Job Strain, Ethnicity, and Sympathetic Nervous System Activity

KaMala S. Thomas, Richard A. Nelesen, Michael G. Ziegler, Wayne A. Bardwell, Joel E. Dimsdale

Abstract—Several studies have demonstrated that blacks have heightened pressor sensitivity in response to the α-agonist, phenylephrine. However, studies examining whether psychosocial factors contribute to this difference are scarce. We examined the effects of job strain on pressor sensitivity in 76 whites and 46 blacks who were enrolled in a study of stress, sleep, and blood pressure. Responses to phenylephrine were examined at an inpatient clinical research center. After a 3-minute baseline period, a 100-microgram phenylephrine bolus was administered to participants intravenously. To measure catecholamines, 24-hour urine samples were also collected from participants. There was a significant relationship between job strain and pressor sensitivity, such that individuals with low decisional control and high job demands experienced a greater increase in diastolic pressure after receiving phenylephrine. Low decisional control was also associated with decreased baroreflex sensitivity. There was an interaction between ethnicity and job control on blood pressure responses to phenylephrine and on 24-hour urinary norepinephrine levels. Blacks who perceived less control experienced a greater increase in diastolic pressure after receiving phenylephrine and had elevated norepinephrine levels. These findings suggest possible mechanisms by which job strain may be associated with cardiovascular disease. (Hypertension. 2004;44:891-896.)

Key Words: baroreflex ■ blood pressure ■ catecholamines ■ norepinephrine ■ blacks

Over the past decade, substantial research has examined the effects of job strain on blood pressure. Generally, these works have measured casual or ambulatory blood pressure (BP). These studies generally demonstrate that job strain is associated with increased BP throughout the day and night. Further, there is a greater incidence of myocardial infarction in individuals who report high job strain. Although, there is considerable evidence that job strain has adverse effects on BP, little work has been performed examining the physiological mechanisms underlying the relationship between job strain and BP.

One of the most venerable ways of examining BP physiology involves pressor sensitivity calculations. In some ways, this is a pharmacological analogue to studies of behavioral stress and BP (ie, both approaches impose a challenge and measure the resulting BP). Pharmacological studies of BP reactivity have found that hypertensive subjects tend to have blunted baroreflex sensitivity and heightened pressor sensitivity in response to an α-agonist. Thus, hypertensive subjects have increased vascular sensitivity to sympathetic output and impaired reflexes that might return BP back toward normal.

Phenylephrine (PE) is an α-1 agonist that stimulates the same pressor receptors as norepinephrine. This drug mimics the short-term effects of stress on BP by increasing vasoconstriction. Although studies consistently demonstrate that PE infusions lead to increased BP, the magnitude of this effect appears to be influenced by demographic factors, including hypertension status, age, gender, and ethnicity. Ethnic and racial differences in pressor sensitivity to PE have been well-documented. Several studies have found that blacks have greater pressor responses to alpha agonists than whites. This increased vascular reactivity may place blacks at greater risk for hypertension. Ethnic differences in vascular reactivity and hypertension rates may partially be explained by a greater exposure to chronic stressors among blacks. Chronic stressors may interact with biological, psychological, and behavioral risk factors to increase SNS activity in blacks. Over time, repeated episodes of stress-induced SNS activation may cause structural vascular changes, leading to the development of hypertension.

High levels of psychosocial stress may also lead to increased sensitivity to sympathetic nervous system (SNS) activation. Laboratory studies have shown that individuals who report high job strain have greater vascular reactivity to behavioral challenges. Psychosocial stress might increase pressor sensitivity by increasing sympathetic nervous responses to stress or by increasing vascular responses to sympathetic nerve activity.

The primary purpose of this study was to examine the relationship between job strain, catecholamines, and pressor sensitivity to PE. We wanted to determine if job strain...
TABLE 1. Ethnic Differences in Sample Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Blacks (%)</th>
<th>Whites (%)</th>
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<tbody>
<tr>
<td>SES–Hollingshead*</td>
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<tr>
<td>Upper class</td>
<td>7 (15.2)</td>
<td>23 (31.5)</td>
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<td>Lower class</td>
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<td>21 (28.8)</td>
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<td>Education</td>
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<td>Partial college</td>
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<td>High school</td>
<td>8 (17.4)</td>
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<td>Less than high school</td>
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<td>1 (1.4)</td>
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<tr>
<td>Hypertensive</td>
<td>13 (30.2)</td>
<td>7 (9.7)</td>
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<table>
<thead>
<tr>
<th>Variable</th>
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<tbody>
<tr>
<td>Mean±SEM</td>
<td>38.3±1.1</td>
<td>36.1±0.9</td>
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<tr>
<td>BMI†</td>
<td>28.8±1.0</td>
<td>25.1±0.5</td>
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<tr>
<td>Cigarettes per day</td>
<td>2.6±1.0</td>
<td>2.2±0.8</td>
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<td>JCS decisional control</td>
<td>70.1±1.4</td>
<td>72.9±1.7</td>
</tr>
<tr>
<td>JCS psychological demands</td>
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<td>31.0±0.6</td>
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<tr>
<td>High job strain</td>
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<td>8</td>
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<tr>
<td>Baseline SBP (mm Hg)‡</td>
<td>129.8±2.6</td>
<td>122.5±2.0</td>
</tr>
<tr>
<td>Baseline DBP (mm Hg)‡</td>
<td>73.7±1.9</td>
<td>69.2±1.5</td>
</tr>
<tr>
<td>SBP pressor response (mm Hg)†</td>
<td>34.7±2.7</td>
<td>26.6±1.3</td>
</tr>
<tr>
<td>DBP pressor response (mm Hg)†</td>
<td>19.9±1.1</td>
<td>15.7±0.9</td>
</tr>
<tr>
<td>DBP baroreflex response (mm Hg/ms)‡</td>
<td>22.9±3.4</td>
<td>34.9±3.2</td>
</tr>
<tr>
<td>Urine NE levels (ng/h)‡</td>
<td>31.5±2.5</td>
<td>26.4±2.9</td>
</tr>
<tr>
<td>Urine E levels (ng/h)‡</td>
<td>13.3±2.5</td>
<td>7.27±0.93</td>
</tr>
</tbody>
</table>

*Upper class = groups I and II; middle class = group III; lower class = groups IV and V.
‡P<0.01. †P<0.05.

Subjects and Methods

Sample characteristics are listed in Table 1. Participants consisted of employed (≥30 hours per week) men and women recruited from the local community via advertisement and referrals. As a result of these recruitment strategies, a total of 385 individuals contacted us and expressed interest in being in the study. Approximately 300 individuals responded to advertisements about the study and ~100 individuals were referred by physicians and previous participants. Of those who contacted us, 122 completed the study. Individuals who did not enroll in the study either were outside of the inclusion criteria or were unable to be excused from work to be in the study.

Ethnicity was assessed via self-report. Thus, individuals who self-identified as blacks or whites were counted as such. Forty-six of the participants were black (22 men and 24 women) and 76 were white (43 men and 33 women). Participants were between the ages of 25 and 52, with a body weight between 90% and 130% of ideal (Metropolitan life tables24), and resting BP <180/110 mm Hg at screening. Screening BP was taken using Dinamap model 1846-SZ with appropriate size cuffs. BP readings were taken in the right arm by registered nurses and defined as the average of 3 seated BP measurements. Individuals were excluded from the study if they had increased BP by increasing sympathetic nervous activity, by increasing the pressor response to sympathetic neurotransmitters, or both. Secondly, we examined whether job strain moderated ethnic differences in pressor sensitivity and catecholamines.

Job strain was measured using the Karasek Job Demand–Control (DC) model. This model combines 2 dimensions of the work environment, “job demands” and “decisional control,” to assess job strain. Decisional control refers to the ability of an individual to make important decisions at work and to control work activities. However, job demands refer to the task requirements or workload of an individual. According to the DC model, having high job demands and low decisional control will lead to job strain. Two scales of the Job Content Questionnaire were used to assess the DC model (decisional control and psychological demands). Nine items comprise the decisional control subscale and 5 items comprise the psychological demands subscale. This scale has been found to have sound psychometric properties, with Cronbach α=0.74 and 0.83 for job demands and control, respectively. Further, several studies support the use of the DC model in predicting cardiovascular disease risk.2–4,7,25–31

Two-Factor Index of Social Position

The 2-factor index of social position measures an individual’s social status. The 2 factors that determine social position include occupation and education. Each factor has a range from 1 to 7, with lower scores representing a higher social status. Scores on the education and occupation factor can be combined to obtain an index of social class. Social class is scaled in 5 categories, with lower scores representing a higher social class. Validation studies support the use of this scale as a reliable and valid measure of social status.34

Baroreflex Testing

The ECG (Hewlett-Packard 78352C) and Finapres BP (Ohmeda, 2300) signals were relayed to an A/D converter (Data Translation, DT2801), sampling at 1 kHz per channel (Global laboratory software, Data Translation) and stored in an IBM PC compatible computer in 3-minute epochs. The BP cuff of the Finapres was placed on the third or fourth digit of the hand opposite the venous injection site. Hand position and cuff location were adjusted so that the Finapres readings were within 5 mm Hg of casual BP determinations.

The subjects were tested for their response to PE in the General Clinical Research Center in the afternoon. Participants rested supine for at least 20 minutes and baseline data were collected 3 minutes before the PE infusion. Immediately after baseline, a 100-μg PE bolus was administered intravenously.

Baroreflex sensitivity was calculated by recording the changes in the BP responses to PE over time. A linear regression was plotted and calculated using BP over the R-R interval. The slope of this function provided an estimate of baroreflex sensitivity.35,36 The pressor slope was calculated as the change in BP over time. We also calculated the maximal change in BP (Δ systolic BP and Δ diastolic BP) and heart rate (Δ heart rate) as the peak level minus baseline level.

Assays

The 24-hour urine samples were collected from participants and stored at −80°C until they were assayed. Samples were obtained from participants during an overnight stay at the University of California San Diego General Clinical Research Center. Samples...
were obtained at 2 collection intervals: a sample was obtained from 10 PM to 6 AM and one was obtained from 6 AM to 10 PM. These samples were combined to assess 24-hour catecholamines. Epinephrine (E) and norepinephrine (NE) were measured by radio-enzymatic assay according to the method described by Kennedy and Ziegler.37

Statistical Analysis
Data were analyzed using SPSS 11.0 for Windows. Job strain was calculated through the traditional quadrant term approach using the median split of job demands and decisional control as cutoffs,7,10,25,38–40 Similar to Fauvel, individuals who were above the median split on job demands and below the median split on decisional control were classified as having high job strain. All other individuals were characterized as nonhigh strain. Before conducting analyses on pressor sensitivity, log transformations were performed to normalize skewed pressor data. MANCOVAs were conducted to examine the effect of job strain on pressor sensitivity. Job strain was included as an independent variable in these analyses. Covariates included age, number of cigarettes smoked per day, body mass index, socioeconomic status, and screening BP. Dependent variables included log-transformed systolic and diastolic pressor responses to PE.

Secondary Analyses
MANCOVAs were conducted to determine whether ethnicity moderates the relationship between job strain and pressor sensitivity. In these analyses, we examined the interaction between ethnicity and job strain on pressor sensitivity. Ethnicity, job demands, and decisional control were included as independent variables. Covariates and dependent variables remained the same as described. MANCOVAs were also conducted examining the effects of ethnicity and job strain on baroreflex sensitivity and urinary catecholamines. In these analyses, independent variables included ethnicity, job strain, job demands, and decisional control. Dependent variables included baroreflex sensitivity, E, and NE. Covariates remained the same as described. Power analyses were conducted to determine the amount of power we had to detect differences between ethnic and job strain groups on these secondary analyses in the study. Given the sample size, average power across outcomes was 0.61.

Results
Job Strain and Pressor Sensitivity
There was a significant effect of job strain on systolic pressure responses to PE ($F=4.5$, $P=0.041$). Individuals with high job strain experienced a greater increase in log systolic pressure after receiving PE (Table 2). There was no significant effect of job strain on log diastolic pressure responses to PE.

Job Strain and Baroreflex Sensitivity
There was no significant effect of overall job strain on baroreflex sensitivity. However, there was a significant effect of the decisional control component of job strain on diastolic baroreflex sensitivity ($F=13.7$, $P=0.001$). Individuals with low control had smaller diastolic baroreflex slopes than those with high control (Figure 1). No other effects were significant.

Job Strain as a Moderator of Ethnicity and Pressor Sensitivity
There was no significant interaction between ethnicity and job strain on pressor sensitivity. Thus, within this study, job strain did not moderate the relationship between ethnicity and pressor sensitivity. However, there was a significant interaction between ethnicity and decisional control on log diastolic pressure responses to PE ($F=7.74$, $P=0.009$). Blacks who perceived less control at work experienced a greater change

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonhigh Strain (%)</th>
<th>High Strain (%)</th>
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<tbody>
<tr>
<td>Social class–Hollingshead*</td>
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<td></td>
</tr>
<tr>
<td>Upper class</td>
<td>22 (28.9)</td>
<td>5 (29.4)</td>
</tr>
<tr>
<td>Middle class</td>
<td>30 (39.5)</td>
<td>6 (35.3)</td>
</tr>
<tr>
<td>Lower class</td>
<td>24 (31.6)</td>
<td>6 (35.3)</td>
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<tr>
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<td></td>
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*Upper class = groups I and II; middle class = group III; lower class = groups IV and V.
†$P<0.05$.

Figure 1. Effect of job strain on diastolic BP baroreflex slope (ie, increase in heart rate mm Hg/ms in response to PE). Individuals with low control have smaller baroreflex slopes ($P<0.01$).
sensitivity observed in those with high job strain was the result of impaired baroreflexes. We conducted responses to PE.

Individuals who reported more job strain had greater systolic pressor reactivity by a pharmacological challenge. Individuals who observed an association between job strain and BP changes on BP. Similar to these studies, we also found a relationship between job strain and the development of hypertension in longitudinal studies. Others have not found such an association. Our results show that high job strain is associated with increased BP reactivity to an alpha agonist. This supports the results of a study conducted by Steptoe et al in which individuals with high job strain had greater BP reactivity to behavioral stress than those with low job strain. It has been suggested that hypertension may result from increased vascular resistance due to exposure to chronic stress. The results of the current study support this assertion. Within this study, individuals who reported high job strain had greater BP reactivity than did those in the nonhigh strain group. Because increased BP reactivity can be a risk factor for cardiovascular disease, the current results provide further evidence that high job strain places individuals at risk for cardiovascular disease.

Secondary analyses were conducted to determine whether job strain moderated the relationship between ethnicity and pressor sensitivity. Specifically, we wondered whether the heightened pressor sensitivity in blacks that we observed in previous studies could be partially explained by job strain. These analyses revealed an interaction between decisional control and pressor sensitivity. Low decisional control was related to increased BP reactivity in blacks but not in whites. Similarly, blacks who reported low control had elevated NE levels. Because of the limited sample size on which these subgroup analyses were conducted, it is possible that these results were caused by chance and do not reflect the true relationship between decisional control and SNS activity among blacks in the general population. However, the fact that other researchers have also found that blacks who report low decisional control have increased BP lends more credence to our finding that control moderates the relationship between ethnicity and SNS activity.

Our finding that low decisional control was related to elevated NE levels in blacks is consistent with the results of a study conducted by Wilson et al in which black adolescents who were exposed to violence had elevated 24-hour NE levels. Together, these findings suggest that there is increased SNS activation in blacks who report high levels of stress. It is interesting that we did not find a relationship between job strain and NE levels in whites. Other studies have also found that blacks have greater SNS reactivity to stress than whites. However, the physiological mechanisms that lead to increased SNS responsiveness in blacks are unclear. Moreover, it is unclear what role ethnic differences in SNS function play in the greater rates of hypertension in blacks.

Perhaps future studies in this area will shed light on the difficulties associated with cardiovascular disease. Previous studies have demonstrated that job strain has adverse effects on BP. Similar to these studies, we also found a relationship between job strain and BP. Most importantly, we observed an association between job strain and BP changes elicited by a pharmacological challenge. Individuals who reported more job strain had greater systolic pressor responses to PE.

The baroreflex decreases SNS output when BP is increased. Thus, increased BP responsiveness to stress or PE may be the result of impaired baroreflexes. We conducted additional analyses to determine whether the increased pressor sensitivity observed in those with high job strain was related to baroreflex sensitivity. These analyses revealed smaller diastolic baroreflex slopes in those who reported low control. Thus, the relationship between job strain and pressor sensitivity may be partially mediated by baroreflex sensitivity.

Several studies have shown that individuals who report high job strain have increased BP. However, there still remains some controversy regarding whether high job strain is a major risk factor for hypertension. Although some researchers have found an association between job strain and the development of hypertension in longitudinal studies, others have not found such an association. Our results show that high job strain is associated with increased BP reactivity to an alpha agonist. This supports the results of a study conducted by Steptoe et al in which individuals with high job strain had greater BP reactivity to behavioral stress than those with low job strain. It has been suggested that hypertension may result from increased vascular resistance due to exposure to chronic stress. The results of the current study support this assertion. Within this study, individuals who reported high job strain had greater BP reactivity than did those in the nonhigh strain group. Because increased BP reactivity can be a risk factor for cardiovascular disease, the current results provide further evidence that high job strain places individuals at risk for cardiovascular disease.

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relationship between stress, SNS function, and cardiovascular health in blacks.

Within the current study, participants were part of a larger study of stress, sleep, and BP. Because of their interest in participating in research on stress and sleep, participants may not be representative of the general population. It is possible that individuals who selected to be in this study were more “stressed” than individuals in the general population. If so, then participants would have greater SNS activation and would be more likely to report job strain than the general population. However, participants did not demonstrate elevated scores on diverse self-report measures of stress (data not shown).

We observed that individuals with high job strain had greater BP reactivity to PE. Low control was also associated with decreased baroreflex sensitivity. This suggests that job strain is associated with increased BP responsiveness to stress. How might job strain lead susceptible individuals to have increased NE excretion, depressed baroreflexes, and increased pressor responses? Stress activates the SNS, leading to increased NE and BP. The vasculature responds to increased BP by hypertrophy, resulting in thickened, muscular, and rigid blood vessels. Hypertrophied blood vessels respond to pressors such as NE and PE with exaggerated vasoconstriction. Thickened blood vessels also stretch poorly, causing impaired baroreflex activation. Blacks are particularly susceptible to the development of hypertension and thickened blood vessels. This scenario might explain the clustering of increased NE release, increased pressor responses, and impaired baroreflexes among blacks exposed to high job stress. Further studies should address whether vascular changes are associated with the pressor responses we have observed.

Acknowledgments

This work was supported by grants HL36005 and RR00827 from the National Institutes of Health.

References

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