Mental Stress–Induced Increase in Blood Pressure Is Not Related to Baroreflex Sensitivity in Middle-Aged Healthy Men

Jean Pierre Fauvel, Catherine Cerutti, Pierre Quelin, Maurice Laville, Marie Paule Gustin, Christian Zacharie Paultre, Michel Ducher

Abstract—The baroreflex that acts to blunt blood pressure (BP) variations through opposite variations in heart rate should limit the BP increase produced by an emotional challenge. However, relations between baroreflex sensitivity and BP reactivity induced by a psychological stress in a large group of adults have never been firmly established. In 280 healthy men, rest (10 minutes) and stress (5 minutes) BP and heart rate were recorded beat to beat by a blood pressure monitor. The mental stress was elicited by a well-standardized computerized version of a word color conflict stress test (Stroop Color Test). Rest and stress baroreflex sensitivity was assessed by the cross-spectral analysis of BP and heart rate and by the sequence method. The stress-induced increase in systolic BP (22.4±0.1 mm Hg) was not correlated with resting baroreflex sensitivity but was slightly correlated (r=0.2, P<0.001) with BP variability assessed either by standard deviation or by mid-frequency band spectral power. Our results suggested that a centrally mediated sympathetic stimulation overcame cardiac autonomic regulation and emphasized the role of the sympathetic vasoconstriction in the pressure response at the onset of the stressing stimulation. During the sustained sympathoexcitatory phase, the cardiac baroreflex blunts BP variations but at a lower sensitivity. (Hypertension. 2000;35:887-891.)

Key Words: baroreflex ■ blood pressure ■ men ■ spectral analysis ■ stress, mental

Blood pressure (BP) reactivity to stress was reported to be associated with an unfavorable cardiovascular risk profile in men1 and to be predictive of future hypertension2 and carotid atherosclerosis in women.3 Furthermore, a depressed baroreflex sensitivity (BRS) was significantly associated with bad cardiovascular prognosis.4 The baroreflex, which acts to blunt BP variations through opposite variations in heart rate (HR), should limit BP increase to an emotional challenge. Parati et al5 reported that BP variability in humans after atropine administration was decreased at rest but was increased during a physical challenge. Thus, BP reactivity to challenge may not be related to BP regulation in resting conditions. However, to our knowledge, no study has investigated relations between resting cardiac BRS and BP response during a sympathetic stimulation induced by a psychological stress in a large group of adults. Therefore, the present study aimed to clarify relations that could exist between sympathetically induced increases in BP and HR and indices of cardiac autonomic control, including BRS, in a large sample of normotensive men. Furthermore, because BRS variation during stress is controversial,6–8 the second purpose of the present study was to investigate BRS variations during a well-standardized mental stress. This study was carried out by using techniques developed in our laboratory. The sympathetic stimulation was elicited by use of a computerized version of the Stroop word color conflict stress test (CWT), which has been reported to provoke a steady and reproducible increase in HR and BP9 that is associated with an increase in plasma catecholamines.10 BP was recorded by means of a Finapres device (model 2300, Ohmeda), which has previously been validated as a reliable method to study beat-to-beat BP variability.11 Indices of spontaneous variability were assessed by use of standard deviation and spectral analysis of beat-to-beat noninvasive recordings of BP12–14 signals in Mayer’s and respiratory frequency bands. The BRS was estimated both by the modulus of the transfer function in the Mayer’s band and by the sequence method, which estimates the mean slope of the linear reverse simultaneous variations of systolic BP (SBP) and HR.

Methods

Participants

The study was conducted in a cohort of men, aged 18 to 55 years, who worked in a chemical company. Among the 355 eligible subjects, 302 volunteered to participate in the study. Of these, 280 subjects (mean age 37 years) were included if their BP was <140/90 mm Hg (mean BP 119±1/67±1 mm Hg, by mercury

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From the Département de Néphrologie et d’Hypertension Artérielle (J.P.F., M.L., M.D.), EA 645 Université C. Bernard, Hôpital E. Herriot, Lyon, France; CNRS ESA 814 (C.C., M.P.G., C.Z.P.), Faculté de Pharmacie, Lyon, France; and Médecine du Travail (P.Q.), Rhodia, Saint-Fons, France.

Correspondence to Jean Pierre Fauvel, Département de Néphrologie et d’Hypertension artérielle, Hôpital E. Herriot, 69437 Lyon, France. E-mail jean-pierre.fauvel@chu-lyon.fr

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sphygmomanometer), if their dipstick urinalyses were within normal limits, and if they were free of any current medication. The protocol was approved by the local Ethics Committee and written informed consent was obtained from each subject.

**Mental Stress**

Mental stress was induced by a computerized version of the CWT.9 Successive series of 4 color words written in incongruent colors appeared in a random order on the screen. The subjects had to type the color of the word on selected keys from the keyboard. An audio signal was provoked if a wrong response was made. The examiner encouraged subjects to perform the stress test at their maximum speeds but kept an emotionally neutral attitude throughout the test.

**BP Measurement**

The experiment was conducted in quiet room with a controlled temperature at 20°C. BP was recorded using a Finapres device. The cuff was wrapped around the forefinger of the nondominant arm, which was resting on a table, the level of which was adjusted to obtain <5 mm Hg difference from the previously determined BP (by mercury sphygmomanometer). The equipped arm of the subject, sitting in front of the screen computer, was held in the same position throughout the procedure. After a 2-minute period for familiarization, the automatic calibration was switched off, and BP was recorded for 15 minutes. Each patient was recorded during 10 minutes at rest and 5 minutes during the mental stress.

**Signal Acquisition and Data Processing**

Signal acquisition and data processing were previously described.14 In brief, the analog output from the Finapres was connected to the analog-to-digital converter (ATMIO 16H, National Instrument) to perform data acquisition, storage, and analysis. Finapres signals were sampled at a rate of 100 Hz with 8 precision bits. Our own algorithm to detect SBP is accurate enough to compute HR, so ECG signal recording was not necessary. Data processing was carried out on a 4-minute recording both at rest and during stress after a delay of 1 minute and 30 seconds, respectively (Figure 1). Rest and stress data were obtained during these two 4-minute periods. These delays were chosen to obtain stationary conditions during rest and stress (Figure 1) as necessary to perform a fast Fourier transformation (FFT). Frequency domain analyses of HR and SBP oscillations were performed by spectral analysis using the FFT algorithm. The FFT was applied on 342 points from a 4-minute recording resampled at 1.4286 Hz (0.7 seconds) and completed to 512 points by the zero-padding technique to enhance the spectral resolution (1.7 MHz).15 BP variability was expressed as standard deviation and as power spectra in the mid-frequency (MF) band (0.07 to 0.14 Hz) and in the high-frequency (HF) band (0.14 to 0.40 Hz). As previously described, the BRS was estimated by the computation of the average modulus of the transfer function between SBP and HR spectra in the 2 frequency bands.14

**Statistical Analysis**

Data are expressed as mean±SEM in text, tables, and figures. Normal distribution of each parameter was tested by use of the Kolmogorov-Smirnov test. For the data for which the distribution was normal (SBP, HR, and their standard deviations; stress-induced increase in SBP and HR; and spectral BRS and sequence BRS at rest and stress), a Student t test and a Pearson correlation were used. If the distribution was not normal (spectral power in the MF and HF bands), a nonparametric rank test for paired data (Wilcoxon) or a Spearman rank correlation test was applied.

**Results**

**Age-Related Spontaneous BP and HR Variabilities and Spectral BRS**

Mean SBP and HR levels were not associated with age. BP and HR variabilities were significantly and negatively correlated with age (Table 1). Correlations were higher with HR indices than with SBP indices. Spectral BRS between SBP and HR were highly negatively correlated with age, whereas sequence BRS was not (Table 1).

**Stress-Induced Variations in SBP and HR Levels, Variabilities, and BRS at Rest**

Stress induced a significant increase in SBP (22.4±0.1 mm Hg, P<0.001) and HR (7.6±0.4 bpm, P<0.001). Stress-induced increases in SBP and HR were related neither with age nor with their basal values. Although SBP and HR standard deviations were not altered by stress, spectral indices were significantly modified (Figure 2). Stress-induced increase in SBP was significantly correlated with its resting SD and power spectrum in the MF band (Table 2). Spectral BRS and sequence BRS were highly significantly correlated (r=0.66, P<0.001). Stress-induced increase in SBP was related neither with the spectral BRS nor with the sequence variability.
BRS. Stress-induced increase in HR was correlated with spectral BRS but not with the sequence BRS at rest (Table 2).

**Discussion**

A centrally modulated BRS during psychological stress has been suspected to contribute to the development of human hypertension. However, relations between BRS and stress-induced increases in BP have never been clearly demonstrated. The present study provides a comprehensive evaluation of relations between sympathetically induced increases in BP and HR and cardiac autonomic control, including BRS, in a large sample of normotensive men. Our results demonstrated that stress-induced increase in SBP was not related to resting cardiac BRS and only slightly related to resting SBP variability (assessed either by standard deviation or spectral indices).

The accuracy of BP Finapres recordings has been assessed and compared with intra-arterial BP recordings at rest and during sympathetic stimulation. The accuracy of Finapres BP determination implies a simultaneously determined BP with a validated technique. In the present study, Finapres resting BP was adjusted with a sphygmomanometer. However, because we focused on BP variability, absolute BP levels should not alter our results. The sympathetic stimulation was elicited by use of a computerized version of the CWT that involved sensory rejection and that has been used as a model of defense reaction in humans. The CWT provoked a steady and reproducible increase in HR and BP associated with an increase in plasma catecholamines and in muscle sympathetic nerve activity. However, because BP increase was not related to catecholamine release, these indices were not determined in the present study. The magnitude of the stress-induced increase in SBP (22.4 mm Hg) confirmed that our version of the CWT provided a major sympathetic stimulation. The main function of the CWT, instead of mental arithmetic, was to elicit a sustained increase in BP (Figure 1) that could allow spectral analysis of BP and HR signals. Thus, in our experimental conditions, our methods were valid in the determination of cardiac BRS and indices of BP and HR variabilities. BRS assessed the efficiency of the cardiac sympathetic and parasympathetic pathways to buffer BP variations via HR. Evidence suggests that BRS should limit BP reactivity to profound challenge. Thus, BP would be expected to rise more in subjects with lower BRS. Because cardiac BRS was not related to the BP stress reactivity, our results do not support this hypothesis. Adjustment for age and basal SBP did not alter our results.

In response to a peripheral vasoconstriction, the cardiac baroreflex decreases HR through parasympathetic stimulation. Opposite hemodynamic cardiac patterns were observed in response to emotional stress that provoked a vasoconstriction associated with an increase in HR. For a few beats after the onset of the stressing stimulation, the cardiac baroreflex appeared to be overcome, because HR and BP increased simultaneously. Interestingly, Zhang et al reported a delay in BP increase in intact rats compared with sinoaortic-

**Figure 2.** Rest and stress, SBP and HR, indices of SBP and HR variabilities (standard deviation [SD] and spectral power in the MF [PMF] and HF [PHF] bands), and BRS determined by the spectral method in the MF bands and by the sequence method. Values are mean ± SEM. *P < 0.05 and **P < 0.001 for stress vs rest (n = 280 subjects).

**Table 2.** Correlation Coefficients Between Rest SBP or HR Indices of Variability and Their Respective Reactivity to Stress

<table>
<thead>
<tr>
<th>Variable</th>
<th>SD SBP</th>
<th>HR</th>
<th>PMF SBP</th>
<th>HR</th>
<th>PHF SBP</th>
<th>HR</th>
<th>PMF/PHF SBP</th>
<th>HR</th>
<th>Spectral BRS</th>
<th>HR</th>
<th>Sequence BRS</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>r=0.2*</td>
<td>NS</td>
<td>P=0.15†</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>r=0.2*</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS indicates nonsignificant. *P < 0.001; † P < 0.05.
denervated rats that involved the role of the cardiac BRS during the critical period after the onset of the sympathetic stimulation. The BRS could be involved in the kinetics of the pressor response. To verify this hypothesis, it would be of interest to study the relation between BRS and the delay to obtain the plateau of stress BP. Unfortunately, in humans, because many individual parameters may interfere (eg, alert reaction to the entry of the physician, comprehension of the test, and sagacity), the slope of the BP increase cannot be precisely measured during a psychological stress test. Stress induced a centrally mediated stimulation on vasomotor centers and induced a parasympathetic withdrawal, as elegantly shown by Zhang et al.23 These authors showed, with the use of sinoaortic-denervated rats, that intact baroceptor afferents limited the centrally mediated sympathetic BP response to stress but did not influence the parasympathetic withdrawal. Our results confirmed, in humans, these findings. The magnitude of the stress-induced increase in BP, which was not influenced by the cardiac baroreflex, could be modulated by the arterial baroreflex. Consistently, resting BP variability (standard deviation and spectral power in the MF band), which is influenced not only by the cardiac baroreflex but also by the arterial sympathetic tone, was slightly but significantly related to the stress-induced BP increase in accordance with the reports of Parati et al5 and Mounier-Vehier et al.24

The prolonged sympathetic stimulation led to a BP and HR plateau. Because spectral and sequence methods could determine BRS during stress, it has been suggested that BP is regulated by inverse variations of HR during the plateau. Furthermore, the calculated BRS during stress was lower than during resting conditions, as reported by Tulen et al.25 Although not recorded, the increase in respiratory frequency that has been reported to be 2 breaths per minute (see Reference 26) could not explain the stress-induced decreases in BRS and in HF bands observed only with greater increases in breathing frequency.27 BP regulation during stress could be compared with what is observed in established hypertension, eg, a resetting of the BRS that becomes able to buffer BP variations but at a higher level. In humans, the stress-induced sustained BP increase was preserved even during a sustained stimulation of arterial baroreceptors produced by infusing phenylephrine,28 and BRS during stress was reported to be impaired.29 In light of this result, the stress-induced reduction in BRS should originate from a central inhibition of the cardiac BRS rather than from a diminished sensitivity of the arterial baroreceptors.

In conclusion, resting BP variability was slightly but significantly related to stress-induced BP reactivity. Resting cardiac BRS that limits BP variability at rest did not blunt BP increase produced by a mental challenge. Our results suggest that a centrally mediated sympathetic stimulation overcame cardiac autonomic regulation at the onset of the stressing stimulation and emphasized the role of the sympathetic vasoconstriction in the pressor response. During the sustained sympathoexcitatory stimulus, a cardiac baroreflex controls BP variations but at a lower sensitivity. Because BP reactivity to challenge was reported to be associated with an unfavorable cardiovascular profile, our results are of major clinical interest.

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References


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