Original Article

Psychological and Physical Stress-Induced Cardiovascular Reactivity and Diurnal Blood Pressure Variation in Women with Different Work Shifts

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There is increasing evidence that diurnal blood pressure (BP) variation, in addition to high BP *per se*, is related to target organ damage and the incidence of cardiovascular events. However, the determinants of diurnal BP variation are not adequately understood. This paper tests the hypothesis that cardiovascular reactivity to acute stress and/or delayed recovery predicts greater diurnal BP variation (*i.e.*, a lower sleep/awake BP ratio). We studied the relationship of diurnal BP variation (assessed by ambulatory BP monitoring) to mental stress (mental arithmetic and anger recall tasks) and physical stress (treadmill)-induced cardiovascular reactivity and recovery in 87 female nurses who worked different shifts. The sleep/awake systolic BP (SBP) ratio was negatively correlated with relative SBP reactivity (maximum SBP increase/baseline SBP: $r = -0.21$, $p = 0.06$) and relative stress response (average of SBP during stress/baseline SBP: $r = -0.23$, $p = 0.04$) induced by anger recall, while the correlations of the sleep/awake SBP ratio with other parameters of reactivity or recovery in the anger recall or mental arithmetic task were not significant. When subjects were divided into day-shift workers ($n = 54$) and night-shift workers ($n = 33$), the sleep/awake SBP ratio was negatively correlated with relative SBP reactivity ($r = -0.41$, $p = 0.02$) and relative stress response of SBP ($r = -0.48$, $p = 0.006$) induced by anger recall, and positively correlated with recovery rate ($r = 0.34$, $p = 0.06$) in the latter group, while these correlations were not significant in the former group. The sleep/awake SBP ratio was inversely correlated with the exercise-induced SBP increase in the day-shift workers ($r = -0.30$, $p = 0.03$), while this association was not found in the night-shift workers. In conclusion, cardiovascular reactivity triggered by psychological and physical stress in the laboratory may be a weak, but significant, determinant of diurnal BP variation; in addition, work shift (day or night) appears to moderate the relationship between these two pressor mechanisms. (*Hypertens Res* 2002; 25: 543–551)

Key Words: diurnal blood pressure variation, cardiovascular reactivity, cardiovascular recovery, psychological stressor, physical stressor, shift worker

Introduction

Ambulatory blood pressure (ABP) varies widely due to various environmental conditions, including psychological and

physical stress (1–4). Similarly, many laboratory studies have reported increases in blood pressure triggered by both physical and psychological acute stressors (4), and there is considerable interindividual variation in the magnitude of these increases (4). Several theorists have hypothesized that

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This study was supported in part by a grant (HL-47540) from the National Heart, Lung and Blood Institute.

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Received January 30, 2002; Accepted in revised form March 26, 2002.

cardiovascular reactivity and recovery induced by psychological stress may be markers of target organ damage (5), or possibly risk factors, for future hypertension (6, 7), especially when there is a positive family history of hypertension (8, 9). However, the role of both cardiovascular reactivity and recovery remain controversial (4).

Ambulatory BP monitoring (ABPM) has been used to show that not only high blood pressure (BP) levels but also a lack of diurnal BP variation is associated with an increased risk for cardiovascular disease in hypertensive patients (10–14). Non-dippers, *i.e.*, those who exhibit a diminished BP decrease during sleep, constitute a subgroup whose abnormal diurnal BP variation is associated with increased rates of damage to all target organs (brain, heart, and kidney) and poorer prognosis following cardiovascular events, compared to dippers with a normal sleep BP fall (10–13). Among dippers, we recently identified a second potential high risk group, “extreme” dippers, who exhibit an exaggerated fall in BP during sleep, and have found that among elderly hypertensive patients (*i.e.*, 60 years and older), extreme-dippers have more marked cerebrovascular damage than dippers (14). Thus, it seems clear that the diurnal BP pattern is an important factor in target organ damage. However, the determinants of diurnal BP variation remain unclear (15). Various changes in autonomic nervous function (16–19), neurohumoral factors (20), hemodynamic factors (21–23), sleep quality (24), and behavioral and genetic factors (1, 2, 25, 26) might be involved in the pathogenesis of abnormal BP variation patterns. In addition, given the hypothesized role of cardiovascular reactivity and recovery in the development of hypertension, these variables may play a role in diurnal variation. However, to our knowledge, the relationship of diurnal BP variation to cardiovascular reactivity and recovery has not been investigated.

We recently reported that ethnicity and shift work are independent predictors of non-dipping status in working women (25). Shift workers (*i.e.*, night workers) are hypothesized to be at higher risk for coronary artery disease than day workers (27, 28). However, the mechanism underlying the relationship between shift work and coronary artery disease remains unclear. Some coronary risk factors have been reported to be higher in shift workers than day workers (29). Munakata *et al.* reported that psychological disturbances after night work were associated with altered cardiovascular and endocrine response (30). The diurnal changes of BP and heart rate variability are predominantly determined by extrinsic factors (sleep and awake behavior status) rather than by intrinsic diurnal rhythm (2). Shift work might moderate the relationship between diurnal BP variation and BP reactivity.

In the present study, we investigated the relationship of diurnal BP variation (assessed by ambulatory BP monitoring) to mental stress (mental arithmetic and anger recall tasks) and physical stress (treadmill)-induced cardiovascular reactivity and recovery in 87 females with different work shifts.

We hypothesized that women who were more reactive and/or exhibited delayed recovery would exhibit a greater difference between their sleep and awake BPs (*i.e.*, a lower sleep/awake ratio).

Subjects and Methods

Subjects

We studied 87 women aged 30 to 59 years (mean $\pm$ SD: 40 ± 7.5 years) who had participated in the Work Site BP Study. All were employed as full-time nurses (registered nurses, nurse practitioners, or nurse aids) at a large private hospital (25). All participants had originally been part of a BP screening of 727 of the 764 nursing staff of the medical/surgery, child/maternity, and critical care departments (95%). Eligibility criteria for participation included: age 30 to 60 years, full-time employment at the hospital for at least 1 year, body mass index (BMI) < 30 kg/m², screening BP $< 160/105$ mmHg, absence of clinically overt cardiovascular disease, renal disease, and diabetes mellitus, and no current use of antihypertensive medication. Further details on inclusion/exclusion criteria have been reported previously (25). A total of 232 nurses met all eligibility criteria. In all, 166 nurses were invited to participate in the larger study, and 105 (99 women and 6 men, 65%) completed the protocol after giving written informed consent. Participants completed a comprehensive evaluation that included 24-h ABPM, an echocardiogram, psychosocial, demographic, and medical history questionnaires, a laboratory-based psychological stress test, and a treadmill exercise stress test. The stress tests were conducted in the late morning or early afternoon, almost always on a non-workday. In the present study, we analyzed the data of 87 women who completed the psychological stress test, treadmill exercise test, and ABPM. The protocol and consent form were approved by the New York Hospital-Cornell Medical Center Institutional Review Committee for Research Involving Human Subjects.

Clinic BPs were measured by sphygmomanometer in the sitting position, according to the American Heart Association's recommended protocol. BMI was calculated as weight (kg) / [height (m)]², as measured by a nurse/technician.

Psychological Stress Test

Beat-to-beat BP and heart rate were noninvasively recorded using a Finapres 2300 BP monitor (Ohmeda, Englewood, USA) during the psychological stress test, as described previously (8). This method uses a finger cuff, which was worn on the third finger of the non-dominant hand following the previously established protocol (8, 31, 32). Systolic (SBP) and diastolic BPs (DBP) and heart rate, averaged for successive pairs of heart beats, were output to a computer file. When the subject arrived at the laboratory, the experimenter explained the procedures, fitted her with the BP cuff, and

Fig. 1. Cardiovascular reactivity and recovery parameters derived from psychological stress test. (A) Baseline: mean of the smoothed data for the 2 min of the baseline period that precede the final 15 s. (B) Reactivity parameters: 1) reactivity: peak value during the stress task (maximum value of smoothed data) - the baseline value; 2) relative reactivity: reactivity/baseline; 3) stress response (based on area under the curve [AUC]): Area S1/duration of stress task period; 4) relative stress response: stress response/the baseline value; 5) delayed response rate: Area S2/(Area S1 + Area S2 + Area S3); 6) desensitization: Area S3/(Area S1 + Area S2 + Area S3). (C) Recovery parameters: 1) 50% recovery: number of seconds after the start of the recovery period when smoothed data first drop below the baseline value + $0.50 \times$ reactivity; 2) 75% recovery: number of seconds after the start of the recovery period when smoothed data first drop below the baseline value + $0.25 \times$ reactivity; 3) recovery AUC: Area R2/(Area R1 + Area R2).

asked her to sit quietly during a 15-min baseline period. After this, the subject engaged in the serial-subtraction task for 2 min (mental arithmetic test), during which she counted backwards by 13 s from a large number (1,084). During this task, the subject was encouraged by the experimenter to count as quickly and accurately as possible. When the task was ended, the subject sat quietly during a second 15-min rest period. Each subject then engaged in an anger-recall task, during which she was asked to recall and describe a recent situation that made her very angry (33). The subject was asked to describe the event/circumstances (3 min) and then to describe her feelings at the time of the event (3 min). Following the anger recall task, the subject sat through a third rest period (15 min), to provide measurements of BP and pulse rate during recovery from the anger recall task.

Cardiovascular Reactivity and Recovery Parameters for the Psychological Stress Test

The 15-point moving average of the raw data was used to smooth the SBP, DBP and pulse-rate time-series data for each participant. Prior to conducting analyses with the diurnal BP variation data, the following parameters assessing cardiovascular reactivity to and recovery from psychological stress (both the mental arithmetic test and anger recall test) were defined and calculated, as illustrated in Fig. 1A: Baseline: mean of the 2 min of the baseline period that preceded the final 15 s; Fig. 1B: Reactivity parameters, including 1) reactivity: peak value during the stress task (maximum value of the smoothed data [15-point moving average]) - the baseline value; 2) relative reactivity (the % increase in BP or pulse rate): $100\% \times \text{reactivity/baseline}$; 3) stress response (based on area under the curve [AUC]): Area S1/duration of stress task period; 4) relative stress response: $100\% \times \text{stress response/the baseline value}$; 5) delayed response rate: $100\% \times \text{Area S2}/(\text{Area S1} + \text{Area S2} + \text{Area S3})$; and 6) desensitization: $100\% \times \text{Area S3}/(\text{Area S1} + \text{Area S2} + \text{Area S3})$; Fig. 1C: Recovery parameters, including 1) 50% recovery: number of seconds after the start of the recovery period when smoothed data first drop below the baseline value + $0.50 \times$ reactivity; 2) 75% recovery: number of seconds after the start of the recovery period when smoothed data first drop below the baseline value + $0.25 \times$ reactivity; and 3) recovery AUC: $100\% \times \text{Area R2}/(\text{Area R1} + \text{Area R2})$.

Each participant engaged in a multistage exercise treadmill test according to the Cornell protocol (34). The subject remained on the treadmill for up to five 3-min stages. SBP, DBP, and pulse rate were recorded by cuff when the subject was standing immediately before testing (baseline) and during the last min of each 3-min exercise stage. Subjects exercised until reaching an age-specific target heart rate or development of symptoms necessitating termination of the test. The recovery phase was 4 min, and the BP and pulse rate were recorded with the subject in a seated position at the end of each min of this period. Physical exercise-related BPs and pulse rate parameters were calculated as follows. The exercise-induced increase (reactivity) was calculated as the value at the last exercise stage - baseline value; the relative exercise-induced increase (relative reactivity) as $100\% \times (\text{value at the last exercise stage} - \text{baseline}) / \text{baseline}$; and recovery as $100\% \times (\text{the value at the last exercise stage} - \text{the value at the end of the 4-min recovery})/\text{reactivity}$.

Exercise Treadmill Methods

Each participant engaged in a multistage exercise treadmill test according to the Cornell protocol (34). The subject remained on the treadmill for up to five 3-min stages. SBP, DBP, and pulse rate were recorded by cuff when the subject was standing immediately before testing (baseline) and during the last min of each 3-min exercise stage. Subjects exercised until reaching an age-specific target heart rate or development of symptoms necessitating termination of the test. The recovery phase was 4 min, and the BP and pulse rate were recorded with the subject in a seated position at the end of each min of this period. Physical exercise-related BPs and pulse rate parameters were calculated as follows. The exercise-induced increase (reactivity) was calculated as the value at the last exercise stage - baseline value; the relative exercise-induced increase (relative reactivity) as $100\% \times (\text{value at the last exercise stage} - \text{baseline}) / \text{baseline}$; and recovery as $100\% \times (\text{the value at the last exercise stage} - \text{the value at the end of the 4-min recovery})/\text{reactivity}$.

24-h ABPM

Noninvasive ABPM was carried out on a normal workday with an automatic ABPM (SpaceLabs 90207, Redmond, USA), which recorded BP and pulse rate every 15 min during the awake period, and every 60 min during anticipated sleep. The monitor was fitted either while the subject was at work or during a research visit to the Hypertension Center of New York Presbyterian Hospital/ Weill Medical College of Cornell University and calibrated by comparison of 5 successive SBP and DBP readings against simultaneously deter-

mined auscultatory readings taken by a trained technician with a mercury column in the sitting position. It was required that the means of the monitor's and technician's readings be within 5 mmHg for the 24-h monitoring to proceed. Each subject was asked to remain as motionless as possible each time the monitor took a reading during waking hours and then to record his or her position, location and activity in a diary.

Sleep BP was defined as the mean BP from the time at which the patient went to bed until the time of awakening (as reported in a diary kept by each subject), and the awake BP was defined as the mean BP during the remaining portion of the day. The average $\pm$ SD number of ambulatory BP readings used for the determination of awake and sleep BPs were 42 ± 9.4 and 6.7 ± 1.8 , respectively. Means based on three or fewer sleep readings, or 15 or fewer awake readings, were treated as missing. The sleep/awake SBP ratio was calculated and, based on this ratio, each patient was categorized as a dipper (ratio < 0.9) or non-dipper (ratio > 0.9) (14). The SDs of BP and pulse rate during the awake and sleep periods were calculated and used as indicators of BP variability. We note that the sleep/awake ratio is not equivalent to the night/day ratio, especially for the night-shift workers.

Statistical Analysis

Data are expressed as a percentage or as the mean $\pm$ SD. Student's *t*-test or Wilcoxon's rank-sum test were used to test differences of means between groups. The χ^2 test was used to evaluate group differences. Pearson's correlation coefficient was used to measure the relationship between continuous measures. Differences/associations with a two-tailed *p*-value < 0.05 were considered to indicate statistical significance.

Results

ABP of Day-Shift Workers and Night-Shift Workers

Table 1 shows the characteristics of the day-shift workers and night-shift workers. As the table shows, sleep SBP was 6 mmHg higher in night-shift workers than in day-shift workers ($p < 0.005$), while there were no significant differences in awake SBP or DBP between the two groups. The non-dipping pattern was significantly more common in the night-shift workers, with 46% of the night-shift nurses showing this pattern, compared to 15% of day-shift nurses ($p < 0.005$). Awake variability (SD) of SBP and pulse rate were significantly higher in night-shift workers than in day-shift workers.

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Figure 2 shows the data for a subject with a typical reaction

Table 1. Ambulatory Blood Pressure and Pulse Rate in Different Shift Workers

Measures	Day-shift (<i>n</i> = 54)	Night-shift (<i>n</i> = 33)
Age (years)	41 $\pm$ 7.7	40 $\pm$ 7.5
African-American (%) [<i>n</i>]	33 [18]	36 [2]
Body mass index (kg/m ²)	24.2 $\pm$ 3.1	24.8 $\pm$ 3.8
Systolic BP (mmHg)		
Clinic	105 $\pm$ 11	110 $\pm$ 13
Awake	116 $\pm$ 8.1	118 $\pm$ 9.2
Sleep	99 $\pm$ 7.7	105 $\pm$ 11 **
SD of systolic BP (mmHg)		
Awake	7.8 $\pm$ 1.3	8.6 $\pm$ 1.6 *
Sleep	6.0 $\pm$ 1.9	6.8 $\pm$ 2.4
Sleep/awake ratio	0.86 $\pm$ 0.05	0.89 $\pm$ 0.06 **
Non-dipping pattern (%) [<i>n</i>]	15 [8]	46 [15] **
Diastolic BP (mmHg)		
Clinic	70 $\pm$ 7.4	76 $\pm$ 9.4 **
Awake	77 $\pm$ 6.1	77 $\pm$ 6.3
Sleep	60 $\pm$ 6.1	63 $\pm$ 7.5
SD of systolic BP (mmHg)		
Awake	7.0 $\pm$ 1.5	7.6 $\pm$ 1.6
Sleep	5.6 $\pm$ 2.2	6.0 $\pm$ 2.3
Pulse rate (mmHg)		
Awake	83 $\pm$ 8.2	80 $\pm$ 7.8
Sleep	68 $\pm$ 6.8	68 $\pm$ 6.7
SD of pulse rate (mmHg)		
Awake	8.3 $\pm$ 1.8	9.7 $\pm$ 2.2 **
Sleep	6.5 $\pm$ 2.5	5.7 $\pm$ 2.4

Data are shown as a percentage or as the mean $\pm$ SD. * $p < 0.05$, ** $p < 0.005$, vs. day-shift workers. Day-shift, day-shift workers; night-shift, night-shift workers.

(Fig. 2A) and one exhibiting cardiovascular hyperreactivity (Fig. 2B) during the anger recall test. Tables 2 and 3 show the average of the cardiovascular reactivity and recovery parameters in the mental arithmetic test, anger recall test, and treadmill exercise test in the day-shift and the night-shift workers. Table 2 shows that SBP and pulse rate recovery from the anger recall task were poorer in night-shift nurses compared to day-shift nurses. In addition, a marginally significant effect was observed for exercise-induced pulse rate, with night-shift nurses evidencing a mean increase in pulse rate of 92 bpm, compared to 86 bpm for day-shift nurses ($p = 0.07$). Similarly, a marginally significant difference between day- and night-shift workers was observed with respect to the relative exercise-induced increase in SBP, with day-shift nurses showing a 111% increase, compared to an increase of 123% in night-shift nurses ($p = 0.08$).

Relative SBP reactivity to the mental arithmetic test and the anger recall test were only weakly correlated with each other ($r = 0.20$, $p = 0.07$), while neither was correlated with relative exercise-induced SBP increase. The relative SBP

Fig. 2. A typical hyperreactive case triggered by psychological stress (anger recall). (A) Normal control (relative reactivity, 0.21; relative stress response, 0.14; recovery rate, 0.93). (B) Hyperreactive case (relative reactivity, 0.75; relative stress response, 0.59; recovery rate, 0.79).

Table 2. Psychological Stress-Induced Cardiovascular Reactivity and Recovery in Different Shift Workers

Measures ^{#1}	Mental arithmetic test				Anger recall test			
	Systolic BP		Pulse rate		Systolic BP		Pulse rate	
	Day-shift	Night-shift	Day-shift	Night-shift	Day-shift	Night-shift	Day-shift	Night-shift
Reactivity parameters								
Reactivity (mmHg or bpm)	20 ± 10	23 ± 12	12 ± 8.8	12 ± 5.7	25 ± 15	24 ± 16	11 ± 8.2	10 ± 7.9
Relative reactivity (%)	18 ± 10	20 ± 12	17 ± 12	16 ± 7.5	21 ± 14	21 ± 15	15 ± 11	14 ± 10
Stress response (mmHg or bpm)	15 ± 9.2	18 ± 11	8.0 ± 7.3	7.9 ± 4.5	14 ± 14	14 ± 14	5.2 ± 5.9	5.0 ± 6.7
Relative stress response (%)	13 ± 9.1	16 ± 10	11 ± 9.9	11 ± 6.1	12 ± 12	11 ± 12	7.1 ± 8.1	6.8 ± 8.8
Delayed response rate (%)	2.4 ± 2.4	1.5 ± 1.6*	0.89 ± 1.4	0.81 ± 1.1	6.2 ± 3.6	6.1 ± 3.2	2.8 ± 2.5	2.8 ± 2.2
Desensitization rate (%)	1.5 ± 1.6	1.8 ± 1.8	3.9 ± 2.9	3.5 ± 3.0	1.2 ± 1.7	1.0 ± 1.0	3.6 ± 3.5	3.2 ± 2.7
Recovery parameters								
50% recovery (s)	92 ± 250	27 ± 34	61 ± 218	32 ± 50	17 ± 25	49 ± 91*	4.3 ± 10	25 ± 89
75% recovery (s)	118 ± 248	157 ± 264	117 ± 252	85 ± 101	115 ± 243	159 ± 281	14 ± 23	68 ± 150*
Recovery rate (%)	89 ± 6.2	88 ± 6.2	87 ± 7.3	88 ± 5.0	86 ± 6.7	87 ± 6.0	89 ± 6.7	90 ± 5.0

^{#1} Absolute values of BP measures are shown as mmHg, and those of pulse rate measures are shown as bpm. All values are shown as the mean ± SD. * $p < 0.05$, vs. day-shift workers. Day-shift, day-shift workers; night-shift, night-shift workers.

stress response to the mental arithmetic test and the anger recall test were also weakly correlated ($r = 0.21$, $p = 0.06$).

Relationship with Diurnal BP Variation

The sleep/awake SBP ratio was more strongly determined by sleep SBP ($r = 0.63$, $p < 0.001$) than by awake SBP ($r = -0.12$, $p = 0.29$) in the total sample. In the night shift workers and the day shift workers, the results were the same (night shift workers: $r = 0.72$ for sleep SBP, $p < 0.001$; $r = -0.05$ for awake SBP, $p = 0.78$; day shift workers: $r = 0.51$ for sleep SBP, $p < 0.001$; $r = -0.25$ for awake SBP, $p = 0.07$). As hypothesized, the sleep/awake SBP ratio was negatively correlated with relative SBP reactivity (SBP increase/baseline

SBP: $r = -0.21$, $p = 0.06$) and relative stress response (average of SBP during stress/baseline SBP: $r = -0.23$, $p = 0.04$) induced by the anger recall task, while the correlations of the sleep/awake SBP ratio with other parameters of reactivity or recovery in anger recall or mental arithmetic tests were not even marginally significant (all $p > 0.10$).

When the subjects were divided into day-shift workers and night-shift workers (Table 4), the sleep/awake SBP ratio was inversely correlated with SBP reactivity ($r = -0.33$, $p = 0.07$), relative reactivity ($r = -0.41$, $p = 0.02$) and relative stress response ($r = -0.48$, $p = 0.006$) induced by anger recall (Fig. 3A), and positively correlated with recovery rate ($r = 0.34$, $p = 0.06$) in the night-shift group, while these correlations were not significant in the day-shift group. When

Table 3. Psychological Stress-Induced Cardiovascular Reactivity and Recovery in Different Shift Workers

Measures ^{#1}	Systolic BP		Pulse rate	
	Day-shift	Night-shift	Day-shift	Night-shift
Exercise-induced increase (mmHg or bpm)	50 ± 16	51 ± 17	86 ± 15	92 ± 14
Relative exercise-induced increase (%)	48 ± 17	47 ± 14	111 ± 30	123 ± 29
Recovery (%)	22 ± 9.4	21 ± 7.5	34 ± 7.7	33 ± 6.3

^{#1} Absolute values of BP measures are shown as mmHg, and those of pulse rate measures are shown as bpm. All values are shown as the mean ± SD.

Table 4. Correlations between Sleep/Awake Ratio of Systolic Blood Pressure and Psychological Stress-Induced Cardiovascular Reactivity and Recovery in Women with Different Work Shift

Measures ^{#1}	Mental arithmetic test				Anger recall test			
	Systolic BP		Pulse rate		Systolic BP		Pulse rate	
	Day-shift	Night-shift	Day-shift	Night-shift	Day-shift	Night-shift	Day-shift	Night-shift
Reactivity parameters								
Reactivity	0.147	- 0.047	- 0.047	- 0.250	- 0.058	- 0.325	- 0.004	- 0.261
Relative reactivity	0.156	- 0.127	0.091	- 0.212	- 0.030	- 0.411 *	0.040	- 0.213
Stress response	0.168	- 0.082	0.020	- 0.215	- 0.069	- 0.428 *	- 0.106	- 0.244
Relative stress response	0.174	- 0.145	0.050	- 0.163	- 0.048	- 0.478 **	- 0.070	- 0.211
Delayed response rate	- 0.180	0.149	- 0.263	0.052	- 0.021	0.167	0.074	0.160
Desensitization rate	0.171	- 0.091	0.230	- 0.153	0.148	- 0.137	0.166	- 0.187
Recovery parameters								
50% recovery	0.165	0.073	0.179	- 0.091	0.056	- 0.029	- 0.209	- 0.093
75% recovery	0.148	- 0.111	0.144	0.040	- 0.023	- 0.260	- 0.267	- 0.248
Recovery rate	- 0.068	0.147	- 0.012	0.209	0.084	0.343	- 0.057	0.153

^{#1} Absolute values of BP measures are shown as mmHg, and those of pulse rate measures are shown as bpm. Pearson's correlation coefficients are shown. * $p < 0.05$, ** $p < 0.01$. Day-shift, day-shift workers; night-shift, night-shift workers.

Fig. 3. Scatter plots of relative stress response with diurnal blood pressure variation (A) and sleep (closed circles) and awake (open circles) blood pressure (B).

we excluded the two outliers (one with a sleep/awake SBP ratio of 1.08, and one with a relative stress response to the anger recall task of 0.59, both apparent in Fig. 3A), these inverse correlations with the sleep/awake SBP ratio diminished only marginally for relative reactivity ($r = -0.35$, $p = 0.06$)

and relative stress response of SBP ($r = -0.42$, $p = 0.02$). When we examined the two components of diurnal variability separately, relative stress SBP response tended to have an inverse relationship with sleep SBP, but not awake SBP, in night-shift workers ($r = -0.33$, $p = 0.07$; Fig. 3B).

Table 5. Correlations with Sleep/Awake Ratio of Systolic Blood Pressure and Physiological Stress-Induced Cardiovascular Reactivity in Women with Different Work Shifts

Measures ^{#1}	Systolic BP		Pulse rate	
	Day-shift	Night-shift	Day-shift	Night-shift
Exercise-induced increase	- 0.301 *	0.112	0.025	0.084
Relative exercise-induced increase	- 0.275	0.071	0.101	0.094
Recovery	- 0.017	- 0.071	0.162	0.161

Pearson's correlation coefficients are shown. * $p < 0.05$. Day-shift, day-shift workers; night-shift, night-shift workers.

Fig. 4. Physiological mechanisms by which psychological and physical stress may affect blood pressure reactivity in women with different work shift.

The sleep/awake SBP ratio was inversely correlated with the exercise-induced SBP increase ($r = -0.30$, $p = 0.03$) and relative exercise-induced SBP increase ($r = -0.28$, $p = 0.05$) in the day-shift workers, while these associations were not found in the night-shift workers (Table 5). Exercise-induced SBP increase was more closely correlated with awake SBP ($r = 0.22$, $p = 0.12$) than with sleep SBP ($r = -0.02$, $p = 0.88$) in the day-shift workers, although neither correlation was statistically significant.

The various measures of pulse rate reactivity to and recovery from stress were not significantly associated with diurnal SBP variation.

We also conducted the above analyses using DBP in place of SBP, and no significant associations were found.

Discussion

Our first hypothesis was that the diurnal BP variation would be partly predicted by individual patterns of cardiovascular reactivity to and recovery from stress generated in the laboratory. Specifically, we thought that those who were more reactive and/or slower to recover from mental and physical stress would be more prone to elevated awake SBP, and hence would exhibit a lower sleep/awake ratio. The latter

prediction, but not the former, was partially supported: we found that diurnal BP variation was related to different stress parameters in night-shift workers. In contrast, exercise-induced BP reactivity was associated with diurnal BP variation in day-shift workers. This is consistent with the hypothesis that psychological stress predominantly releases noradrenaline to activate sympathetic activity, while physical/exercise stress predominantly releases adrenaline from the adrenal glands (Fig. 4).

The psychological stress-induced BP increase triggered by anger recall in the laboratory was related to the diurnal BP variation in the total sample ($r = -0.24$, $p < 0.04$), and this relationship was enhanced in night-shift workers ($r = -0.48$, $p < 0.006$), but not day-shift workers ($r = 0.05$, n.s.). The greater the psychological stress-induced BP increase in night-shift workers, the greater the BP dipping during night. Logically, this could be due to the BP increase induced by psychological stress being positively related to awake BP and/or negatively related to sleep BP in shift workers. We hypothesized that those exhibiting greater BP reactivity to psychological stress would have higher awake BP due to the greater effect of psychological stress on their BP. However, this prediction was not empirically supported. Although BP dipping is calculated from both sleep BP and awake BP, it is usually more strongly related to sleep BP (35). In the present study, this pattern held for night-shift workers, day-shift workers, and the total sample. Furthermore, in the night-shift workers, anger recall-induced SBP increase was more closely correlated with sleep SBP than awake SBP. Thus, in night-shift workers, the more reactive subjects tended to have greater decreases in SBP during sleep. We speculate that in the night-shift workers, an incomplete diurnal rhythm of neurohumoral factors may cause denervation hypersensitivity and increased cardiovascular reactivity.

In a previous study using heart rate variability to assess autonomic nervous system balance, we found that extreme dippers with a marked decrease ($> 20\%$) in sleep BP exhibited a diminished low/high frequency power ratio during sleep, an indicator of sympathetic nervous activity, indicating that their sleep BP decrease may have been caused by a marked withdrawal of sympathetic nervous activation (15). Perhaps the BP of night-shift workers with higher reactivity is maintained during the awake period by exposure to psychological stress while their basal BP is lower. When their

BP levels return to a basal level during sleep, presumably less affected by psychological stress, more marked BP dipping is observed. Because hyperreactivity is the difference between resting BP and BP during stress, it is possible that more reactive subjects exhibit lower BP levels during the resting (stress-free) baseline period. Psychological stress-dependent BP may play a greater role in maintaining BP during the awake period for the night-shift workers than for day-shift workers. This could explain the finding that awake BP variability, which may reflect variation in stress while awake, was significantly higher in the night-shift workers.

A relationship between BP reactivity and the sleep/awake SBP ratio was found during the anger recall test, but not the mental arithmetic test. This may indicate that different types of psychological stress rely on different mechanisms for triggering an increase in BP or pulse rate, as indicated previously. Also, these psychological pressor mechanisms may vary widely from individual to individual. Thus, the pressor mechanism induced by the anger recall test may be more closely related to the pressor mechanism that maintains awake BP in the night-shift workers. Specifically, the anger recall task may be a more ecologically valid stressor, *vis-à-vis* participants' daily life, than the mental arithmetic task. In addition, the relationship between cardiovascular reactivity and the sleep/awake SBP ratio was only found for BP reactivity, and not pulse rate reactivity. This may indicate that the linkage between diurnal BP variation and BP reactivity to the anger recall task is due to α -adrenergic stimulation or postsynaptic vascular reactivity, instead of general sympathetic arousal which also increases heart rate through β -adrenergic stimulation.

On the other hand, we found an inverse correlation between the sleep/awake SBP ratio and physical exercise-induced BP increase only in day-shift workers. Since exercise-induced SBP increase was more closely correlated with awake SBP than with sleep SBP, exercise-related increased BP may influence diurnal BP variation primarily through increasing awake BP. We previously found that orthostatic stress-induced BP increase was inversely correlated with sleep BP dipping in elderly hypertensives who sleep at night (3, 19). Although there were no significant differences in baseline pulse rate or exercise-induced BP increase between day-shift workers and night-shift workers in the present study, the exercise-induced increase in pulse rate tended to be greater in night-shift workers than in day-shift workers. This may partly explain the previous reports of an increased risk of cardiovascular events in night-shift workers. There was no significant association between the psychological stress-induced increases in BP or pulse rate and those induced by physical stress in the total sample, day-shift workers, or night-shift workers, indicating that the pressor mechanism for psychological stress is probably different than that for physical stress. In a previous study, we calculated ABP reactivity to physical activity using simultaneously collected 24-h ABPM and actigraphy data (24). The ABP reactivity

was defined as the slope of the regression line obtained from regressing SBP against physical activity for those BP readings taken while awake. This ABP reactivity was not associated with nocturnal BP dipping status (24).

Concerning the recovery parameters, the time until 50% recovery of SBP and until 75% recovery of pulse rate after the anger recall task were higher in the night-shift workers than in the day-shift workers, but there were no significant intergroup differences in any of the other parameters. The sleep/awake SBP ratio was positively correlated with recovery rate in the night-shift workers, but this correlation was not significant in the day-shift workers, indicating that those night-shift workers who showed a more rapid BP recovery after psychological stress tended to exhibit smaller dips in BP during sleep.

It is important to note that while most of the estimated associations between cardiovascular reactivity/recovery and sleep/awake SBP ratio were not statistically significant, those that were significant were all in the hypothesized direction of greater reactivity and slower recovery predicting increased sleep dipping (lower sleep/awake SBP ratio). There is thus a possibility that target organ damage, particularly left ventricular hypertrophy, modulates the association between cardiovascular reactivity and diurnal BP variation.

In conclusion, cardiovascular reactivity triggered by psychological and physical stress in the laboratory may be a weak, but significant, determinant of diurnal BP variation; in addition, work shift (day or night) appears to moderate the relationship between these two pressor mechanisms.

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