Sleep Quality and Blood Pressure Dipping in Normal Adults

José S. Loredo, MD[1,3]; Richard Nelesen, PhD[2]; Sonia Ancoli-Israel, PhD[2,4]; Joel E. Dimsdale, MD[2]

Department of Medicine[1] and the Department of Psychiatry[2] University of California, San Diego; Department of Medicine[3] and Psychiatry[4] Veterans Affairs San Diego Healthcare System

Objectives: To investigate the relationship between sleep quality and nocturnal blood pressure dipping in normal subjects. We hypothesized that sleep quality correlates with dipping.
Design: Cross-sectional study.
Setting: Unattended polysomnography in the home followed by a 24-hour ambulatory blood pressure measurement.
Patients: Eighty-eight self-described normal subjects were evaluated; 26 were excluded due to an apnea-hypopnea index ≥ 10. None were taking antihypertensive medications.
Interventions: N/A.
Measurements and Results: Subjects were divided into dippers and nondippers based on ≥ 10% drop in nocturnal mean arterial pressure (MAP). Sleep-quality variables included total sleep time; sleep latency; percentage of stages 1, 2, 3, 4, and rapid-eye-movement sleep; percentage of wake time after sleep onset (WASO); total arousal index; and sleep efficiency. Of the remaining 62 subjects, 17.7% were nondippers, and 7 were hypertensive. There was no difference in age, body mass index, apnea-hypopnea index, blood pressure, or sleep quality between groups. Stage 4 sleep correlated significantly with dipping of diastolic blood pressure and MAP (r = 0.410 and 0.378, respectively, $P \leq .002$), and percentage of WASO was negatively correlated with dipping of diastolic blood pressure (r = -0.360, P = .004), suggesting that greater dipping was associated with better sleep quality. On multivariate analyses, Stage 4 sleep was independently associated with dipping of diastolic blood pressure (P = .034) after adjusting for screening MAP, percentage of WASO, total arousal index, and Stage 1 sleep. The same link was found between Stage 4 sleep and dipping of MAP (P = .05) after adjusting for screening MAP, age, sex, and body mass index. Repeat analyses excluding hypertensives yielded similar findings.
Conclusion: Our data suggest that deeper and less-fragmented sleep is associated with more blood pressure dipping in normal subjects.
Key Words: Sleep quality, dipping, ambulatory blood pressure monitoring, delta sleep.
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INTRODUCTION

THE QUALITY AND DURATION OF SLEEP ARE CONSIDERED TO BE IMPORTANT ASPECTS OF RESTORATIVE SLEEP. A number of physiologic parameters, such as respiration, oxygen consumption, temperature regulation, hormonal balance, and cardiovascular function, change during sleep.[1-4] In many of these systems, sleep has a "toning-down" effect, and it is intuitive to think that the better the quality of sleep, the greater the toning-down effect of sleep on physiologic functions. An example is the effect of sleep on blood pressure. Normally during sleep, blood pressure and heart rate drop by 10% to 20% from their daytime values in both normotensive and hypertensive individuals. This drop in blood pressure is called dipping. However, some individuals do not experience dipping during sleep (nondippers), and occasionally some increase their blood pressure during sleep (reverse dippers). Dipping has been postulated to be a restorative physiologic process.[5] Conversely, nondipping may be associated with an increased risk for hypertensive end-organ damage.[6,7] Few researchers have studied nondipping in normal populations, and, thus, the prevalence of nondipping in normal subjects has not been firmly established. In one study, Cugini et al[8] estimated the prevalence of nondipping among normal individuals to be 16%.

Dipping and nondipping have primarily been studied in patients with various disease states. A higher prevalence of nondippers has been described among subjects with essential hypertension,[9] sodium sensitivity,[10] chronic renal failure,[11] obstructive sleep apnea,[12] Cushing's syndrome,[13] and autonomic nervous system dysfunction. We have reported in previous studies a prevalence of nondippers of greater than 80% in a sample population of severe sleep apneics[14] and higher nondipper to dipper ratios in elderly subjects with hypertension and sleep apnea.[15]

The relationship between sleep quality and blood pressure changes during sleep has not been well described. Some believe that the quality of sleep affects the degree of dipping.[16-18] The few studies that have been published in English that have evaluated the relationship of sleep quality to dipping have looked primarily at patients with hypertension and sleep apnea. The general consensus is that nondippers have more disturbed sleep, as determined by electroencephalography (EEG).[18-20] However, when Hermida et al[21] indexed sleep by physical activity alone, they found no relationship between movement during sleep and dipping in hypertensives. In patients with severe sleep apnea, we found that despite having a high prevalence of nondipping, their sleep quality did not appear to be associated with dipping.[14] In 2 studies of normal individuals,[17,22] nondippers had more disturbed sleep. However, in both of these studies, sleep quality was evaluated only by the degree of nighttime activity as measured by actigraphy rather than by polysomnography, and, therefore, no relationship with sleep stages could be examined. In this study, we tested the hypothesis that sleep quality, as measured by polysomnography, correlates with dipping in self-described normal subjects.

Disclosure Statement
This is not an industry-sponsored study. Dr. Ancoli-Israel serves on the speaker's bureau for King Pharmaceuticals, Takeda, Neurocrine/Pfizer Inc., and Sepracor. Drs. Loredo, Nelesen, and Dimsdale have indicated no financial conflicts of interest.

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Address correspondence to: Dr. José S. Loredo, UCSD Medical Center Department of Medicine, 200 West Arbor Drive, San Diego, CA 92103-0804; Tel: 619 543 5593; Fax: 619 543 7519; E-mail: jloredo@ucsd.edu

MATERIALS AND METHODS

Subjects

All subjects gave informed consent to the protocol, which was approved by the Institutional Review Board. A total of 88 self-described normal adult subjects were studied at the University of California San Diego Clinical Research Center. Subjects were recruited from the community by way of public advertisements and by word of mouth from previous participants. Inclusion criteria included age 25 to 55 years and no major medical, sleep disorders, or psychiatric illnesses. Subjects found to have hypertension on screening were not excluded. Weight ranged from normal to up to 1.5 times the ideal body weight, as determined from Metropolitan Life tables.[23] Subjects were also excluded if they were receiving medications known to affect sleep, if they currently abused alcohol or drugs, or if they were shift workers or normally slept during the day.

Experimental Design

Blood pressure was measured three times on one session after subjects rested in the sitting position for 5 minutes during a morning screening in the sleep laboratory. Subjects with a systolic blood pressure (SBP) consistently greater than 140 mm Hg or with a diastolic blood pressure (DBP) greater than 90 mm Hg, or both, were considered hypertensive. Subjects who were taking medications to control their blood pressure had their antihypertensive medications tapered off with the consent from their primary care physician. Daily blood pressure measurements were made over a 3-week washout period before the subject was further studied. Medications were restarted if blood pressure exceeded 180/110 mmHg at any one time.

An unattended home polysomnogram was performed using the Embla Sleep recording system (Embla, Flaga hf. Reykjavik, Iceland). The overnight sleep recording included central and occipital EEG, bilateral electrooculography, submental and tibialis anterior electromyography, electrocardiography, nasal/oral airflow using a thermistor and nasal cannula, and respiratory effort using chest and abdominal inductance belts. Oxyhemoglobin saturation was monitored using pulse oximetry. The EEG sleep records were scored according to the criteria of Rechtshaffen and Kales.[24] Respiratory events were derived from the nasal-cannula pressure sensors. The thermistor was primarily used to denote mouth breathing. Apneas were defined as decrements in airflow of at least 90% from baseline for a period 10 seconds. Hypopneas were defined as a decrement in airflow of at least 50% but less than 90% from baseline for a period 10 seconds associated with a 4% oxyhemoglobin desaturation or an arousal. The number of apneas and hypopneas per hour of sleep were calculated to obtain the apnea-hypopnea index (AHI). Subjects with an AHI of 10 or more or a periodic limb movement index greater than 5 per hour were considered to have a sleep disorder and were excluded from the study.

After the home sleep recording, a 24-hour ambulatory blood pressure measurement was begun using the SpaceLabs ambulatory blood pressure monitoring system (SpaceLabs Medical, Inc. Model 90207, Redmond Wash). This apparatus was programmed to measure blood pressure every 30 minutes from 10 PM to 6 AM and every 15 minutes from 6 AM to 10 PM. Nighttime or sleeping blood pressure was determined from when the subjects turned the lights off to when they got up the following morning. Daytime (awake) and nighttime (sleeping) average SBP, DBP, and mean arterial pressures (MAP) were recorded.

Dipping Definition

Three measurements of dipping were obtained by subtracting nighttime (sleeping) blood pressure measurements from the daytime (awake) blood pressure measurements. These included SBP, DBP, and MAP changes. Patients were also divided into dippers and nondippers based on a nocturnal drop in MAP of at least 10%.

Sleep-Quality Variables

Ten variables to measure sleep quality were calculated: Total sleep time; sleep latency to the first 3 epochs of stage 1 sleep or the first epoch of any other sleep stage; the percentage of total sleep time spent in Stage 1 sleep (Stage 1%), Stage 2 sleep (Stage 2%), Stage 3 sleep (Stage 3%), Stage 4 sleep (Stage 4%), Stage rapid eye movement (REM) sleep (Stage REM%); the percentage of time awake after sleep onset (WASO) during the sleep period (WASO%); the total arousal index (TAI); and sleep efficiency. The American Academy of Sleep Medicine arousal criteria were used.[25] Briefly, arousals were defined as a sudden rise in EEG frequency to alpha or theta activity lasting at least 3 seconds but less than 15 seconds preceded by at least 10 seconds of sleep.

Statistical Analysis

The various subject characteristics and sleep-quality variables were compared between dippers and nondippers by 2-tailed independent sample *t* tests. Two-tailed Pearson correlations with Bonferroni's correction were performed to examine the association between sleep-quality variables and blood pressure dipping for each of the 3 dipping measurements. A multivariate linear regression model was used to further assess the association of sleep quality on dipping, as measured by SBP, DBP, and MAP changes. Screening MAP was entered first in the model to control for the possible confounding effect of hypertensive status. Only those sleep-quality variables exhibiting a significant or borderline correlation with the dipping variables were included in the models. The variables were entered into the model in descending order of the strength of their correlation. Stage 4% was entered first, followed by WASO%. This order fits our hypothesis that deeper and more efficient sleep constituted better-quality sleep. The TAI and Stage 1% were entered last in the model as variables denoting lower-quality sleep. An α of .05 was considered statistically significant. The analyses were then repeated after excluding the hypertensive subjects to further remove any potential confounding effect of hypertensive status. The significant relationships from these analyses were reevaluated in a regression model while controlling for screening blood pressure, age, sex, and body mass index (BMI). Statistical analyses were performed using the statistical software packages SPSS for Windows 11.0 (SPSS, Inc., Chicago, Ill).

RESULTS

Table 1 provides the subject characteristics and sleep-quality data. Twenty-six subjects were excluded because of having an

elevated AHI (AHI ≥ 10) on the sleep recording. None were excluded due to other sleep disorders. The study sample consisted of 62 subjects. Nearly 18% were nondippers. There was no significant difference in age, AHI, screening blood pressure, or BMI between dippers and nondippers. On average, dippers were of normal weight. Nondippers tended to be slightly overweight, and their blood pressure tended to be higher than that of nondippers, although still within the normal range. Seven of the subjects were classified as hypertensive. Of these, only 1 subject was a known mild hypertensive who required tapering off of antihypertensive medications. Among dippers, 7.8% were hypertensive, whereas 27.3% of nondippers were hypertensive. There was a borderline statistically significant association between hypertensive status and dipping category (odds ratio 4.4, 95% confidence interval 0.826, 23.5; Pearson $\chi^2_{3.41,1}$; $P = .065$). Dippers dropped their nocturnal MAP an average of 17.1%, while nondippers dropped their MAP significantly less (5.8%, $P < .001$), which is a logical and expected consequence of the group selection. There was no statistically significant difference in mean values for all the sleep-quality variables between dippers and nondippers.

Data were also examined using continuous measures of dipping as opposed to the dichotomized "dippers" versus "nondippers." Such continuous measures have greater statistical power. Table 2 presents the univariate correlations between sleep-quality measures and dipping variables. Significance was adjusted using the rather conservative Bonferroni's correction. A significant P value was determined to be .0045 or less on a 2-tailed test. Stage 4% was positively correlated with DBP dipping and MAP dipping ($P \leq .002$) and had a borderline positive correlation with SBP dipping. Stage 3% was not significantly correlated with any of the dipping variables. Slow-wave sleep percentage (Stage 3% and stage 4% combined) had borderline positive correlations with SBP, DBP, and MAP dipping. WASO% was negatively correlated with DBP dipping ($P = .004$) and had a borderline negative correlation with MAP dipping. Stage 1% and TAI were negatively correlated with DBP and MAP dipping; however, these correlations were of borderline significance.

Tables 3 and 4 show the results of the multivariate linear regression procedures where DBP and MAP dipping were the dependent variables, respectively. Stage 4% was independently associated with DBP dipping, after adjusting for screening MAP, WASO%, TAI, and Stage 1% (Table 3). In the case of MAP dipping, Stage 4% was independently associated with MAP dipping when controlling for screening MAP and WASO% (Table 4). None of the variables predicted SBP dipping. Stage 4% explained a modest but significant part of the variance of MAP and DBP dipping after controlling for screening blood pressure (R^2 changes, 8.3% and 9.4%, respectively, $P < .02$).

All analyses were repeated after excluding the 7 hypertensive subjects in order to further eliminate the possible confounding effect of hypertensive status. On dichotomized data, there was no significant difference between dippers and nondippers on age, BMI, AHI, screening blood pressure, or any of the sleep-quality variables, except for the expected difference in MAP dipping (17.3% ± 4.6% vs 5.7% ± 2.8%, $P < .001$ between dippers and nondippers, respectively). Two-tailed Pearson correlations between the sleep-quality variables and dipping showed a significant positive correlation between Stage 4% and MAP ($r = 0.372$, $P = .005$), DBP dipping ($r = 0.407$, $P = .002$), and a borderline correlation with SBP dipping (Bonferroni's correction significant $P \leq .005$). WASO%, TAI, and Stage 1% had negative correlations with DBP and MAP dipping, but these were of borderline significance. Multivariate linear regression showed that Stage 4% was independently associated with DBP dipping after adjusting for

Table 1—Subject Characteristics

Variable	Dippers	Nondippers
Number	51	11
Age, y	34.8 ± 7.7	37.4 ± 7.9
Sex, men/women	25/26	4/7
BMI, kg/m^2	24.9 ± 4.2	26.4 ± 2.8
AHI, events/h	4.8 ± 2.8	5.7 ± 2.8
Dipping MAP, %	17.1 ± 4.6	5.8± 3.3*
Mean screening SBP, mmHg	122.4 ± 11.3	126.9 ± 12.1
Mean screening DBP, mmHg	71.8 ± 9.0	76.0 ± 10.3
Hypertensive subjects, no.	4	3
Total sleep time, min	408 ± 65	411 ± 78
Sleep latency, min	18.2 ± 27.3	15.2 ± 14.3
WASO, %	8.5 ± 7.2	9.8 ± 8.0
Percentage of sleep stage, %		
1	7.4 ± 3.9	7.0 ± 3.4
2	62.8 ± 8.2	63.1 ± 8.0
3	6.7 ± 4.6	6.0 ± 4.0
4	3.5 ± 5.0	1.9 ± 3.0
REM	19.6 ± 5.3	22.0 ± 6.3
Total Arousal Index, events/h	8.1 ± 5.7	10.4 ± 6.6
Sleep efficiency, %	87.6 ± 9.3	87.2 ± 8.6

Data are presented as mean ± SD unless otherwise indicated.
*Statistically significant, $P < .001$.
BMI refers to body mass index; AHI, apnea-hypopnea index; MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; WASO%, percentage of time awake after sleep onset divided by sleep-period time; REM, rapid eye movement.

Table 2—Pearson Correlations of Sleep-Quality Variables and Blood Pressure Dipping

Variable	SBP Dipping	DBP Dipping	MAP Dipping
Sleep efficiency	0.031	0.203	0.163
Sleep latency	0.216	0.116	0.123
Sleep stage			
Stage 1%	- 0.224	- 0.295†	- 0.302†
Stage 2%	- 0.182	- 0.222	- 0.190
Stage 3%	0.173	0.203	0.187
Stage 4%	0.291†	0.410*	0.378*
Stage REM%	0.040	- 0.002	0.007
Stage SWS%	0.277†	0.366†	0.337†
WASO%	-0.223	-0.360*	-0.320†
Total Arousal Index	- 0.217	-0.332†	- 0.294†
Total sleep time	0.017	0.032	0.032

*Statistically significant at $P \leq .0045$ level (Bonferroni corrected) with 2-tailed test.
†Borderline statistically significant (P values ranged from .005 to .036), 2-tailed significance.
SBP refers to systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; REM, rapid eye movement; SWS, slow-wave sleep; WASO%, percentage of time spent awake after sleep onset divided by sleep-period time.

WASO%, TAI, and Stage 1% ($F_{4,46} = 3.2$, significance of F =.02, $\beta = .479$, $t = 2.31$, $P = .026$). In the case of MAP dipping, Stage 4% was independently associated with MAP dipping when controlling for WASO% and TAI ($F_{3,47} = 3.3$, significance of F = .03, $\beta = .360$, $t = 2.18$, $P = .034$). Stage 4% was significantly associated with SBP dipping only when alone in the model ($F_{1,49} = 4.54$, $P = .038$). Stage 4% explained a modest but significant part of the variance of DBP, MAP, and SBP dipping in normal subjects (R^2 change 16.5%, 13.7%, and 8.5%, respectively, $P < .04$).

Regression procedures were repeated to further evaluate the association of Stage 4% with MAP and DBP dipping while controlling for screening MAP, age, sex, and BMI. Stage 4% continued to be independently associated with MAP dipping after adjusting for screening MAP, age, sex, and BMI ($F_{5,54} = 2.45$, significance of F = .045, $\beta = .363$, $t = 2.0$, $P = .05$). Stage 4% had a borderline association with DBP dipping after controlling for the same parameters ($F_{5,54} = 3.34$, significance of F = .011, $\beta = .406$, $t = 1.89$, $P = .064$).

DISCUSSION

These results indicate that in a population of healthy subjects, with or without hypertension, deeper sleep was associated with more blood pressure dipping. Conversely, our data could also suggest that lighter and more disturbed sleep may be associated

Table 3—Regression Table for Dipping in Diastolic Blood Pressure

Independent Variables in Model	R^2	Percentage of Variance Gained	*df*	F	Significance of F	β	*t*	*P*
Screening MAP	0.126	12.6*	1,58	8.34	.005*	-.281	-2.9	.005*
Screening MAP	0.220	9.4*	2,57	8.02	.001*	-.209	-2.16	.035*
Stage 4%						.488	2.62	.011*
Screening MAP	0.233	1.4	3,56	6.68	.002*	-.178	-1.74	.087
Stage 4%						.452	2.38	.021*
WASO%						-.130	-0.99	.324
Screening MAP	0.233	0	4,55	4.18	0.005*	-.176	-1.7	.094
Stage 4%						.446	2.24	.029*
WASO%						-.126	-0.93	.358
TAI						-.024	-0.12	.905
Screening MAP	0.235	0.2	5,54	3.31	0.011*	-.176	-1.68	.098
Stage 4%						.439	2.18	.034*
WASO%						-.110	-0.75	.458
TAI						-.019	0.08	.940
Stage 1%						-.100	-0.30	.762

*Statistically significant at $\alpha = .05$.
MAP refers to mean arterial pressure; WASO%, percentage of time awake after sleep onset divided by sleep-period time; TAI, total arousal index.

Table 4—Regression Table for Dipping in Mean Arterial Pressure

Independent Variables in Model	R^2	Percentage of Variance Gained	*df*	F	Significance of F	β	*t*	*P*
Screening MAP	0.091	9.1*	1,58	5.82	0.019*	-.196	-2.4	.019*
Screening MAP	0.174	8.3*	2,57	6.02	0.004*	-.140	-1.72	.091
Stage 4%						.375	2.4	.02*
Screening MAP	0.184	1.0	3,56	4.21	0.009*	-.118	-1.38	.173
Stage 4%						.350	2.19	.033*
WASO%						-.090	-0.82	.417
Screening MAP	0.189	0.5	4,55	3.2	0.020*	-.113	-1.30	.200
Stage 4%						.325	1.94	.057
WASO%						-.075	-0.66	.515
TAI						-.095	-0.56	.580
Screening MAP	0.192	0.3	5,54	2.56	0.038*	-.112	-1.28	.206
Stage 4%						.317	1.87	.067
WASO%						-.055	-0.44	.659
TAI						-.041	-0.20	.845
Stage 1%						-.125	-0.45	.654

*Statistically significant at $\alpha = .05$.
MAP refers to mean arterial pressure; WASO%, percentage of time awake after sleep onset divided by sleep-period time; TAI, total arousal index.

with less dipping. These relationships were not apparent when the data were examined in a dichotomous fashion. However, utilizing the more powerful continuous data comparisons, we began to discern that deep sleep is significantly associated with more blood pressure dipping despite using the very conservative Bonferroni's correction. We then ran a series of exploratory multiple regressions to see what may be affecting these relationships and found that, with multiple regression, Stage 4 sleep could predict DBP and MAP dipping after controlling for a number of factors.

For many years, sleep had been assumed to be a passive inert state. However, it is now recognized that sleep is associated with a number of physiologic changes such as hormonal surges,[4,26] body-temperature cycles,[2] sympathetic nervous system activation,[1] and complex cerebral activity. Work from Branderberger and associates[27] has shown that sleep stage influences 24-hour variations in heart rate and heart-rate variability. Specifically, oscillations in delta-wave activity during sleep were inversely coupled with heart-rate variability.[28] For some time, it has been recognized that blood pressure drops during sleep: denominated as dipping. It has also been felt that those subjects who do not experience dipping may be at risk for hypertensive end-organ damage and other cardiovascular complications.[6,7]

Little information is available as to the association of the quality of sleep and dipping. Intuitively, investigators have surmised that the better the sleep quality (deeper sleep, less disrupted sleep), the greater the dipping during sleep. This is supported by findings that arousals, which greatly disturb sleep, result in rises in sympathetic nervous output and rises in blood pressure during sleep.[29,30] We have shown that movement arousals can affect even daytime sympathetic activity.[31] Other investigators have observed that nondippers have more arousals during sleep and tend to have more disrupted sleep.[17,19,22,30]

In this study, we set out to test the hypothesis that sleep quality was associated with blood pressure dipping normally seen during sleep. We recruited a sample of self-described normal subjects from the community and determined their sleep quality with an overnight polysomnogram. Subjects with sleep apnea were excluded because sleep apnea is known to elevate blood pressure during sleep and the prevalence of nondipping is high in sleep apnea.[14,15] We also controlled for the use of medicines that could affect sleep and restricted weight to less than 1.5 times the ideal body weight to avoid the confounding effect of obesity on blood pressure and sympathetic nervous system activity.[32,33] Hypertension, as determined by screening blood pressure, was controlled during the statistical analyses because hypertension has been reported to be associated with nondipping.[34] We further controlled for the possible confounding effects of blood pressure by repeating the analyses after excluding hypertensive subjects. In this sample, 17.7% of subjects were classified as nondippers, which is similar to what has been described in a normal population.[8] There were no differentiating characteristics between dippers and nondippers, including no group differences in sleep-quality variables. Although there were no significant demographic differences between dippers and nondippers, nondippers included more women, were slightly older, and were slightly heavier. To make sure that the relationship between deep sleep and dipping was not a statistical artifact, we evaluated the relationship of Stage 4 sleep and dipping while controlling for screening blood pressure, age, sex, and BMI and found that Stage 4 sleep was still predictive of MAP dipping.

Most previous work in normal individuals that has studied the association of sleep quality with dipping assessed sleep quality indirectly using actigraphy.[17,22] We evaluated sleep quality directly with full overnight polysomnography in a normal population and analyzed the data to determine whether sleep quality was associated with dipping (see Table 2). We found that Stage 4 sleep was significantly correlated with DBP and MAP dipping regardless of the presence or absence of hypertensive subjects, suggesting that the greater the percentage of deep sleep, the greater the drop in blood pressure during sleep. This finding is consistent with our hypothesis that better-quality sleep, in this case deeper sleep, is related to a larger drop in nocturnal blood pressure. Conversely, WASO, TAI, and Stage 1 sleep had borderline negative correlations with dipping, suggesting that the lighter and more disturbed the sleep, the higher the nocturnal blood pressure or less dipping. Our findings are consistent with reports in the literature that nondippers have greater sleep activity, as measured by actigraphy in healthy volunteers,[17,22] and higher frequency of microarousals in nondippers in a small sample of hypertensive patients.[19]

We have previously investigated the relationship of sleep quality and dipping in a sample of patients with severe obstructive sleep apnea.[14] In that cohort, the prevalence of nondipping was very high (83%); however, we did not find a significant association between sleep quality and dipping. It is possible that in our apneic sample, sleep was so disturbed by the frequency of the apneas and arousals (mean AHI of 55.3 and 48.4 for dippers and nondippers, respectively) that the effect of sleep quality on nocturnal blood pressure was not detectable. Indirect evidence of the masking effect of AHI in our previous report was that once blood pressure and sleep apnea were controlled for, slow-wave sleep was a significant predictor of DBP dipping.

Stage 4 sleep was independently associated with DBP and MAP dipping even after controlling for WASO, TAI and Stage 1 sleep (see Tables 3 and 4). Stage 4 sleep also explained a modest portion of the variance for DBP and MAP dipping. Stage 4 sleep was still predictive of MAP dipping after controlling for screening blood pressure, age, sex, and BMI. This finding is consistent with our hypothesis that sleep quality is associated with nocturnal blood pressure dipping yet is puzzling, since the absolute number in minutes of Stage 4 sleep was small (14.3 minutes and 7.8 minutes for dippers and nondippers, respectively), (see Table 1). Sleep, especially delta sleep, has been associated with significant metabolic changes, some of which appear to be related to the effects of delta sleep-inducing peptide.[35,36] This neuropeptide has been linked to changes in respiration and circadian cycles and has a stress-mitigating quality that could potentially affect nocturnal blood pressure. In our study, Stage 3 sleep was not correlated with dipping. Combining Stage 3 and Stage 4 sleep, as is often done, yielded a borderline correlation with dipping, suggesting that the association of deep sleep and dipping depended mainly on Stage 4 sleep. Our data suggest that it may be useful to split Stage 3 and Stage 4 sleep when investigating sleep quality and blood pressure. To our knowledge this is the first report in which Stage 4 sleep has been linked to blood pressure dipping in a normal population.

For logistical purposes, in this study, we chose to define dipping by subject-reported bedtime and waking-time blood pres-

sure. Some have argued that measuring dipping using this definition may not be as sensitive as measuring blood pressure during actual sleep.[37] We have previously reported on the reliability of nocturnal blood pressure dipping using 3 different definitions (clock time, bedtime, and sleep time) and have found no significant difference between them.[38]

A weakness in our study is that the blood pressure measurements and sleep study were performed only once and 1 day apart. This study assumed that the quality of sleep and blood pressure-dipping variability were constant from night to night in our population, which may not necessarily hold true. We have previously reported limited test-retest correlation across 2 sleep settings.[39] A better approach would thus have been to perform the nocturnal blood pressure measurements at the same time as the sleep study over several nights. However, this approach could also be counterproductive in that the greater intrusiveness of the protocol and equipment could result in poorer sleep quality. For instance, we and others have previously reported that cuff inflation during ambulatory blood pressure measurements results in significant sleep disruption.[40,41]

This study cannot address the question of what comes first—poor sleep quality or higher blood pressure during sleep. Our findings show that Stage 4 sleep, although small in absolute number of minutes, explained about 8% to 16% of the variance of blood pressure dipping; thus a number of other factors must be playing a prominent role in nocturnal blood pressure variability. In future studies, it would be interesting to examine a larger sample size so that the importance of additional variables could be examined.

In conclusion, in a self-described normal population, sleep quality was associated with nocturnal blood pressure dipping. Our data suggests that deeper sleep (Stage 4 sleep) and less-fragmented sleep is associated with more dipping.

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