no association (22, 27, 30, 32, 43). These discrepancies remain unresolved, but methodological limitations must be considered. Of specific interest to the present study, these prior studies (2, 21, 22, 27, 28, 30-32, 41, 43) have recorded sleep efficiency and nocturnal ambulatory blood pressure concurrently,
despite evidence that nocturnal ambulatory blood pressure monitoring (ABPM) can artificially reduce sleep efficiency (13, 22, 33). Moreover, previous studies have categorized subjects according to blood pressure dipping status instead of sleep efficiency.

Therefore, the purpose of this study was to evaluate the relation between sleep efficiency and 24 hour ABPM in normotensive adults when sleep efficiency is quantified from several nights within two months that are not confounded by ABPM. Moreover, given that the majority of studies have focused exclusively on blood pressure, we also aimed to examine the relations between sleep efficiency and 24 hour heart rate. We hypothesized low sleep efficiency would be associated with blunted nocturnal blood pressure and heart rate dipping.

METHODS

Subjects

Twenty-three healthy young adults (14 male, 9 female; age 18-28 years) participated in this study. All subjects were nonsmokers and had no history of cardiovascular disease, asthma, or diabetes. Female subjects reported regular menstrual cycles and were not taking oral contraceptives or other hormonal supplementations. All subjects were screened for obstructive sleep apnea by a board certified sleep physician using the at-home ApneaLink (ResMed, San Diego, CA), which calculates an apnea hypopnea index (AHI) by measuring airflow during sleep through a nasal cannula connected to a pressure transducer held in place by a belt around the individual’s chest (10, 12, 16, 20). Subjects were excluded based on an AHI ≥ 10
episodes per hour, which disqualified one male subject from participation. The final study population included 13 men and 9 women. The experimental protocol was approved by the Michigan Technological University Institutional Review Board, and written, informed consent was obtained from all subjects.

**Experimental Design**

Subjects wore a wrist actigraph watch (Actiwatch-64; Mini Mitter, Philips Respironics, Bend, OR) for a total of 7 days and nights over the course of approximately one month. The actigraphy data was used to assure adequate sleep time for another study (9). As such, actigraphy was recorded for 3-4 consecutive nights approximately one month apart; all female subjects were studied during early follicular phase both months. Objective measurements of sleep time, sleep efficiency, sleep onset latency (SOL), and wake after sleep onset (WASO) were acquired from the actigraph watch. Actigraphy measurements of these sleep parameters have been validated against gold standard polysomnography (1, 5, 11, 26, 29, 34, 40, 42). Actigraphy sleep measurements were averaged over the 7 nights, with an average of 6±1 nights per subject. Subjects also kept sleep diaries, which were used to estimate sleep time if actigraphy data was unavailable. All actigraphy data was interpreted and scored by a board-certified sleep physician (J. P. DellaValla).

On a separate day in between the two block sessions of actigraphy, subjects were instrumented with an ABPM (90207 Ambulatory Blood Pressure monitor, SpaceLabs Healthcare, Snoqualmie, Washington). This particular ABPM model has been validated as an accurate and reliable device by the British Hypertension Society.
Subjects reported their anticipated sleep and wake times, and this information was used to program the device to record blood pressure and heart rate every 20 minutes during the wake period and every 30 minutes during sleep for 24 consecutive hours. Immediately following the ABPM recording, subjects reported their actual sleep and wake times while wearing ABPM, which were used to determine the final sleep/wake times for data analysis. The ABPM obtained an average of 59 ± 2 blood pressure and heart rate recordings per subject (44 ± 2 during wake and 16 ± 0.3 during sleep) during the 24-hour period.

**Data Analysis**

Actigraphy data were analyzed with Actiware version 5.59.0015 (Mini Mitter, Philips Respironics, Bend, OR). This software utilizes an algorithm where activity levels recorded during any individual epoch are modified by activity levels in the surrounding two-minute time period. All data were collected and analyzed utilizing a 15 second epoch length. Data were separated into mobile and rest intervals in order to determine total time spent in bed.Epochs were scored as mobile when the total activity counts in the epoch was greater than or equal to the epoch length. All epochs were scored as either sleep or wake by comparing the activity level in an epoch against a wake threshold value. Sleep efficiency was calculated as the scored time spent asleep for a given rest interval/length of rest interval x 100. Sleep onset latency was calculated as the elapsed time between the start of a rest interval and the following sleep start time. Wake after sleep onset (WASO) was calculated as the number of epochs scored as wake during a sleep interval multiplied by epoch length.
Consistent with previous studies (38, 39), we classified subjects as low or high efficiency sleepers using the 85% cut-off based on their average sleep efficiency scores. The percent change in nocturnal blood pressure and heart rate were calculated as \([1 - \text{sleep heart rate or blood pressure} / \text{wake heart rate or blood pressure}] \times 100\).

Non-dipping blood pressure was defined as <10% decrease in systolic arterial pressure.

All data were analyzed statistically using commercial software (IBM SPSS Statistics 20.0, SPSS, New York, NY). One-way analysis of variance (ANOVA) was used to compare high vs. low sleep efficiency groups. Paired t-test was used to compare average actigraphy-based sleep measurements calculated across the two 3-4 day blocks of actigraphy (taken approximately one month apart). Correlations between actigraphy data and ABPM data were calculated using two-way Pearson’s correlations. Significance was set as \(P < 0.05\) for all tests. All data are reported as mean ± standard error (SEM).

**RESULTS**

Table 1 depicts subject demographics and key variables sorted by high and low sleep efficiency. With the exception of the sorting variable (i.e., sleep efficiency), there were no differences in demographic data or sleep parameters between the high and low sleep efficiency groups. 24-hour blood pressure and heart rate, and wake blood pressure and heart rate, were not different between sleep efficiency groups. However, subjects with low sleep efficiency had elevated heart rate during sleep compared to subjects with high sleep efficiency. Sleep efficiency (84 ± 1 vs. 84 ± 1%, \(p = 0.603\)) was
not different when compared across the two 3-4 day actigraphy recording sessions approximately one month apart.

As depicted in Figure 1, the low sleep efficiency group also had blunted nocturnal dips in SAP and heart rate compared to the high sleep efficiency group (raw data provided in Table 1). While individuals in the low sleep efficiency group tended to have blunted nocturnal dip in diastolic arterial pressure (DAP), this did not reach statistical significance ($p = 0.42$).

Figure 2 demonstrates that when all data were analyzed in continuum (as opposed to being artificially classified based on the 85% threshold for sleep efficiency), findings were similar. Sleep efficiency scores were correlated to nocturnal dips in SAP ($r = 0.515$, $p = 0.01$) and heart rate ($r = 0.578$, $p = 0.01$), but not DAP ($r = 0.305$, $p = 0.168$). WASO was correlated with sleep efficiency ($r = -0.588$, $p = 0.004$) and the nocturnal dip in HR ($r = 0.493$, $p = 0.020$), but not SAP dipping ($r = 0.290$, $p = 0.191$).

**DISCUSSION**

This study evaluated the relations between actigraphy-based sleep characteristics and 24 hour ambulatory blood pressure and heart rate patterns in normotensive young adults. In our study design, sleep data was acquired for several nights across the span of one month, and ABPM was obtained on a non-actigraphy night to account for the reported impact of ABPM on sleep (13, 22, 33). When controlling for these potential confounds, we observed that low sleep efficiency was significantly associated with blunted SAP and heart rate dipping at night in normotensive young adults. These relations between sleep efficiency were observed
despite no significant difference in total sleep time. These findings suggest that sleep
efficiency, independent of sleep duration, may be an important factor in diurnal
hemodynamic regulation in young adults.

Blunted nocturnal blood pressure dipping has been associated with increased
risk of mortality in large epidemiological studies of hypertensive (14, 46) and
normotensive adults (24). In addition, a longitudinal analysis from the Coronary Artery
Risk Development in Young Adults (CARDIA) study demonstrates that blunted
nocturnal blood pressure dipping in adolescents is associated with an increased risk of
hypertension later in life (48). Given that the present study evaluated healthy young
adults, our findings may be more informative for future risk of hypertension. The
literature is divided on whether nocturnal SAP dipping is associated with sleep efficiency
in hypertension (21, 28, 41). However, the few studies that assessed sleep by
actigraphy with ABPM in normotensive and prehypertensive adolescents and young
adults did not find an association between sleep efficiency and SAP dipping (22, 32).
There are several possibilities that may explain our conflicting results. Mezick et al. (32)
measured actigraphy data for 7 consecutive nights and ABPM for 2/7 nights during that
week and did not account for the differences in sleep efficiency with and without ABPM.
Hughes et al. (22) collected actigraphy and ABPM data within the same 24h period and
even noted that 12% of the subjects reported being awoken by the ABPM which has
been reported to decrease sleep efficiency (13, 22, 33). To our knowledge, the present
study is the first to examine the association of actigraphy-based sleep and ABPM using
an experimental approach that eliminated artificial sleep disruption from the ABPM, and
our findings suggest a statistical association between low sleep efficiency and blunted SAP dipping at night in normotensive young adults.

While blood pressure is routinely assessed in epidemiologic studies, heart rate is not as widely supported as a prognostic indicator of cardiovascular health, and is therefore inadequately reported in hypertension research (36). However, there is strong evidence to support heart rate has prognostic value for future cardiovascular risk and mortality, independent of blood pressure (15, 18, 19). Furthermore, blunted nocturnal dipping of heart rate has been shown to be an independent risk factor for cardiovascular and all-cause mortality (4, 47). Although it is widely understood that heart rate decreases at night compared to daytime measurements, this nocturnal bradycardia is often attributed, perhaps oversimplistically, to nighttime posture and activity levels (37).

In fact, recent evidence suggests that the extent that heart rate dips at night are governed by circadian rhythms and sleep architecture rather than simply activity (8).

Our findings that nocturnal dips in heart rate are blunted in low efficiency sleepers, as well as higher mean nocturnal heart rate, when compared to high sleep efficiency subjects adds novel insight into how sleep modulates heart rate. It has been consistently shown that sympathetic activity is increased during rapid eye movement (REM) sleep and reduced during slow wave sleep (6, 44, 45). Fung et al. (17) demonstrated a significant correlation between the percentage of slow wave sleep and the incidence of hypertension. Thus, it is plausible that young adults with lower sleep efficiency experience reduced slow wave sleep (i.e., “deep sleep”) and experience more REM sleep, which would increase nocturnal sympathetic activity leading to blunted
nocturnal heart rate and SAP dipping patterns. However, the present study did not directly assess wake and nocturnal sympathetic activity or sleep architecture.

One of the more relevant findings of the present study was that the reported associations between sleep efficiency and nocturnal hemodynamic dipping persisted despite no difference in total sleep time between the low and high sleep efficiency groups. This is consistent with emerging epidemiological evidence that attention to both sleep duration and quality are essential, and that investigation of only sleep duration can be misleading. For example, Knutson et al. (25) examined CARDIA data using a longitudinal analysis and reported that not only short sleep duration, but also reduced sleep consolidation (i.e., low sleep efficiency), was significantly associated 5-year increases of resting blood pressure in 578 Caucasian and African American adults aged 33-45 at baseline. Bruno et al. (7) reported that sleep quality, but not sleep duration, was associated with resistance to hypertensive treatment in women. Our findings support the emerging concept that sleep efficiency, independent of sleep duration, may be a key factor to consider regarding the role of sleep in cardiovascular health.

We acknowledge our sample size as an important limitation. A larger sample size would have allowed for other key variables (age, body mass index, gender, etc.) to be incorporated into a more advance multivariate statistical model. That said, Table 1 demonstrates that several of these potential confounders were balanced between our two sleep efficiency groups. Moreover, we observed consistent statistical significance whether we analyzed via an 85% sleep efficiency group analysis or using a continuous regression analysis. Because all actigraphy-based parameters were restricted to the early follicular phase in all female subjects, our findings do not account for potential
variability in sleep patterns across the menstrual cycle (3) or investigate the effects of female sex hormones on nocturnal hemodynamic dipping. Finally, we acknowledge that while several studies have validated actigraphy accessed sleep efficiency against the gold-standard polysomnography (1, 11, 26, 29, 34, 42), some studies have found variation in the calculation of sleep efficiency between the two techniques (5, 40).

Summary and Practical Significance

The primary finding of this study is that low sleep efficiency is significantly correlated to blunted SAP dipping, which a known risk factor for future hypertension in young adults (48). In addition, low sleep efficiency was also associated with higher nocturnal heart rate and blunted heart rate dipping, which are clinically-relevant indices of cardiovascular prognostic value that are often overlooked in this area of research (36). Our methodology attempted to control for potential variation in sleep patterns of young adults, and for the methodological consequences of ABPM on actigraphy data (13, 22, 33). Accordingly, we suggest that the present methodology and findings might serve to inform future epidemiological studies aimed at clarifying the relations between sleep and diurnal hemodynamic patterns in humans.
REFERENCES


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Table 1. Sleep and 24-hour Blood Pressure and Heart Rate

<table>
<thead>
<tr>
<th></th>
<th>High Sleep Efficiency (N=10)</th>
<th>Low Sleep Efficiency (N=12)</th>
<th>P-values</th>
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<tbody>
<tr>
<td>Female (%)</td>
<td>40</td>
<td>42</td>
<td>0.94</td>
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<tr>
<td>Age (years)</td>
<td>22 ± 1</td>
<td>22 ± 2</td>
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<tr>
<td>Weight (kg)</td>
<td>77 ± 5</td>
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<tr>
<td>Height (cm)</td>
<td>174 ± 3</td>
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<td>BMI</td>
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<td><strong>Sleep</strong></td>
<td></td>
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<tr>
<td>Sleep Time (hours)</td>
<td>8 ± 0</td>
<td>7 ± 0</td>
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<tr>
<td>Sleep Efficiency (%)</td>
<td>87 ± 1</td>
<td>82 ± 1*</td>
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<tr>
<td>SOL (minutes)</td>
<td>19 ± 3</td>
<td>24 ± 3</td>
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<tr>
<td>WASO (minutes)</td>
<td>35 ± 3</td>
<td>45 ± 5</td>
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<tr>
<td>Awakenings (#)</td>
<td>40 ± 2</td>
<td>43 ± 3</td>
<td>0.59</td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
<td></td>
<td></td>
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<tr>
<td>24-hour SAP (mmHg)</td>
<td>123 ± 3</td>
<td>126 ± 3</td>
<td>0.41</td>
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<tr>
<td>24-hour DAP (mmHg)</td>
<td>69 ± 1</td>
<td>70 ± 1</td>
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<tr>
<td>Wake SAP (mmHg)</td>
<td>128 ± 3</td>
<td>130 ± 3</td>
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<td>Wake DAP (mmHg)</td>
<td>73 ± 1</td>
<td>74 ± 1</td>
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<tr>
<td>Sleep SAP (mmHg)</td>
<td>109 ± 3</td>
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<td>Sleep DAP (mmHg)</td>
<td>58 ± 2</td>
<td>61 ± 2</td>
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<td>SAP dip (%)</td>
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<td>DAP dip (%)</td>
<td>20 ± 2</td>
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<td><strong>Heart Rate</strong></td>
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<td>24-hour HR (bpm)</td>
<td>66 ± 2</td>
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<td>HR wake (bpm)</td>
<td>70 ± 2</td>
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<td>HR sleep (bpm)</td>
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<tr>
<td>HR dip (%)</td>
<td>21 ± 3</td>
<td>12 ± 3*</td>
<td>0.03</td>
</tr>
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</table>

Sleep Onset Latency (SOL), Wake After Sleep Onset (WASO), Systolic Arterial Pressure (SAP), Diastolic Arterial Pressure (DAP), Heart Rate (HR). * P < 0.05 vs. high sleep efficiency.
**FIGURE LEGENDS**

**Figure 1.** Nocturnal dips in systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and heart rate (HR) in high and low efficiency sleepers. Nocturnal dip in SAP and HR were blunted in the low sleep efficiency group compared to the high sleep efficiency group * P < 0.05 vs. high sleep efficiency.

**Figure 2.** Correlations of sleep efficiency to nocturnal dips in systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and heart rate (HR). Sleep efficiency scores were correlated to nocturnal SAP and HR dips, but not DAP dip.
Figure 1. Nocturnal dips in systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and heart rate (HR) in high and low efficiency sleepers. Nocturnal dip in SAP and HR were blunted in the low sleep efficiency group compared to the high sleep efficiency group * P < 0.05 vs. high sleep efficiency.
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