Neither Perceived Job Stress Nor Individual Cardiovascular Reactivity Predict High Blood Pressure

Jean Pierre Fauvel, Ignasse M’Pio, Pierre Quelin, Jean-Pierre Rigaud, Maurice Laville, Michel Ducher

Abstract—We have reported that high job strain was associated with a significantly higher diastolic blood pressure (DBP) of 4.5 mm Hg during the working hours, irrespective of BP reactivity to a stress test. We report the final results of the first 5-year follow-up study, which aimed to assess the respective influences of perception of professional strain and cardiovascular reactivity to a mental stress test on BP. A cohort of 292 healthy subjects (mean ± SEM age, 38 ± 1 years) was followed up for progression to hypertension outcome, which was defined as an increase in systolic blood pressure (SBP) or DBP >7 mm Hg or a DBP >95 mm Hg during follow-up. None of the subjects was lost to follow-up, and 209 subjects completed the study. The high-strain (HS) group, representing 20.9% of the subjects, was compared with the remaining subjects (non–high-strain [NHS]). Similarly, the subjects with the highest BP stress reactivity (HR; 20.9% of subjects) were compared with the remaining subjects (NHR). Progression to hypertension was reached by 93 subjects (31.8%). Kaplan-Meier survival estimates revealed that neither HS nor HR increased the incidence of progression to hypertension. End-of-follow-up 24-hour ambulatory BPs that were similar in HS and NHS (120 ± 2 vs 120 ± 1 mm Hg, respectively) and in HR and NHR (122 ± 2 vs 120 ± 1 mm Hg, respectively) confirmed our findings. Age, alcohol, salt diet, body mass index, and occupation did not interfere with our results. In conclusion, cardiovascular HR and HS do not appear to be major risk markers for future high BP in healthy, young adults. (Hypertension. 2003;42:1112-1116.)

Key Words: epidemiology ■ stress ■ clinical trials ■ hypertension, essential ■ blood pressure monitoring, ambulatory

Psychological stress is hypothesized as 1 of the major environmental factors implicated in the genesis of hypertension. Among various psychological stresses, the most investigated has been job-related stress. It was defined by Karasek et al1 as the combination of high psychological demand and low latitude on the job. To date, only 3 studies designed to assess the long-term effect of job strain on blood pressure (BP) have produced controversial results.2-4 The most convincing 1 was a case-control study, which found that high job strain was associated with a 3-year increase in systolic BP (SBP)/diastolic BP (DBP) of 5/3 mm Hg, supporting the hypothesis that job strain might be an etiologic factor in the genesis of essential hypertension.4

The effects of stressors on cardiovascular regulation involve 2 components that have never been studied concomitantly. The first component is individual stress perception, quantified by questionnaires, and the second is individual cardiovascular reactivity to stress, assessed by a BP surge in response to stress tests. We recently reported the results of a cross-sectional analysis5 of a prospective study in which subjective perception of job strain was evaluated by the questionnaire developed by Karasek et al,1 and stress cardiovascular reactivity was measured by the Stroop stress test. The main results were that high professional strain but not stress BP reactivity was associated with a higher DBP of 4.5 mm Hg during working periods. We hereby report the final results of the 5-year follow-up study that aimed to evaluate the potential influence of the 2 stress components (cardiovascular reactivity and quantification of professional strain) on progression to hypertension, defined as an increase in SBP and/or DBP >7 mm Hg or a DBP >95 mm Hg during follow-up. Furthermore, to increase the reliability of our study, major factors known to influence BP were analyzed, and ambulatory blood pressure (ABP), which is more relevant than casual BP, was assessed at the end of follow-up.

Methods

Study Population

The study was conducted on full-time-employment subjects working in a chemical company, aged between 18 and 55 years (mean ± SD age, 38 ± 1 years). Among the 473 eligible subjects, 370 volunteered to participate in the study. Of them, 303 nonmedicated, healthy, normotensive (BP <140/90 mm Hg) subjects (278 men and 25 women) were included if their dipstick urinalysis results were within normal limits and if they were free of any current medication that could interfere with BP regulation. After inclusion in 1995, subjects were followed up for outcome until 2001. The mean length of the follow-up period was 5.0 ± 1.4 years, ranging from 1 to 6 years. Two hundred ninety-two subjects were followed up for at least 1 year and
were analyzed. Two hundred eighty-three subjects were followed up 2 years; 266, for 3 years; 245, for 4 years; and 208 for at least 5 years. The main reasons for discontinuation during follow-up were retirement (40 subjects) and job transfer (35 subjects). Five subjects discontinued because of hypertension, and 4 died (1 cardiac failure, 1 sudden death, and 2 cancer). None of the subjects was lost to follow-up, and each subject who was planned to discontinue the study had a final evaluation.

**Definition of High-Strain and High-Reactivity Groups**

High-strain (HS) and high-reactivity (HR) groups were defined on the inclusion data as previously described but were not revealed to the investigators (P.Q. and I.M.) to ensure blinded measurement of outcomes. In brief, the self-administered questionnaire included 18 items to assess job demand and job decision latitude. The medians representing the HS group (n=61) were compared with the remaining subjects (NHS group, n=232; 17 nonvalid questionnaires). Similarly, the 61 subjects exhibiting the highest stress-induced SBP increase were considered the HR group and were compared with the remaining subjects (NHR, n=226; 7 nonvalid stress test results). Mental stress was induced by a computerized version of Stroop’s color conflict test. Rest and stress BPs were recorded beat to beat by using a Finapres device (model 2300, Ohmeda).

**Protocol**

The planned sample size of 300 subjects was calculated after assuming an SE for BP measurement of 7 mm Hg, group sizes of 25% for the HS group versus 75% for the NHS group, and a difference in DBP of 3 mm Hg between groups. On these bases, it was estimated that the study would have at least 80% power to detect the expected difference between groups with a risk α of 0.05. The mean 5-year increase in DBP was ~3 mm Hg for the whole group. Thus, for the Kaplan-Meier analysis, the primary end point was a 5-year increase in DBP >7 mm Hg (a mean increase in DBP of 7 mm Hg plus a difference between groups of 3 mm Hg) and/or a DBP >95 mm Hg. During follow-up at the annual working visit, subjects were given a routine medical examination, which included a full history, physical examination, body mass index (BMI) determination, and assessment of alcohol intake. Worksite BP was measured 3 times to the nearest 2 mm Hg with a mercury sphygmomanometer after a 5-minute rest in a reclining position. The mean of variation. All other abbreviations are as defined in text. Values are mean±SEM.

**Statistical Analysis**

Data are expressed as mean±SEM in text, tables, and figures. A linear multivariate analysis was first performed to evaluate the determinants of the 5-year BP (office and ambulatory) evolution. Mean values at inclusion and at end of follow-up were compared between complementary groups (HS vs NHS and HR vs NHR) with an ANCOVA with gender, age, alcohol intake, BMI, occupation, and sodium intake as intersubject factors. Cox proportional-hazards models were used to evaluate the multivariate relations between the characteristics at entry and the progression to hypertension. The Kaplan-Meier method was used to estimate the cumulative incidence of progression to hypertension according to the characteristics identified at entry, and the log-rank test was used to assess the significance of unadjusted differences among the incidence curves. A value of P<0.05 was considered significant.

**Results**

The only significant determinant of 5-year BP (office and ambulatory) evolution was age. BMI was the second but did not reach significance (P=0.07). A positive family history of hypertension (first-degree relatives) was associated with a higher SBP (130±9 vs 127±11 mm Hg, P<0.05) and a higher DBP (84±6 vs 81±8 mm Hg, P<0.05) at the end of follow-up. The rate of discontinuation from the study was broadly similar between groups. At entry, the main characteristics of the subjects of complementary groups were similar, as shown in Table 1.

**Table 1. Baseline Characteristics of the 4 Groups, Classified by Job Strain and SBP Response to Mental Stress**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HS</th>
<th>NHS</th>
<th>HR</th>
<th>NHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>61</td>
<td>213</td>
<td>61</td>
<td>232</td>
</tr>
<tr>
<td>Gender, M/F</td>
<td>53/6</td>
<td>198/15</td>
<td>57/4</td>
<td>21/204</td>
</tr>
<tr>
<td>Age, y</td>
<td>36±1</td>
<td>38±1</td>
<td>37±1</td>
<td>38±1</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.0±0.5</td>
<td>24.7±0.2</td>
<td>25.2±0.4</td>
<td>24.7±0.2</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>124±1</td>
<td>125±1</td>
<td>126±1</td>
<td>124±1</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>77±1</td>
<td>78±1</td>
<td>78±1</td>
<td>78±1</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>63±1</td>
<td>63±1</td>
<td>62±1</td>
<td>63±1</td>
</tr>
<tr>
<td>Sodium, g/24 h</td>
<td>9.4±0.4</td>
<td>9.7±0.3</td>
<td>9.6±0.5</td>
<td>9.6±0.3</td>
</tr>
<tr>
<td>Alcohol mean score</td>
<td>1.9±0.1</td>
<td>2.1±0.1</td>
<td>1.9±0.1</td>
<td>2.1±0.1</td>
</tr>
<tr>
<td>ΔSBP, mm Hg</td>
<td>22±2</td>
<td>22±1</td>
<td>40±1</td>
<td>17±1*</td>
</tr>
<tr>
<td>ΔDBP, mm Hg</td>
<td>10±1</td>
<td>10±1</td>
<td>15±1</td>
<td>9±1*</td>
</tr>
<tr>
<td>ΔHR, bpm</td>
<td>9.0±1.2</td>
<td>7.5±0.5</td>
<td>11±1</td>
<td>6.8±0.5*</td>
</tr>
</tbody>
</table>

HR indicates heart rate, in beats per minute (bpm); Δ, stress-induced variation. P<0.001 between complementary groups (HS vs NHS or HR vs NHR).

![Figure 1. Cumulative incidence of “progression to hypertension” in normotensives as a function of job strain (HS and NHS groups).](image-url)
Multifarious mechanisms link psychological stress to hypertension is of major interest but still remains debated. The hypothesis that chronic stress exposure could lead to hypertension is typically associated with increased BP. The cardiovascular response to mental stress represents a complex interplay between a personal integrative feeling of stress, the autonomic nervous system, and cardiovascular function and/or structure. This study was designed to test long term-effects of stress exposure on BP. The individual integrative perception of stress (job strain) was measured by a questionnaire, whereas BP response to the Stroop stress test evaluated personal physiologically stress-induced increases in BP. The main result of our study was that neither job strain nor stress BP reactivity was associated with an increase in the incidence of “progression to hypertension.” In our study, progression to hypertension was defined as an increase in SBP >7 mm Hg or a DBP >95 mm Hg during follow-up.

Categorization of patients was based on estimated job strain and cutoff scores to separate subjects. Medians of demand and latitude scores were respectively 26 and 35. The HS group included 61 subjects (21%). The stress-induced increase in SBP of the HR group (61 subjects) was at least 32.0 mm Hg.

Progression to hypertension was reached by 93 subjects (31.8%) in the whole group, 17 (27.9%) in the HS group, 71 (33.3%) in the NHS group, and 5 (29%) of the 17 whose questionnaire could not be analyzed. The log-rank test assessed that there was no significant difference among the incidence curves between HS and NHS groups, as shown in the Kaplan-Meier curves represented in Figure 1. Eighteen HR subjects (29.5%), 72 NHR subjects (33.8%), and 3 subjects (47.7%) whose stress test was not reliable progressed to hypertension. The log-rank test revealed that the difference among the incidence curves was not significant between HR and NHR groups, as shown in Kaplan-Meier curves represented in Figure 2. End of follow-up ABPs were similar in HS and NHR groups and in HR and NHR groups (Table 2). We checked a posteriori that the main characteristics (age, BMI, SPB/DBP, salt diet, alcohol consumption, gender ratio, and ratio of positive family history of hypertension) of the subjects who had an ABPM did not differ in the mean and distribution when compared with those of the whole population. Subjects whose job strain was high both at entry and at the end of study (HS-HS group) had similar BP compared with subjects whose job strain was high only at entry (HS-NHS), was high only at the end of follow-up (NHS-HS), or was never high (NHS-NHS group; Table 3). Suspected confounding factors (age, gender, BMI, alcohol intake, and sodium intake) were not different between groups, and ANCOVA, controlling for these variables, provided similar findings.

Discussion

Acute stress is typically associated with increased BP. The hypothesis that chronic stress exposure could lead to hypertension is of major interest but still remains debated. Multifarious mechanisms link psychological stress to hypertension. The cardiovascular response to mental stress represents a complex interplay between a personal integrative feeling of stress, the autonomic nervous system, and cardiovascular function and/or structure. This study was designed to test long term-effects of stress exposure on BP. The individual integrative perception of stress (job strain) was measured by a questionnaire, whereas BP response to the Stroop stress test evaluated personal physiologically stress-induced increases in BP. The main result of our study was that neither job strain nor stress BP reactivity was associated with an increase in the incidence of “progression to hypertension.” In our study, progression to hypertension was a composite outcome associating an increase in SBP or DBP >7 mm Hg or a DBP >95 mm Hg at the end of follow-up. This composite criterion was chosen because in this rather young cohort of subjects, the incidence of hypertension was expected to be low. Similar ABPs between complementary stress groups reinforced our results. However, until now, many but not all published studies tended to find a relation between stress and BP. Among them, only 5, specifically designed for that pur-

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HS-HS</th>
<th>HS-NHS</th>
<th>NHS-HS</th>
<th>NHS-NHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>n, group/n, ABP</td>
<td>17/14</td>
<td>19/13</td>
<td>19/13</td>
<td>103/71</td>
</tr>
<tr>
<td>Worksite SBP</td>
<td>128±2</td>
<td>127±2</td>
<td>127±2</td>
<td>128±1</td>
</tr>
<tr>
<td>Worksite DBP</td>
<td>82±2</td>
<td>81±2</td>
<td>81±1</td>
<td>82±1</td>
</tr>
<tr>
<td>24-Hour SBP</td>
<td>118±2</td>
<td>123±3</td>
<td>123±3</td>
<td>120±1</td>
</tr>
<tr>
<td>24-Hour DBP</td>
<td>76±2</td>
<td>81±2</td>
<td>81±2</td>
<td>77±1</td>
</tr>
<tr>
<td>Working SBP</td>
<td>123±3</td>
<td>128±3</td>
<td>128±3</td>
<td>126±1</td>
</tr>
<tr>
<td>Working DBP</td>
<td>82±3</td>
<td>87±3</td>
<td>87±3</td>
<td>83±1</td>
</tr>
<tr>
<td>Nonworking SBP</td>
<td>117±3</td>
<td>119±1</td>
<td>119±1</td>
<td>119±1</td>
</tr>
<tr>
<td>Nonworking DBP</td>
<td>75±2</td>
<td>76±2</td>
<td>76±2</td>
<td>74±1</td>
</tr>
</tbody>
</table>

HS-HS indicates high strain both at entry and at the end of follow-up; HS-NHS, high strain only at entry; NHS-HS, high strain only at the end of follow-up; NHS-NHS, no high strain both at entry and at the end of follow-up; n, ABP, No. of ABP measurement in the group of n; All other abbreviations are as defined in text. Values are mean±SEM.
pose, were conducted prospectively. At a 1-year interval, change in job strain was associated with a change in BP, whereas at a 5-year interval, persistently high job strain was not associated with a change in BP. Three prospective studies that used ABP measurements provided evidence that chronic stress exposure could lead to higher BP in the long run and that changes in stress exposure were associated with a change in ABP. The most convincing was a prospective case-control study, which reported that 15 subjects with high strain (both at entry and at the end of follow-up) had a significant 4 mm Hg higher DBP at the end of follow-up (after controlling for initial BP). However, cases were hypertensives (DBP > 85 mm Hg or being treated for hypertension), and controls were unmedicated normotensives. Because BP evolution is linked to baseline BP, such a case-control design could have amplified the stress effect on BP. Case-control studies that have underlined a potential relation between job strain and BP level might generate methodological bias. Thus, to minimize potential bias, our study was conducted in a normotensive population to quantify the association between job strain and BP. Furthermore, most known risk factors for elevated BP were controlled for, and none of the subjects was lost to follow-up. We also verified that the 95 premature withdrawals (main reasons for withdrawal were retirement or job transfer) were not related to stress status. These subjects whose professional status changed might have been less concerned by their actual job strain and thus, were not asked to complete the job strain questionnaire. The percentage of subjects who did not fill out the questionnaire was similar between groups (41% in the HS group vs 37% in the NHS group) According to Schnall et al., we compared BPs in groups in relation to their change in job strain level between entry and the end of follow-up. In our study, BP values at the end of follow-up were independent of the level of strain at entry and 5 years apart (Table 2). Job strain might vary in 5 years. This is a limitation to our study, which is common to all observational studies. The questionnaire developed by Karasek et al. is well suited to record job strain at present. It does not provide any information on either past or future evolution of job strain. In that view, job strain might be related only to simultaneously recorded BP. Because cross-sectional studies, including our analysis at inclusion, consistently reported that job strain was associated with a higher BP level, job strain might be related to concomitant BP but would not predict BP in the long run.

A lower median job demand and higher median job latitude could in part explain the lack of job strain effects on BP evolution. However, median levels are not far from those reported by Schnall et al. Because there is no accepted threshold, we compared subjects in the high-strain quadrant (high demand and low latitude) to the remaining subjects, as recommended by Karasek et al. One of the main interests of our study was to simultaneously evaluate job stress and BP reactivity to mental stress. Several studies have addressed the issue that physical stress BP reactivity was predictive of future hypertension, stress being exercise or a cold test. Few studies reported a weak predictive value of mental stress reactivity on BP level. We could not find any predictive value of stress BP reactivity even when using a reproducible stress test that elicited a major and sustained BP response (22±1/10±1 mm Hg for SBP/DBP).

**Perspectives**

Our study is the first to report a lack of job strain effect and of stress reactivity on 5-year BP evolution. However, the design of our study increases the confidence in our results. This is the first study designed to analyze the effects of job strain and reactivity to mental stress, which was conducted in a cohort of nonselected normotensive subjects. The number of subjects was calculated to obtain a power of 80%. The convergence of our results from the use of various statistical tools attests to the robustness of our conclusions. If job strain increases BP in the long run, it might be true only in receptive subjects. Main BP-related factors (alcohol consumption, BMI, sodium diet, age, gender, and occupation), which were equally distributed between complementary groups, did not influence our conclusions.

**Acknowledgments**

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**References**

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