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Overcommitment to Work Is Associated With Changes in Cardiac Sympathetic Regulation

TANJA G.M. VRIJKOTTE, PhD, LORENZ J.P. VAN DOORNEN, PhD, AND ECO J.C. DE GEUS, PhD

Objective: Work stress is associated with an increased risk for cardiovascular disease (CVD). Exaggerated cardiovascular reactivity to work-related stressors or incomplete recovery after work is a proposed mechanism underlying this increase in risk. This study examined the effects of work stress on 24-hour profiles of the pre-ejection period (PEP), a measure of cardiac sympathetic activity, obtained from ambulatory measurement of the impedance cardiogram. **Methods:** A total of 67 male white-collar workers (age 47.1 ± 5.2) underwent ambulatory monitoring on 2 workdays and 1 non-workday. Work stress was defined according to Siegrist's model as 1) a combination of high effort and low reward at work (high imbalance) or 2) an exhaustive work-related coping style (high overcommitment). **Results:** High overcommitment was associated with shorter absolute PEP levels during all periods on all 3 measurement days, reduced wake-to-sleep PEP differences and reduced PEP variability, as indexed by the SD. **Conclusions:** Overcommitment to work was associated with an increase in basal sympathetic drive and a reduction in the dynamic range of cardiac sympathetic regulation. Both findings are compatible with the hypothesis that overcommitment induces β -receptor down-regulation. **Key words:** ambulatory impedance cardiogram, pre-ejection period, work stress, ionotropic cardiac regulation.

BP = blood pressure; **BMI** = body mass index; **CVD** = cardiovascular disease; **ERI** = effort-reward imbalance; **HR** = heart rate; **ICG** = impedance cardiograms; **MANOVA** = multivariate analysis of variance; **PAI-1** = plasminogen activator inhibitor; **PEP** = pre-ejection period; **SDPEP** = SD pre-ejection period; **VU-AMS** = Vrije Universiteit Ambulatory Monitoring System; **WHR** = waist to hip ratio.

INTRODUCTION

Over the past years, a number of studies have shown that work stress is associated with an increase in the risk for cardiovascular disease (CVD) (1–5). This relationship is often attributed to recurrent sympathetic nervous system activation in response to work-related stressors in subjects with high work stress (6). So far, the main methods to infer sympathetic activity in a work setting are either ambulatory measurements of heart rate (HR) and blood pressure (BP), or urinary catecholamines (7–9). Recently, various systems became available (10–12) for the ambulatory monitoring of thoracic impedance cardiograms (ICG) that allows noninvasive assessment of the pre-ejection period (PEP). PEP is the time interval between the onset of ventricular depolarization and the opening of the semilunar valves. Changes in PEP reliably index changes in β -adrenergic inotropic drive to the left ventricle as shown in laboratory studies manipulating β -adrenergic tone by epinephrine infusion (13,14), adrenoceptor blockade (15), exercise (16–18), or emotional stress (19–21).

This study examined the effects of work stress on ambulatory PEP in a group of middle-aged male white-collar workers. In studies so far, high work stress was mostly defined by the combination of high psychological job demands and low

decision latitude, according to the Karasek model (4,22,23). Siegrist developed an alternative model, called the effort-reward imbalance (ERI) model, to take into account the considerable individual variation in patterns of appraisal and coping in work-related situations (3,23,24). The model defines two summary measures of work stress: *imbalance*, the ratio between extrinsic effort (demands on the job) and rewards (money, esteem, and status control) and *overcommitment*, a psychological coping style associated with the inability to withdraw from work obligations. Work stress defined with this model has yielded strong prospective evidence for CVD (1,5,22,24). In support of the model, we previously observed higher HR reactivity to work in men with high imbalance, and increased levels of insulin and plasminogen activator inhibitor (PAI-1) in men with high overcommitment (25,26).

Both HR hyperreactivity and increased metabolic risk may result from repeated and exaggerated sympathetic activation (27,28). A direct test of this exaggerated sympathetic reactivity in subjects with high work stress is lacking, however, and forms the basis of the present study. Twenty-four hour recordings of thorax impedance cardiograms were made in 67 male white-collar workers on 2 workdays and 1 non-workday. These subjects represented the four work stress quadrants obtained by combinations of high/low imbalance with high/low overcommitment. From these ambulatory registrations, 24-hour PEP values were computed as an index of overall cardiac sympathetic activity. Differences between the workdays versus the non-workday were computed as indices of sympathetic reactivity to work. Also, for each of the measurement days, PEP variability within each of the periods (sleep, work, leisure) was indexed by the SD of PEP during that period (SDPEP). This measure is comparable to blood pressure variability computed from intermittent BP measurements (29,30) and was used as a putative index of lability of the sympathetic nervous system. Finally, the increases in PEP from work to leisure and from awake to sleep were used to index sympathetic recovery.

Shifts in posture and physical activity affect cardiac afterload and preload (31,32) and may cause PEP to change independently of changes in cardiac sympathetic drive. Because such shifts occur frequently during ambulatory recordings, we based our PEP comparisons across the groups on carefully

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selected periods with unchanged posture and physical activity only.

We hypothesized that subjects high in work stress are characterized by an overall increase in cardiac sympathetic activity, larger sympathetic reactivity to work, higher lability during work, and incomplete recovery during leisure and sleep.

MATERIALS AND METHODS

Subjects

One hundred and twenty six male, middle-aged white-collar workers, all working at the same large computer company and performing mainly sedentary work, participated in a study on work stress and CVD risk (25,26). Perceived work stress was assessed by the Dutch version of the ERI questionnaire, based on Siegrist's model (2,3,5,23,24). The ERI model explicitly distinguishes two sources of high effort at work: 1) the demands of the job (extrinsic) and 2) the personal motivation and ability to cope with a demanding working situation (intrinsic). Reward refers to money (adequate salary), esteem (e.g., respect and support), and status control (e.g., promotion prospects, job security). Work stress was expressed by two summary measures: imbalance and overcommitment. First, we computed the ratio between the ERI scores for extrinsic effort and reward. We dichotomized this ratio into a single imbalance score with subjects scoring > 1 assigned to the high imbalance group, and subjects scoring ≤ 1 assigned to the low imbalance group. Overcommitment was computed as the summed score of four intrinsic effort factors: 1) need for approval, 2) competitiveness, 3) impatience with a disproportionate level of irritability, and 4) inability to withdraw from work obligations. This component is by itself a mismatch score. Those individuals who score high on overcommitment tend to spend an inadequate amount of effort that is not met by externally defined rewards (24). The overcommitment score was dichotomized so that subjects in the lower two tertiles were considered low in overcommitment and subjects in the upper tertile high in overcommitment. Combining classifications for imbalance and overcommitment yielded four groups: low imbalance/low overcommitment, high imbalance/low overcommitment, low imbalance/high overcommitment, and high imbalance/high overcommitment.

From the total sample ($N = 126$), 17 subjects were not eligible for the ambulatory monitoring study for different reasons (e.g., moving, retirement, long-term illness, medication for hypertension, experience of major life event in the past three months, attrition during ambulatory monitoring). The remaining subjects ($N = 109$) participated in ambulatory cardiovascular monitoring between September 1996 and December 1997. During the week of ambulatory monitoring, the subjects received questionnaires on demographic information like, age, years of services and education level, subjective sleep quality (33), and physical habitual activity. They also filled out the ERI questionnaire to obtain the work stress scores that applied at the time of ambulatory monitoring.

To reduce the burden of the interactive data-analysis of ambulatory recorded thorax impedance, a selection of subjects was made to retain the four most interesting work stress groups. All males with high work stress scores on either imbalance or overcommitment were included: 13 subjects scoring high on imbalance and low on overcommitment, 24 subjects scoring low on imbalance and high on overcommitment, and 10 subjects scoring high on imbalance and high on overcommitment. From the remaining and largest group, ie, low in imbalance and low in overcommitment ($N = 62$), a subset of 20 subjects were selected at random. To verify whether this constituted a representative subset we compared the 20 selected and 42 non-selected subjects on a number of key measures (age, years of service, education level, percentage smoking, physical habitual activity, BMI, coffee and alcohol consumption), and found no significant differences. Importantly, using previously scored ambulatory HR and BP in this sample (26) we confirmed the selected subjects to be representative for the entire low imbalance/low overcommitment group. Comparing selected vs. non-selected we found for HR during work 76.0 versus 78.0 bpm, for HR during leisure 75.5 versus 76.2

bpm, for HR during sleep 63.9 versus 64.0 bpm, for SBP during work 134.8 versus 136.8, and for SBP during leisure 132.5 versus 133.9 mm Hg.

None of the final 67 subjects received treatment for hypertension, hyperlipidemia, or diabetes mellitus, and all subjects were free of overt CVD. The study protocol was approved by the Ethics Committee of the Vrije Universiteit and all subjects gave written consent before entrance to the study.

Ambulatory Monitoring

Subjects participated in 24-hour ambulatory monitoring on 3 days of the same workweek.

Blood pressure was recorded every 30 minutes during the waking hours with a SpaceLabs ABP monitor. In addition, ambulatory recording of the ECG and the ICG signal, defined as the first derivative of pulsatile changes in the transthoracic impedance (dZ/dt), was performed continuously by the Vrije Universiteit Ambulatory Monitoring System (VU-AMS) from a 6-spot electrode configuration. Detailed information on this ambulatory recording device and its recording procedures has been given elsewhere (26,34–36).

Subjects were measured on 2 workdays (Monday and Thursday), and 1 non-workday (Saturday or Sunday), always in that order. They came to the health department of the computer company for the first time on Monday morning between 8:00 AM and 11:00 AM. After the ambulatory monitors were attached, the subjects left to their departments to follow their normal working routines. The next morning, they returned and the monitors were removed. This procedure was repeated on Thursday morning. On Friday, subjects were shown how they could attach the VU-AMS device and electrodes themselves, and they took the ambulatory monitors home for the 24-hour non-workday registration. Subjects were instructed to use the electrode locations that were identified and marked by the trained research assistants during the workday measurements. Various measures were taken to increase the reliability of such self-attachment, eg, simple 5-step instruction cards, electrodes that are both numbered and color-coded, feedback beeping to alert to *incorrect* as well as *correct* attachment, and continuous availability of assistance by phone. Equal signal quality (in terms of percentage data loss during interactive signal scoring) was found on the self-attachment (weekend) and nonself attachment days (workday).

Body weight, height, waist circumference and hip circumference were measured on Monday before instrumentation. BMI was calculated as the weight in kilograms divided by the square of height in meters and waist to hip ratio (WHR) was calculated as the ratio between waist circumference and hip circumference.

Integration of Diary and Physical Activity Measurement With Ambulatory Recording Vertical Accelerometry

To measure physical activity during the registration, the VU-AMS also monitored the amount of body movement of the subject by an in-built vertical accelerometer. Because the device was always placed on the hip, the signal indexes gross body movements, ie, transitions in posture and activity. The measuring circuit consisted of an active acceleration sensor. Its output was amplified, rectified, and fed into a hardware integrator. Every five seconds this integrator was sampled and reset by the microprocessor. The integrated values have a range of 0 to 3.2 gsec with a resolution of 0.008 gsec. Average vertical acceleration across 30-second periods was stored throughout the 24-hour recording time.

Diary Prompting

The VU-AMS produced an audible alarm approximately every 30 minutes (± 10 minutes randomized) to prompt the subject to fill out their activity diary. They were instructed to write down the time, activities, and bodily postures during the last 30-minute period in chronological order. The number of consumed cups of coffee, glasses of alcohol, and cigarettes smoked was also noted. In the 5 minutes preceding each diary prompt, a beat-to-beat registration had been started during which the complete time series of R-waves and all 1-minute ICG ensembles were stored. One-minute ensemble averages are most often reported for the ICG because they optimally reduce the impact of impedance signal fluctuation through respiration and thorax

movement (20,31,37). Each of these five ICG ensembles was visually inspected using the ICG software module of the VU-AMS software. PEP was defined as the interval between R-wave and B-point plus a fixed Q-R interval of 48 ms. An average PEP value was obtained for each of the diary entries, allowing a direct link to ongoing posture and physical activity at the time of PEP recording. Diary prompting was disabled during sleep, but regular beat-to-beat recording of the ICG was maintained throughout the night.

Data Reduction and Analysis

Information from the diary about types of activities and (changes in) posture was combined with the vertical accelerometer information using interactive graphical software that displayed the amount of body movement as a function of time. This made it possible to accurately specify the start and end times of the activities/posture changes that the subjects had reported in the diary. Stationary fragments were coded for posture and physical activity: lying (sleep), sitting activities (e.g., desk work, dinner, meetings, watching TV), upright activity (standing, standing and walking about), mild to moderate physical activity (walking, household activities, bicycling), period (work, leisure, sleep), and day (Monday, Thursday and non-workday) were stored by the program simultaneously with the duration of that fragment. Mean values of PEP for the different work, leisure, and sleep periods were determined. Also, for each of the measurement days, PEP variability (SDPEP) in each of the periods (sleep, work, leisure) was indexed by the SD of PEP during that period.

We examined the resulting PEP distributions to identify outliers (Box plots). These were followed up by independent visual re-inspection of the original ICG fragments by two of the authors (Vrijkotte and de Geus). Resulting PEP and SDPEP distributions had acceptable skewness and kurtosis at each of the eight periods. To check the assumption of homogeneity of the covariance matrices across the eight periods we performed, Box M tests for repeated measures; Levene's test was used to establish equal variance across the low and high overcommitment groups.

Multivariate analysis of variance (MANOVA) with the SPSS-General Linear Model (SPSS-GLM) procedure was then used to test for main and interaction effects of imbalance (high, low), overcommitment (high, low), and measurement period (work Monday, leisure Monday, sleep Monday, work Thursday, leisure Thursday, sleep Thursday, awake non-workday, sleep non-workday) on PEP and SDPEP. Differences between the work stress groups with respect to age, BMI, WHR, coffee consumption, alcohol consumption, years of service, education level, and physical habitual activity were tested by one-way analysis of variance (ANOVA). Percentage of smokers was compared across groups by a χ^2 -test. When appropriate, these variables were entered as covariates into the MANOVA on work stress effects. To indicate reactivity to the work setting, preplanned group by period contrasts tested awake (work+leisure) time on the workdays vs. awake time on the non-workday. For both workdays, short-term sympathetic recovery was tested as the increase in PEP during leisure time over the PEP during work time. Long-term recovery was tested as the increase in PEP during sleep over PEP during the awake (work+leisure) time. For SDPEP, preplanned group by period contrasts tested whether the high work stress group had greater lability at work than during leisure time or sleep, or whether SDPEP was greater on workdays than on non-workdays.

The above MANOVAs (and contrasts) were repeated twice. The primary analysis used PEP values during sitting activities only, whereas the secondary analysis used PEP values during all activities, i.e., summing PEP across all postures and different levels of physical load. The latter values in principle have higher ecological validity, since changes in sympathetic activity due to physical activity may meaningfully contribute to individual differences in disease risk. The former, however, have the advantage of not being confounded by the effects of preload (end diastolic volume) and afterload (mean aortic pressure). Because of preload and afterload effects, variations in PEP during changes in posture or physical load may not adequately measure a change in sympathetic nervous system activity (38,39).

RESULTS

The mean number of 1-minute ensemble averaged ICG-complexes on Monday, Thursday, and the non-workday per subject was 225 ± 35 , 233 ± 30 , 221 ± 38 respectively. Visual inspection of morphology of the ICG signal resulted in rejection of 14.0%, 15.2%, and 15.3% of the complexes on the consecutive days. The percentage of complexes that could not be coded due to ambiguous diary information resulted in additional data loss of 9.3%, 8.9%, and 8.5% across the three measurement days. There was no systematic relation between this data loss and work stress status (Table 1). Surprisingly, more ICG complexes were rejected during sleep (19.2%) compared with sitting activity (12.4%), upright activity (10.8%), and physical activity (8.4%). Ambiguous B-point scoring was the main reason for rejection.

Table 1 shows the personal characteristics as a function of high and low overcommitment and imbalance. The four work stress groups had similar composition with respect to the confounding factors: age, BMI, WHR, percentage of smokers, coffee consumption, alcohol consumption, years of service, education level, and physical habitual activity. The exception was sleep quality. High overcommitment was associated with reduced subjective sleep quality (higher score) compared with the low overcommitment group ($p < .01$), and high imbalance was also associated with reduced subjective sleep quality ($p < .05$). All these characteristics had no significant effect on PEP levels or SDPEP, with the exception of the amount of alcohol consumed during the measurement day. Alcohol consumption showed an acute effect on absolute PEP during sleep. More alcohol consumption was associated with shorter PEP. On Monday this correlation was -0.31 , on Thursday -0.31 , and on the weekend day -0.23 .

Effects of Posture and Physical Activity

Posture and the level of physical load during the measurements were expected to be important determinants of sympathetic activity (40–42). As expected, an ANOVA contrasting mean ambulatory PEP across the four posture/physical activity categories showed a significant effect ($F = 27.5$; $p < .0001$). PEP decreased from sleep (101.12 ± 14.06 ms) to sitting activity (94.71 ± 9.45 ms), to upright activity (93.59 ± 9.45 ms), and to mild to moderate physical activity (90.56 ± 8.51 ms). However, because of the confounding effects of differences in end diastolic volume and mean aortic pressure across different posture and levels of physical load, this PEP effect cannot unambiguously be attributed to the sympathetic nervous system.

Because individual differences in posture and physical activity are uncontrolled when measuring in a naturalistic setting, their effects on PEP may interfere with our work stress group comparison, particularly if one of the groups had been more physically active. However, a comparison of the absolute time (number of minutes) or relative time (% of total time) spent in different physical activity categories showed that the four work stress groups did not differ in the total duration of sleep, sitting activity, upright activity, and physical

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TABLE 1. Subject Characteristics (Mean $\pm$ SD) and Time Spent in Different Postures as a Function of Imbalance Nested Under Overcommitment

Imbalance	Overcommitment Low		Overcommitment High		Total (N = 67)	(N = 67)
	Low (N = 20)	High (N = 13)	Low (N = 24)	High (N = 10)		
Imbalance	0.61 $\pm$ 0.13	1.23 $\pm$ 0.23	0.73 $\pm$ 0.16	1.33 $\pm$ 0.26	0.88 $\pm$ 0.35	^a
Overcommitment	7.8 $\pm$ 2.7	10.9 $\pm$ 0.7	15.7 $\pm$ 2.8	16.2 $\pm$ 3.6	12.5 $\pm$ 4.5	^b
Age (yr)	47.2 $\pm$ 5.8	45.9 $\pm$ 4.5	47.3 $\pm$ 5.3	47.0 $\pm$ 5.3	47.1 $\pm$ 5.2	–
BMI (kg/m ²)	24.8 $\pm$ 3.6	25.5 $\pm$ 2.8	24.9 $\pm$ 3.6	27.1 $\pm$ 3.9	25.2 $\pm$ 2.8	–
WHR	0.94 $\pm$ 0.11	0.87 $\pm$ 0.10	0.90 $\pm$ 0.08	0.90 $\pm$ 0.06	0.92 $\pm$ 0.09	–
Alcohol (glasses/week)	15.5 $\pm$ 11.0	17.8 $\pm$ 13.0	13.8 $\pm$ 13.1	14.2 $\pm$ 11.0	15.2 $\pm$ 11.0	–
Coffee (cups/day)	5.0 $\pm$ 2.6	5.6 $\pm$ 1.9	4.8 $\pm$ 2.4	4.7 $\pm$ 2.6	4.9 $\pm$ 2.4	–
Current smokers (%)	27.0	30.8	20.8	30.0	26.6	–
Education level*	5.5 $\pm$ 1.2	4.8 $\pm$ 2.0	5.2 $\pm$ 1.2	5.7 $\pm$ 1.4	5.3 $\pm$ 1.5	–
Physical habitual activity [†]	1.6 $\pm$ 1.4	1.2 $\pm$ 1.2	1.5 $\pm$ 1.2	1.8 $\pm$ 1.1	1.4 $\pm$ 1.1	–
Years of service (yr)	21.2 $\pm$ 8.6	20.5 $\pm$ 7.0	22.1 $\pm$ 7.3	20.6 $\pm$ 6.7	22.2 $\pm$ 7.1	–
Subjective sleep quality [‡]	2.0 $\pm$ 2.1	4.4 $\pm$ 3.7	3.7 $\pm$ 3.7	6.6 $\pm$ 4.2	3.7 $\pm$ 3.6	^{a,c}
Workday						
Total registration time (hh:mm)	23:11 $\pm$ 1:38	22:36 $\pm$ 2:07	22:39 $\pm$ 1:25	23:12 $\pm$ 1:01	22:53 $\pm$ 1:34	–
Lying (%) (only during sleep)	24.2 $\pm$ 7.8	24.0 $\pm$ 6.5	20.3 $\pm$ 5.6	26.2 $\pm$ 2.9	23.0 $\pm$ 6.2	–
Sitting (%)	37.6 $\pm$ 9.0	35.3 $\pm$ 7.9	35.2 $\pm$ 6.9	38.5 $\pm$ 5.0	37.3 $\pm$ 7.5	–
Standing (%)	11.8 $\pm$ 5.3	10.90 $\pm$ 2.9	10.9 $\pm$ 1.2	8.3 $\pm$ 1.7	10.9 $\pm$ 3.1	–
Physical active (%)	5.7 $\pm$ 2.1	3.8 $\pm$ 2.8	5.7 $\pm$ 3.3	3.7 $\pm$ 3.1	5.0 $\pm$ 2.8	–
Data loss (%)	20.7 $\pm$ 6.0	26.0 $\pm$ 6.7	28.0 $\pm$ 6.9	23.2 $\pm$ 7.1	23.8 $\pm$ 6.0	–
Nonworkday						
Total registration time (hh:mm)	22:37 $\pm$ 1:56	22:52 $\pm$ 3:00	22:15 $\pm$ 2:50	22:47 $\pm$ 3:53	22:33 $\pm$ 2:43	–
Lying (%) (only during sleep)	27.1 $\pm$ 7.1	24.3 $\pm$ 5.8	22.4 $\pm$ 6.5	28.1 $\pm$ 6.4	25.0 $\pm$ 6.5	–
Sitting (%)	30.6 $\pm$ 6.8	30.9 $\pm$ 9.0	30.8 $\pm$ 8.3	28.4 $\pm$ 4.3	30.4 $\pm$ 7.7	–
Standing (%)	17.5 $\pm$ 1.3	12.8 $\pm$ 2.8	15.6 $\pm$ 1.6	15.9 $\pm$ 4.3	15.7 $\pm$ 2.7	–
Physical active (%)	6.1 $\pm$ 4.7	4.6 $\pm$ 5.4	3.8 $\pm$ 3.0	3.8 $\pm$ 2.9	4.6 $\pm$ 4.3	–
Data loss (%)	18.7 $\pm$ 5.4	27.3 $\pm$ 6.7	27.4 $\pm$ 6.6	23.7 $\pm$ 5.9	24.2 $\pm$ 5.4	–

* 7-point scale ranging from primary school to university level.

[†] “How many times a week do you exercise till sweating in your leisure time?” Answers ranged from 0 (zero times a week) to 4 (four or more times a week).

^a Significant main effect of imbalance, $p < .01$; ^b Significant main effect of overcommitment, $p < .01$; ^c Significant main effect of imbalance, $p < .05$.

[‡] 15-point scale.

activity during on all 3 days (Table 1). This suggests that any ambulatory cardiovascular differences between the imbalance and overcommitment groups would not reflect different activity patterns during the ambulatory monitoring days. Indeed, primary analyses on values during sitting activities only, and secondary analysis on all values, ie, regardless of posture and physical activity, gave essentially the same results. For brevity, work stress effects on the values obtained during sitting activities only will be presented below.

Temporal Stability of PEP Level, SDPEP, and PEP Reactivity and Recovery

Ambulatory PEP levels during the workday constitute a highly stable trait. Test-retest correlations from Monday to Thursday were high for average PEP at work, during leisure time, and during sleep (Table 2). More modest test-retest reliability was found for PEP variability.

In the main MANOVA a highly significant main effect of period was found on PEP ($F = 6.67$, $p = < 0.001$). There was no significant difference between PEP levels during the awake time on the workdays vs. the awake time on the non-workday, although, as shown in Table 3, large individual differences were found that were reliable across the 2 workdays. On the workdays, the expected difference between PEP

TABLE 2. Means ($\pm$ SD) of PEP and SDPEP and Their Test-retest Reliability Across the Two Workdays

	Monday	Thursday	R
Absolute PEP			
Work	94.2 $\pm$ 9.6	95.1 $\pm$ 10.6	0.92
Leisure	94.8 $\pm$ 9.8	95.2 $\pm$ 10.2	0.85
Sleep	102.3 $\pm$ 14.6	101.7 $\pm$ 15.1	0.93
SDPEP			
Work	5.0 $\pm$ 2.8	4.8 $\pm$ 2.5	0.75
Leisure	5.2 $\pm$ 3.1	5.2 $\pm$ 2.3	0.49
Sleep	5.5 $\pm$ 3.0	4.6 $\pm$ 2.3	0.53

level during work and leisure periods was not found, but the contrast between wake and sleep was significant and accounted for the entire main effect of period. In addition, this measure of long-term recovery was highly stable across the 2 workdays.

Work Stress Effects

Neither imbalance nor the interaction of over*commitment with imbalance showed significant effect on the absolute PEP level, long-term PEP recovery, or SDPEP. There was, however, a significant main effect of overcommitment ($F = 5.83$, $p = .019$). The upper panel of Figure 1 displays the PEP level

TABLE 3. Means ($\pm$ SD) of PEP Reactivity and Recovery Contrasts and Their Test-retest Reliability Across the Two Workdays

	Monday	Thursday	R
Reactivity PEP			
Awake workday vs. awake nonworkday	0.5 $\pm$ 5.2	1.0 $\pm$ 4.9	0.65
Recovery PEP			
Work vs. leisure	0.2 $\pm$ 4.0	0.3 $\pm$ 4.6	0.38
Wake vs. sleep	7.6 $\pm$ 10.5	5.5 $\pm$ 9.7	0.90

across all 3 measurement days for the high and low overcommitment groups. Men in the high overcommitment group showed shorter PEP (5.6 ms on average) in all periods on all measurement days than men in the low overcommitment group. Inspection of the total variance of the two overcommitment groups showed mild heteroscedasticity for PEP such that total variance in the low overcommitment group was higher than in the high overcommitment group. However,

Levene's test was significant during one period (leisure weekend-day) only. Because PEP showed adequate normal distribution in both groups this small violation is unlikely to have distorted the results.

Tests of preplanned contrasts showed that the shorter absolute PEP in the high overcommitment group was coupled to a *decreased* PEP wake-sleep difference on both workdays in comparison to the low overcommitment group ($F = 6.14$, $p = .016$ on Monday and $F = 5.86$, $p = .018$ on Thursday). The same wake-sleep contrast by overcommitment was not significant on the non-workday ($F = 1.78$; $p = .19$). This suggests that long-term sympathetic recovery is less complete in the highly overcommitted subjects, but only on workdays.

In addition to absolute PEP and PEP wake-sleep difference, variability in PEP also showed a significant group difference ($F = 7.15$, $p = .010$) such that high overcommitment was associated with less PEP variability (Figure 1, lower panel). There was no overcommitment by period interaction effect on PEP variability, and the preplanned contrasts did not find

Figure 1. Preejection period (upper panel) and pre-ejection period variability (lower panel) during work, leisure and sleep on 2 workdays and the nonworkday for the high ($N = 34$) and low ($N = 33$) overcommitment group. Vertical bars denote the SD.

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evidence for a larger increase in PEP variability during work vs. non-work settings in the high overcommitment group.

DISCUSSION

Exaggerated sympathetic nervous system reactivity to work-related stressors has been proposed as a possible mechanism explaining the association of work stress and increased risk for CVD (1–3,6,42). The present study tested this hypothesis with regard to cardiac inotropic activity, by comparing ambulatory PEP profiles across the work week in high and low work stress groups. Work stress was defined as an *imbalance* in the ratio between extrinsic effort (demands on the job) and rewards (money, esteem, and status control), and as *overcommitment*, a psychological coping style associated with the inability to withdraw from work obligations. Both work stress measures, either by themselves or in interaction, have been shown to predict the occurrence of heart disease in Germany, Finland, and England (1,2,5,23,24). The main finding of this study was that high overcommitment was associated with shorter absolute PEP levels during all periods on all three measurement days, reduced wake/sleep PEP differences, and reduced PEP variability, as indexed by the SD. Neither imbalance nor the interaction of overcommitment with imbalance had an effect on PEP, SDPEP, PEP reactivity or recovery.

Overcommitment has evolved from a critical analysis of the global pattern of type A behavior and reflects the individual's way of coping with work demands. Individuals who score high on overcommitment are competitive, impatient, have a high need for approval, and are unable to 'let go.' It strongly resembles the hostile behavior style that precedes 'vital exhaustion,' a powerful predictor of heart disease, characterized by excess fatigue, a decrease in energy, and feelings of helplessness or the sense of a loss of control (43–45). It is tempting to interpret the altered ambulatory PEP profile of overcommitted subjects as indicative of a chronic increase in cardiac β -adrenergic drive. Furthermore, this increase appears to be most noticeable during sleep, when high overcommitted subjects fail to show the degree of PEP elongation seen in the other groups. Intriguingly, this loss of PEP recovery was coupled to reduced subjective sleep quality in the high overcommitment group.

In support of this interpretation of the PEP profile, many studies have shown that *within-subject* changes in PEP reliably index changes in cardiac (nor) epinephrinergic drive (13–21,46,47). It is further likely that *between-subject* differences in absolute PEP reflect differences in chronic β -adrenergic inotropic cardiac drive, although the experimental confirmations of this idea are still scant. The best evidence so far comes from a study in 13 female undergraduate students (21) that showed a high correlation (0.82) between absolute PEP and heart period increases in response to sympathetic blockade. In further support, a significant inverse correlation between a subjects' absolute PEP and their plasma adrenaline level was found (48). Endurance athletes showed longer PEP than untrained controls (49). Finally, a chronic increase in

cardiac sympathetic activity would be in keeping with the increases in insulin, glucose, and PAI-1 activity levels that we previously found in this population (25). The levels of these risk factors are known to respond to increased sympathetic nervous system activity (50,51).

As a consequence of the chronic increase in cardiac β -adrenergic drive, overcommitted subjects may suffer from a loss of ionotropic responsiveness to normal daily fluctuations in cardiac sympathetic drive on the 2 workdays, explaining the observed reduction in the overall PEP variability on these days. A decreased ionotropic responsiveness in overcommitment would be congruent with the conclusions of previous studies showing chronic psychological stress (52) or personality characteristics like anxiety, depression (53,54), and hostility (55) to be associated with lower β -adrenergic receptor responsiveness. The mechanism that could explain all these findings is decreased responsivity of β -receptors by the effect of chronic exposure to catecholamines. Decreased responsivity of adrenoceptors (as well as many other G-protein coupled receptors) in response to continued exposure to agonists is well-established (56,57). In the face of chronic work stress, down-regulation of cardiac β -receptors may constitute an example of 'allostatic load' (58,59), where a temporary cardio-protective compensatory response comes at the cost of increased long-term risk, for instance for chronic heart failure (60,61).

In these same subjects, we previously showed that the other component of work stress, effort-reward imbalance, was associated with higher HR reactivity to work (26). Daytime HR on the workday was significantly higher than daytime HR on the non-workday in the high imbalance men, but no difference between workday and non-workday HR was found in the low imbalance men. The effect of imbalance on workday HR was coupled to a chronically low vagal tone in these men during the workdays (26). Because vagal tone and sympathetic drive often act reciprocally, we expected to additionally find shorter PEP during work than during leisure, and shorter PEP on the workday in comparison to the non-workday, selectively in subjects with high scores on effort-reward imbalance. This was not confirmed. Part of the reason may be that the expected contrasts between PEP at work and during leisure or between PEP at work versus non-workdays were not significant. We based our expectation of this PEP difference on the robust short-term decrease in PEP found in the laboratory in response to stress tasks. To obtain an adequate measure of ambulatory PEP reactivity a different paradigm may be needed than was used here. A possible approach would be to contrast moments of high subjective work-related stress with periods of low subjective work-related stress.

In the epidemiological studies that have used the ERI work stress model, a significant interaction of overcommitment and effort-reward imbalance was found at the level of the disease end points, like acute myocardial infarction, sudden cardiac death, or stroke (3,23,24). This led us to hypothesize an interactive effect of overcommitment and imbalance on each of the risk factors as well. The pattern that we have found here

and in previous studies, however, suggest that the interactive effect arises across different risk factors, not within. Specifically, we found an influence of overcommitment on cardiac sympathetic drive, insulin, glucose, and PAI-1 levels (25), and an influence of imbalance on heart rate, vagal tone, and blood pressure (26). These risk factors each exert an effect on the disease processes by themselves, but may also act synergistically, explaining the interaction term found at the level of actual disease end points.

CONCLUSION

The shorter overall PEP combined with the reduced variation in PEP suggests that overcommitment is associated with an increase in sympathetic drive coupled with a decrease in the dynamic range of cardiac inotropic regulation, possibly through β -receptor down-regulation.

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