Erschienen in: The Journal of clinical endocrinology and metabolism : JCEM ; 91 (2006), 10. - S. 3857-3865

Low Social Support and Poor Emotional Regulation Are Associated with Increased Stress Hormone Reactivity to Mental Stress in Systemic Hypertension

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Context: There is strong evidence for a physiological hyperreactivity to stress in systemic hypertension, but data on associated or potentially moderating psychological factors are scarce.

Objective: The objective of the study was to identify psychological correlates of physiological stress reactivity in systemic hypertension.

Design: This was a cross-sectional, quasiexperimentally controlled study. Study participants underwent an acute standardized psychosocial stress task combining public speaking and mental arithmetic in front of an audience.

Setting: The study was conducted in the population in the state of Zurich, Switzerland.

Subjects: Subjects included 22 hypertensive and 26 normotensive men (mean ± SEM 44 ± 2 yr).

Main Outcome Measures: We assessed the psychological measures social support, emotional regulation, and cognitive appraisal of the stressful situation. Moreover, we measured salivary cortisol and plasma epinephrine and norepinephrine before and after stress and several times up to 60 min thereafter as well as blood pressure and heart rate.

Results: We found poorer hedonistic emotional regulation (HER) and lower perceived social support in hypertensives, compared with normotensives ($P < 0.01$). Compared with normotensives, hypertensives showed higher cortisol, epinephrine, and norepinephrine secretions after stress ($P < 0.038$) as well as higher systolic and diastolic blood pressure ($P < 0.001$). Cortisol reactivity and norepinephrine secretion were highest in hypertensive men with low HER ($P < 0.05$). In contrast, hypertensives with high HER did not significantly differ from normotensives in both cortisol and norepinephrine secretion after stress. Epinephrine secretion was highest in hypertensives with low social support but was not different between hypertensives with high social support and normotensives.

Conclusions: The findings suggest that both low social support and low HER are associated with elevated stress hormone reactivity in systemic hypertension.

THE CONCEPT OF cardiovascular hyperreactivity posits that studying short-term cardiovascular responses to controlled physiological, cognitive, and emotional challenges serves as a window into complex psychological and physiological processes that are involved in the development of cardiovascular disease (1). There is evidence suggesting that systemic hypertension is characterized by physiological hyperreactivity to psychosocial stressors (2). Compared with normotensive controls, hypertensive individuals showed exaggerated cardiovascular responses if confronted with laboratory stressors (for reviews see Refs. 3 and 4). Cardiovascular hyperreactivity has been established in hypertensives or hypertension-prone persons for a variety of physical and mental stressors (4–12) and was also predictive for the development of hypertension (13–16). Cardiovascular hyperreactivity is proposed to be a consequence of a hyperreactive sympathetic branch of the autonomic nervous system (14, 16, 17). Sympathetic hyperreactivity is often accompanied by enhanced activation of the hypothalamus-pituitary-adrenal (HPA) axis (2, 18–20). Although findings are not uniform (21, 22), there is reason to assume that hypertension is associated with altered HPA function in response to stress. More precisely, enhanced stress reactivity of the HPA axis has been associated with an increased risk of hypertension (5, 23, 24), and hypertensives exhibited larger cortisol elevation during and after mental stress (2, 7, 23–25). Likewise, hypertension-prone persons such as normotensives with a parental history of hypertension show stronger cortisol and ACTH responses to stress (5, 8, 24, 26).

According to definition, systemic or essential hypertension has no definite cause (27). Psychological factors could help explain some of its hitherto unexplained variance. Although several psychological differences between hypertensives and normotensives have been identified (for reviews see Refs. 28 and 29), studies investigating whether psycho-

Abbreviations: AUC, Area under the total response curve; AUCg, AUC ground from baseline to peak response; AUCi, increase in AUC; BMI, body mass index; BP, blood pressure; BSSS, Berlin Social Support Scale; DAR, distress-augmenting regulation; EM, emotional moderation; ERI, Emotional Regulation Inventory; HER, hedonistic emotional regulation; HPA, hypothalamus-pituitary-adrenal; MBP, mean arterial pressure; PASA, Primary and Secondary Appraisal; PSS, perceived social support; TSST, Trier Social Stress Test.

logical factors affect stress reactivity in hypertensives are scarce (29). Based on an extensive metaanalysis, Jorgensen *et al.* (29) previously elaborated a conceptual framework for psychosocial factors contributing to both tonic elevations of sympathetic drive and frequent and intense bouts of stressor evoked reactivity; among these factors they highlighted ineffective coping processes including cognitive appraisal of harm-loss and threat, poor affect management, and low social support. Of note, poor affect management or emotional regulation and cognitive appraisal can both be considered to be parts of coping. Coping is defined as cognitive and behavioral efforts to manage specific external and/or internal demands including actions aiming at both nonemotional goals and regulation of emotions (30, 31).

Cognitive coping processes like primary and secondary appraisal of a stressful situation predicted the magnitude of the cortisol stress response (32, 33). Moreover, social support may attenuate both HPA and cardiovascular stress reactivity (34–36). Social support has been associated with lower rates of hypertension (37), and hypertensives reported lower social support than normotensives (38). Therefore, one could assume that low social support might be associated with exaggerated physiological stress reactivity in hypertensive individuals. The role of affect management or emotional regulation in hypertension has also been discussed (29, 39). In particular, a hedonistic way of emotional regulation, *i.e.* a person's capability to intensify or maintain positive affect and practice mood repair when facing negative affect, is thought to facilitate stress-recovery and stress-protection (40). In contrast to psychological factors like hostility and anger both being associated with elevated physiological stress responses in hypertension-prone persons (41, 42), the role of emotional regulation in the interface between physiological stress reactivity and hypertension remains elusive (39). Also, whether cognitive stress appraisal and social support account for differences in the physiological stress reactivity between hypertensives and normotensives has not been studied.

The aim of this study was to investigate psychological correlates of physiological stress reactivity to acute psychosocial stress in unmedicated, otherwise healthy, middle-aged hypertensive men, compared with age-matched normotensive controls. We measured the stress hormones cortisol, epinephrine, and norepinephrine as well as the hemodynamic measures blood pressure and heart rate. The psychological correlates of interest were social support, emotional regulation, and cognitive appraisal of the stressful situation. We wondered whether these psychological factors would differ between hypertensives and normotensives and whether these differences would be associated with group differences in stress hormone reactivity.

Subjects and Methods

Study population

The final study sample consisted of 48 subjects who provided written informed consent. By aid of the Swiss Red Cross of the State of Zurich and advertisement, we recruited apparently healthy, nonsmoking men who did not take any medication. In detail, members of our study team accompanied the mobile blood donating unit of the Swiss Red Cross of the State of Zurich that routinely records blood pressure before blood donation. If a male person was found to have an elevated blood pressure, this person was asked whether he was interested in participating in the study. Interested subjects were given the advertisement text asking for the following inclusion criteria: aged 20–65 yr; systolic blood pressure 140 mm Hg or greater and/or diastolic blood pressure 90 mm Hg or greater; nonsmoker; no regular medication intake, particularly no antihypertensive medication; and no alcohol or illicit drug consumption. All potentially eligible individuals expressing interest in participating in the study were then screened by a telephone interview using an extensive health questionnaire. Specific exclusion criteria, as obtained by subjects' self-report, were: clinical psychosomatic and psychiatric diseases; regular heavy exercise; alcohol and illicit drug abuse; any heart disease, varicosis, and thrombotic diseases; elevated blood sugar and diabetes; elevated cholesterol; liver and renal diseases; chronic obstructive pulmonary disease, allergies and atopic diathesis; rheumatic diseases; HIV; cancer; and current infectious diseases. If personal history was not conclusive, the subjects' primary care physician was contacted for clarification. A previous diagnosis of high blood pressure was not an exclusion criterion. For each hypertensive subject enrolled in the study, we recruited an age-matched normotensive control subject also by aid of the Swiss Red Cross. All controls met inclusion and exclusion criteria as specified for hypertensive study participants. After reading the advertisement, 32% of interested subjects were eventually enrolled. The Ethics Committee of the State of Zurich, Switzerland, formally approved the research protocol. The study was carried out in accordance with the Declaration of Helsinki principles.

Assessment of hypertension

After a 15-min rest, three seated blood pressure (BP) measurements were obtained by a fully automated sphygmomanometry device (Omron 773; Omron Healthcare Europe B.V., Hoofddorp, The Netherlands) on three different days, and the average BP was computed. Two measurements were taken by trained members of the study team and one by the subject himself after careful instruction and training. Based on screening BP, subjects were categorized into hypertensive and normotensive individuals following the World Health Organization/International Society of Hypertension definition (systolic BP $\geq$ 140 mm Hg and/or diastolic BP $\geq$ 90 mm Hg) (27). This screening procedure left 22 hypertensive and 26 normotensive men (mean $\pm$ SEM age, 44.0 $\pm$ 2 yr) whose characteristics are listed in Table 1.

Psychosocial stress procedure

All experimental sessions commenced between 1400 and 1600 h and lasted for approximately 2 h. Participants abstained from food and drink (other than water) for 2 h before the experiment and from physical exercise, alcohol, and caffeinated beverages starting the evening before the test day. To inflict acute psychosocial stress, we used the well-standardized Trier Social Stress Test (TSST) comprising 5 min of preparation, a mock job interview (5 min), and mental arithmetic (serial subtraction, 5 min) in front of an unknown panel of one man and one woman (43). The TSST enables a naturalistic exposure to a psychosocially stressful situation and has repeatedly been found to induce profound endocrine and cardiovascular responses (43, 44). During the 45 min before introduction to the TSST and another 60 min after task completion, subjects remained seated in a quiet room.

Samples of saliva (by chewing on cotton rolls) were taken in this same room 1 min before subjects were introduced to the TSST to assess resting levels as well as immediately thereafter and 10, 20, 30, 40, 50, and 60 min after completion of the TSST. Via an indwelling catheter, blood samples were also obtained under resting conditions 1 min before subjects were introduced to the TSST and immediately after completion of the TSST. Additional blood samples were drawn 10 and 60 min after completion of the TSST. At the end of saliva and blood sampling, participants were debriefed and participation was financially remunerated with 80 Swiss francs.

Hemodynamic measures

Heart rate data were obtained continuously via a portable heart rate monitor (Polar system, S810; Polar, Kempele, Finland) (45–47). Blood pressure was measured under resting conditions 1 min before the start

TABLE 1. Group characteristics of normotensive (NT) and hypertensive (HT) men

	NT (n = 26)	HT (n = 22)	*P* value
Systolic blood pressure (mm Hg)[a]	121 ± 1.6	149 ± 1.9	<0.0001
Diastolic blood pressure (mm Hg)[a]	77.6 ± 1.3	95.2 ± 1.8	<0.0001
Age (yr)	42.0 ± 2.6	46.3 ± 3.0	0.28
BMI (kg/m^2)	24.9 ± 0.5	27.1 ± 0.6	0.007

Values given are mean ± SEM.
[a] Mean of the three screening BP measurements.

of the TSST procedure (Omron baseline reading) and immediately after stress as well as 10 and 20 min after stress by Omron sphygmomanometry and continuously from 5 min before beginning of the TSST introduction to 5 min after TSST completion (*i.e.* average of speech and arithmetic BP) by the Vasotrac APM205A device (Medwave Inc., St. Paul, MN) (48, 49). For statistical analyses, average BP values during stress were adjusted to Omron sphygmomanometry readings to take into account overestimation of BP due to measurement via the Vasotrac device. In detail, adjusted Vasotrac readings were calculated by adding the difference between the Vasotrac reading of a given time point and the Vasotrac baseline reading (mean of 5 min before beginning of the TSST procedure) to the Omron baseline reading.

Stress hormone measures

For assessment of salivary free cortisol levels, saliva was collected by subjects using Salivette collection devices (Sarstedt, Rommelsdorf, Germany) and stored at −20 C until biochemical analysis. Saliva samples were thawed and spun at 3000 rpm for 10 min, yielding low-viscosity saliva. Cortisol concentrations were measured using a commercially available competitive chemiluminescence immunoassay with high sensitivity of 0.16 ng/ml (LIA; IBL, Hamburg, Germany). Intra- and interassay variability were less than 7.7 and 11.5%, respectively. For assessment of plasma norepinephrine and epinephrine levels, blood was drawn into EDTA-coated monovettes (EDTA; Sarstedt, Numbrecht, Germany), and immediately centrifuged for 10 min at 2000 × *g*; obtained plasma was stored at −80 C until analysis. Plasma norepinephrine and epinephrine were determined by HPLC [detection limit 0.25 pg/ml; inter- and intraassay variance < 5%; Laboratory for Stress Monitoring, Göttingen, Germany (50, 51)]. To reduce systematic measurement errors, all samples from one subject were analyzed in the same run.

Psychological assessment

We used validated German versions of the following questionnaires.

Social support. The first part of the Berlin Social Support Scale (BSSS) consists of 17 items assessing perceived social support (PSS), support seeking, and need for support (52). Previous literature on social support and cardiovascular disease guided us in using the PSS for the purpose of this study (53). Using a 4-point rating scale ranging from 1 (completely wrong) to 4 (completely right), participants were asked whether they agree with certain statements on their perception of social support (*i.e.* there are people who help me if I need help). Higher scores mean higher PSS. Cronbach's alpha (n = 437) is 0.83 for the PSS subscale (52).

Emotional regulation. The 34-item Emotional Regulation Inventory (ERI) is specially suited for assessment of behavioral regulation of emotions and comprises a hedonistic way of emotional regulation, *i.e.* hedonistic regulation (HER), buffering of emotions, *i.e.* emotional moderation (EM), and intensifying of negative emotions, *i.e.* distress-augmenting regulation (DAR) (40). Using a 6-point rating scale ranging from 1 (almost never) to 6 (almost always), participants were asked to rate how often they use specific strategies (*e.g.* listen to cheerful music, go out with friends) to regulate their emotions. Higher scores mean higher HER, stronger buffering of emotions in EM, and higher distress augmenting regulation in DAR. Cronbach's alphas (n = 1800) were 0.91 (HER), 0.90 (EM), and 0.92 (DAR) for the three subscales. The three subscales are correlated in the expected way with conceptually relevant constructs (n = 425; $P < 0.01$): Negative Mood Repair (54) [HER (r = 0.43), DAR (r = −0.38), EM (r = 0.17)] and the dimension Repair of the Trait Meta-Mood Scale (55) [HER (r = 0.55), DAR (r = −0.42), EM (r = 0.21)] (40).

Cognitive coping: primary and secondary appraisal. The 16-item questionnaire for Primary and Secondary Appraisal (PASA) construed to fit with the respective description of the transactional stress model proposed by Lazarus and Folkman (31) assesses four cognitive stress appraisal processes relevant for the TSST, which are threat and challenge (*i.e.* primary appraisal) as well as self-concept of own abilities and control expectancy (*i.e.* secondary appraisal) (33). A global PASA scale termed Stress Index combines primary and secondary appraisal providing an integrated measure of transactional stress perception (33). Each scale comprises eight items, on which subjects have to evaluate the extent to which the particular statement applies to them on a 6-point scale ranging from 1 (strongly disagree) to 6 (strongly agree). Higher scores in the Stress Index mean higher stress appraisal. Cronbach's alphas (n = 81) were 0.83 (threat), 0.63 (challenge), 0.81 (self-concept of own competence), and 0.77 (control expectancy). The Stress Index correlates in the expected way with competence and control orientation (56), a conceptually relevant construct (n = 81; $P < 0.05$): the subscales self-concept of own competence (r = −0.47), control expectancy (internality) (r = −0.31), control expectancy (powerful others control) (r = 0.25), and control expectancy (chance control) (r = 0.23) (33).

Statistical analyses

All calculations were performed using SPSS Inc. (version 11.0.1) software packages (SPSS, Chicago, IL). Data are presented as mean ± SEM. The optimal sample size of n = 48 to detect an expected large effect size of $f^2 = 0.35$ (representing a large effect size) with a power 0.85 or greater and alpha = 0.05 was calculated *a priori* with the statistical software G-Power (57). Results were considered statistically significant at the $P \leq 0.05$ level, and all tests were two tailed. In case of missing data, cases were excluded listwise. Data were tested for normal distribution and homogeneity of variance using Kolmogorov-Smirnov and Levene's tests before statistical procedures were applied. Across the two subject groups, univariate ANOVAs were calculated for group characteristics (Table 1), questionnaire scales (Tables 2 and 4), and baseline group differences in stress hormones and hemodynamic measures. ANOVAs for repeated measures were computed to reveal possible stress (time from 1 min before to 60 min after stress) and group (hypertensives *vs.* normotensives) effects for cortisol, norepinephrine, and epinephrine. To

TABLE 2. Psychological characteristics of normotensive (NT) and hypertensive (HT) men

Psychological factor	Scale	NT (n = 26)	HT (n = 22)	*P* value
Social support (BSSS)	PSS	3.73 ± 0.05	3.46 ± 0.09	0.010
Emotional regulation (ERI)	HER	49.5 ± 1.27	41.9 ± 1.97	0.002
	DAR	34.5 ± 1.82	31.26 ± 1.84	0.23
	EM	32.5 ± 1.62	30.0 ± 2.01	0.33
Cognitive appraisal (PASA)	Stress index	2.37 ± 0.47	2.09 ± 0.54	0.70

Values given are mean ± SEM.

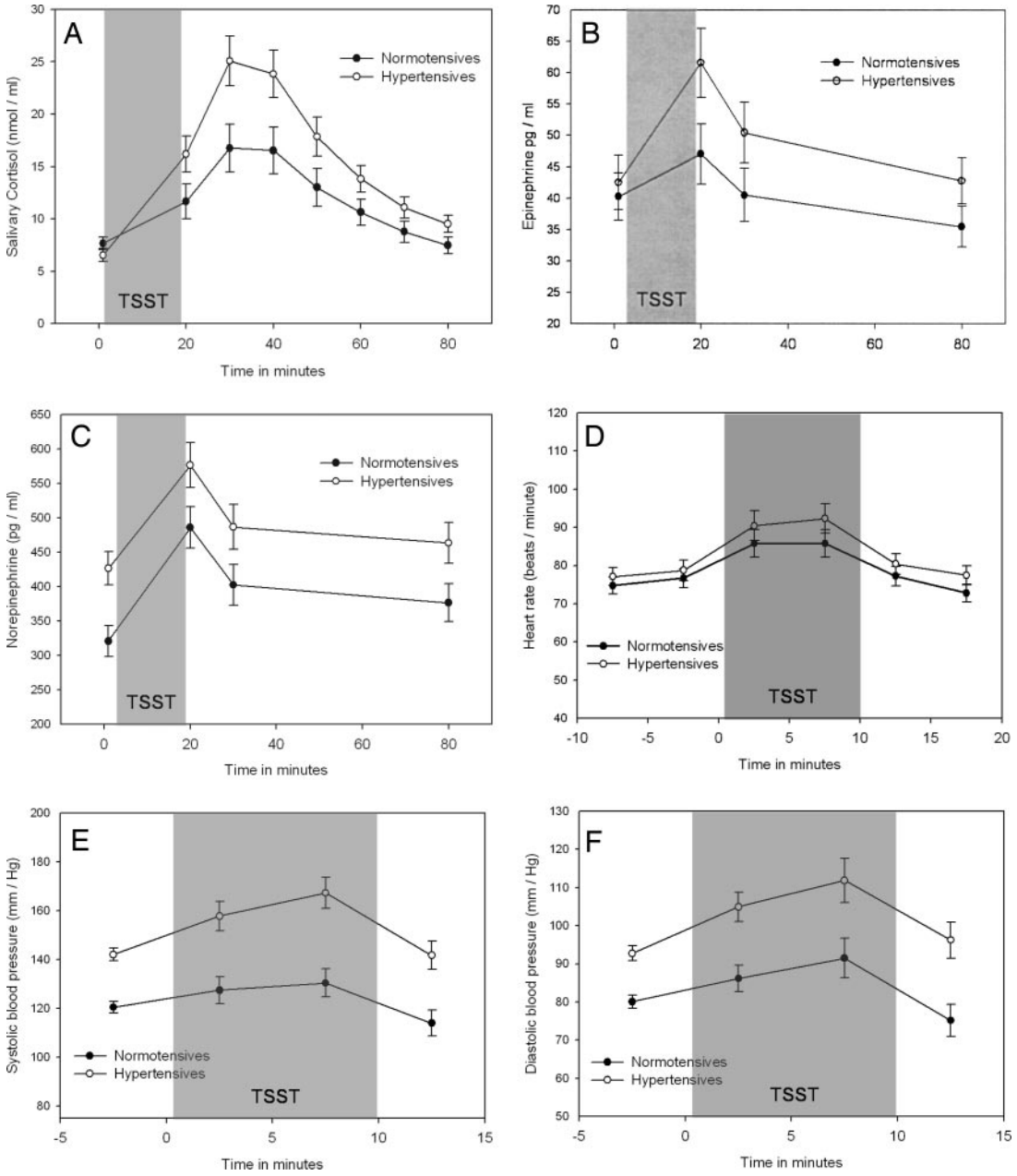

FIG. 1. A–F, Values are means ± SEM. Across all subjects, the stressor (TSST) elicited a significant response in hormone (A–C) and hemodynamic (D–F) measures. Hypertensive men showed higher cortisol ($P = 0.007$), catecholamine (epinephrine: $P = 0.038$; norepinephrine: $P = 0.019$), and blood pressure ($P < 0.0001$) but not heart rate responses from rest to stress ($P = 0.48$). Stress hormone (A–C) and hemodynamic (D and E) reactivity to psychosocial stress in hypertensive and normotensive men are shown.

control for differences in body mass index (BMI) between hypertensives and normotensives, we calculated analyses of covariance for psychological characteristics, physiological stress reactivity, and associations between psychological parameters and stress hormones with BMI as a covariate. We applied Huynh-Feldt correction for repeated measures. Correlations were computed as Pearson product-moment correlations. For stress hormones, areas under the total response curves (AUCs), expressed as area under the measured time points, with respect to increase (AUCi) and ground from baseline to peak response (AUCg), were calculated using the trapezoid formula (58). Whereas AUCg mostly captures baseline differences, AUCi is a measure reflecting differences between baseline and task values.

For assessment of associations between psychological factors and stress hormone reactivity, we used a five-step procedure. First, we identified psychological factors significantly differing between hypertensive and normotensive subjects. Second, we correlated these psychological factors with the AUCs of stress hormones. To avoid multiple testing in further analyses, we used those AUCs of stress hormones, which were significantly different between groups. We used AUCi for correlation analyses testing for a significant interaction effect and AUCg for correlation analyses testing for a significant group effect (Table 3). Third, in case of a significant bivariate correlation, we performed a median split on psychological scales rendering four subgroups of hypertensives and normotensives with either high or low values in the particular psychological measure (*e.g.* hypertensives with high and low PSS and normotensives with high and low perceived social support). In these four groups, ANOVAs for repeated measures were performed for stress hormones. Fourth, significant subgroup effects were further tested

TABLE 3. Correlations between psychological factors differing between hypertensives and normotensives and AUCs of stress hormones expressed as AUCi and AUC whole

Parameter	AUC	HER (ERI)	Social support (BSSS)
Cortisol	AUCi	-0.560^{c}	-0.440^{b}
Epinephrine	AUCi	-0.315	-0.457^{b}
Norepinephrine	AUCg	-0.377^{a}	-0.172

Values given are mean ± SEM.
[a] $P < 0.017$.
[b] $P < 0.01$.
[c] $P < 0.001$.

by calculating linear regression analyses (enter method) with the AUC of the respective stress hormone as the dependent variable. We considered three potential predictors, namely the mean arterial pressure [MBP; calculated by the formula (2/3 ∗ diastolic BP) + (1/3 systolic BP)], differing psychological factor, and the interaction term (MBP × psychological factor). This type of analysis investigates whether psychological parameters independently of each other affect stress hormone secretion or whether they interact in doing so. All regression parameters were Z transformed before regression analyses to allow computation of interaction terms. Because AUCs are aggregated measures reducing information on the reactivity pattern, we validated regression results by, fifth, performing general linear models with repeated measurement for each stress hormone as dependent variable and the respective psychological scale as continuous independent variable. Because catecholamines peak immediately after stress, we present calculations on all time points (−1 to +60 min) and baseline and peak (−1 and +1 min).

Results

Group characteristics

Table 1 provides the characteristics of the 22 hypertensive subjects and 26 normotensive controls studied. According to definition, hypertensive subjects had higher average systolic and diastolic BP than normotensive subjects. In addition, hypertensives had higher BMI than normotensives.

Psychological characteristics

Table 2 shows psychological characteristics of hypertensives and normotensives. Whereas there were no differences in cognitive appraisal of the stress situation between groups, hypertensives and normotensives differed in terms of emotional regulation and social support. Hypertensive subjects regulated their emotions in a less hedonistic way ($F(1/39) = 11.11$, $P = 0.002$). Furthermore, hypertensives perceived lower social support ($F(1/46) = 7.25$, $P = 0.010$). HER and PSS correlate positively ($r = 0.33$, $P = 0.04$).

Physiological stress responses

The TSST caused significant increases in all physiological parameters measured ($P < 0.05$) (Fig. 1).

Stress hormones. Hypertensives showed higher cortisol reactivity from baseline to 60 min after psychosocial stress, compared with normotensive controls (interaction group by stress: $F(2.4/94.3) = 4.77$, $P = 0.007$). Resting cortisol ($P = 0.20$) and epinephrine levels ($P = 0.99$) were not different between groups, but hypertensives showed higher epinephrine reactivity than normotensives (interaction group by stress: $F(3.0/124.3) = 2.90$, $P = 0.038$). Also, hypertensives showed elevated norepinephrine levels both at rest and after psychosocial stress (group effect: $F(1/46) = 5.95$, $P = 0.019$).

Hemodynamic measures. As expected hypertensives showed higher resting systolic and diastolic blood pressure before stress ($P < 0.0001$). These differences were maintained during and after stress (group effect: systolic BP, $F(1/40) = 23.31$, $P < 0.0001$; diastolic BP, $F(1/41) = 20.86$, $P < 0.0001$). Although hypertensives had higher absolute heart rate at all time points than normotensives, this difference did not reach statistical significance, neither at rest nor during or after stress.

Associations between psychological parameters and stress hormone secretion

Correlation analyses. To test for associations between psychological factors and secretion of stress hormones, we tested those psychological variables that showed a difference between hypertensives and normotensives, *i.e.* HER and PSS. First, HER and PSS were correlated with AUCs of stress hormones (Table 3). HER correlated negatively with aggregated cortisol secretion (AUCg: $r = -0.344$, $P = 0.028$; AUCi: $r = -0.446$, $P = 0.004$) and aggregated epinephrine increase (AUCi: $r = -0.336$, $P = 0.039$). PSS correlated negatively with both cortisol (AUCg, $r = -0.348$, $P = 0.018$; AUCi, $r = -0.448$, $P = 0.002$) and epinephrine (AUCg, $r = -0.344$, $P = 0.021$).

Subgroup analyses. Second, subgroup analyses were performed to further explore the associations between psychological parameters and stress hormones differing between hypertensives and normotensives. In each group, a median split was performed for HER and social support, yielding two groups of hypertensives and normotensives, each with high *vs.* low HER and high *vs.* low social support (Table 4).

HER. For hypertensives and normotensives with high and low HER, there was a significant group-by-stress interaction for cortisol reactivity ($F(8.52/90.84) = 2.53$, $P = 0.014$, Fig. 2A) and a significant group effect for norepinephrine secretion ($F(3/36) = 2.91$, $P = 0.047$, Fig. 2B). There were no group differences or group-by-stress interactions for epinephrine. *Post hoc* tests revealed that hypertensives with low HER showed higher cortisol reactivity than normotensives with both high ($P = 0.018$) and low HER ($P = 0.045$) but failed to reach statistical difference, compared with hypertensives with high HER ($P = 0.12$). Similar results were observed for norepinephrine: Hypertensives with low HER showed higher norepinephrine secretion than both hypertensives ($P = 0.042$) and normotensives with high HER ($P = 0.007$) and marginally than normotensives with low HER ($P = 0.09$).

Social support. Hypertensives with low social support showed significantly higher epinephrine stress reactivity,

TABLE 4. HER and PSS in hypertensive and control men after median split

Group	Median split	HER (ERI)	Social support (BSSS)
Hypertensives	Low	35.3 ± 1.2	3.11 ± 0.10
	High	49.2 ± 2.0	3.81 ± 0.04
Normotensives	Low	46.0 ± 1.3	3.51 ± 0.06
	High	54.3 ± 1.0	3.92 ± 0.02

Values given are mean ± SEM.

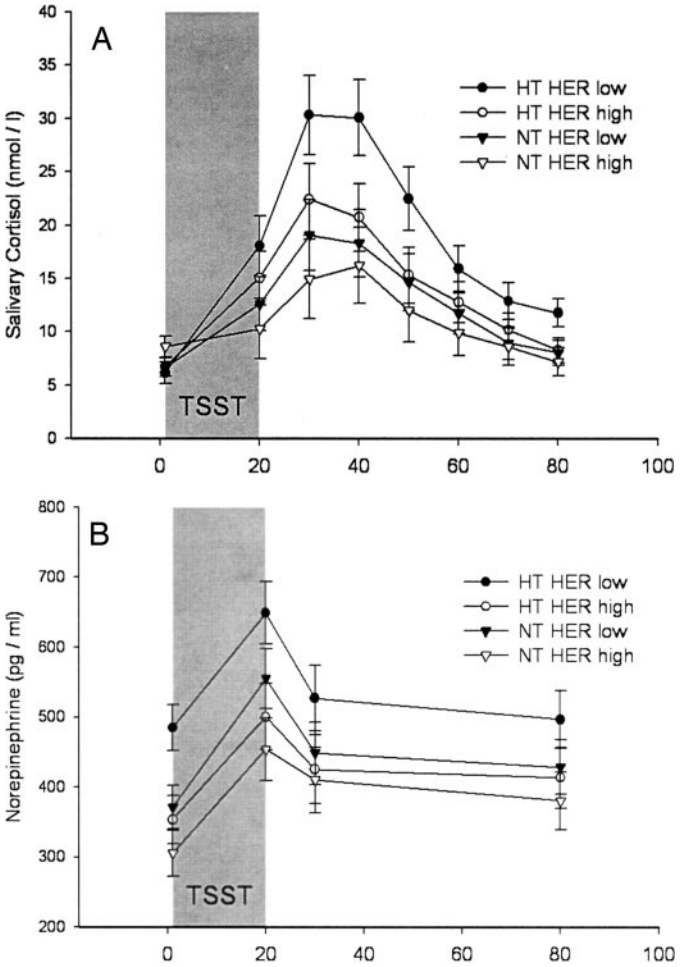

FIG. 2. A and B, Values are means ± SEM. Hypertensive men with low HER show higher cortisol reactivity to psychosocial stress than normotensives with either high or low HER ($P < 0.045$), whereas hypertensives with high HER did not significantly differ from normotensives (A). Similarly, highest norepinephrine secretion could be observed in hypertensives with low hedonistic regulation (B) ($P < 0.042$). A and B, Cortisol and norepinephrine reactivity to psychosocial stress (TSST) in hypertensive (HT) and normotensive (NT) men with high and low HER.

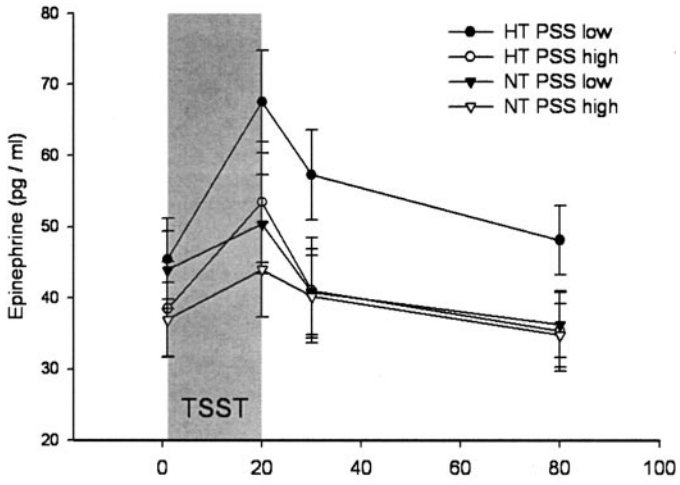

FIG. 3. Values are means ± SEM. Whereas hypertensives with high social support did not differ from normotensives, hypertensives with low social support showed higher epinephrine secretion than normotensives with high social support ($P < 0.043$). Epinephrine reactivity to psychosocial stress (TSST) in hypertensive (HT) and normotensive (NT) men with high and low perceived social support (PSS) are shown.

compared with normotensives with high social support ($P = 0.043$), whereas hypertensives with high social support did not differ from normotensives with either low or high social support (Fig. 3). Compared with normotensives with high social support, *post hoc* tests showed higher norepinephrine secretion in hypertensives with high social support ($P = 0.016$). Although there was a significant group-by-stress interaction for hypertensives and normotensives with high and low PSS ($F(7.68/94.7) = 2.27$, $P = 0.03$) in terms of cortisol stress reactivity, social support did not account for differences between hypertensives and normotensives. Compared to normotensives with high social support, *post hoc* tests revealed higher cortisol reactivity in hypertensives with both low ($P = 0.029$) and high social support ($P = 0.044$).

Regression analyses. To further explore subgroup analyses, we calculated hierarchical regression analyses. To predict AUCi of cortisol, we entered in a first step MBP and HER as independent variables and the interaction thereof in a second step. In contrast to MBP and the interaction term, only HER significantly predicted AUCi of cortisol (beta = −0.535, $P = 0.002$, $R^2 = 0.314$). Similarly, AUCi of epinephrine was predicted by PSS (beta = −0.390, $P = 0.014$, $R^2 = 0.209$) but not MAP or the interaction between MAP and PSS. AUCg of norepinephrine from baseline to peak was significantly predicted when entering MAP and HER as independent variables ($R^2 = 0.195$, $P = 0.014$); entering their interaction in a second step did not change R^2. We also calculated regression analyses to address whether PSS and HER independently influence stress hormone secretion or whether they interact in doing so. To assess the independent influence of HER on AUCi of cortisol, we entered PSS (step 1) followed by HER (step 2). HER significantly changed R^2 ($\Delta R^2 = 0.203$, $P = 0.002$) independently of PSS. Similarly, HER significantly changed R^2 ($\Delta R^2 = 0.124$, $P = 0.023$) independently of PSS to predict AUCg of norepinephrine. PSS significantly changed R^2 ($\Delta R^2 = 0.159$, $P = 0.012$) to predict AUCi of epinephrine independently of HER. Interaction of HER and PSS marginally changed R^2 ($\Delta R^2 = 0.066$, $P = 0.056$) to predict AUCi of cortisol, but not AUCs of catecholamines.

General linear models. To validate regression results, we applied general linear models with repeated measures of stress hormones as dependent variables and significant psychological predictors as independent variables. In terms of repeated cortisol secretion (all measurements), the main effect of HER ($F(1/34) = 8.3$, $P = 0.007$) and the interaction of HER by stress ($F(2.7/92.8) = 8.31$, $P > 0.0001$) were significant. The main effect of HER on norepinephrine secretion was significant for all norepinephrine measures ($F(1/39) = 4.37$, $P = 0.043$) and norepinephrine baseline and peak ($F(1/39) = 7.39$, $P = 0.010$). The interaction PSS by stress, however, failed to reach statistical significance for all repeated epinephrine measurements as dependent variable ($F(2.9/121.2) = 2.17$, $P = 0.097$) but was significant for the two repeated epinephrine measurements from baseline to peak ($F(1/45) = 4.3$, $P =$

0.044). The main effect of PSS on epinephrine measures was significant for all repeated measures ($F(1/42) = 4.2$, $P = 0.047$).

Influence of BMI on psychological characteristics, physiological stress reactivity, and associations between psychological parameters and stress hormones

Because BMI differed between hypertensives and normotensives, we controlled for BMI. Whereas psychological differences and cortisol effects did not significantly change, epinephrine stress reactivity lost its significance (interaction group by stress: $F(3.0/122.8) = 1.83$, $P = 0.15$). Norepinephrine levels remained higher in hypertensives with borderline significance (group effect: $F(1/45) = 2.9$, $P = 0.096$) after entering BMI as covariate. Concerning associations between HER/PSS and stress hormone secretions, planned comparisons indicated that only significance of epinephrine stress reactivity was marginally changed after controlling for BMI. In detail, higher epinephrine stress reactivity in hypertensives with low HER, compared with all other HER subgroups, became of borderline significance ($P = 0.052$). Controlling for BMI in a first step did not significantly change results of regression analyses. Controlling for BMI in general linear models with repeated measures did not significantly change results on cortisol and norepinephrine; only epinephrine results lost significance ($P = 0.079$).

Discussion

Hypertensive unmedicated and otherwise healthy men showed higher cortisol, epinephrine, and norepinephrine secretions after stress as well as higher systolic and diastolic blood pressures than normotensive controls. Moreover, we found lower HER and lower PSS in hypertensives, compared with normotensives, but no differences in cognitive appraisal of the stressful situation. This finding may reflect the conceptual differences between emotional regulation and stress appraisal as different domains of coping. In contrast to the PASA items, which are directly related to the anticipated stress situation and which therefore do not assess general coping processes but specific ones, the ERI items ask for general emotional regulation strategies not related to a specific situation.

The main finding of our study is that hypertensive men with low HER show higher cortisol reactivity to psychosocial stress and higher norepinephrine secretion than normotensives and hypertensives with high HER independent of PSS. Interestingly, only HER significantly predicted cortisol stress reactivity. This finding suggests that the observed cortisol differences between hypertensives and normotensives are more likely related to different HER levels than BP or the interaction between HER and continuous BP levels. Moreover, as indicated by the marginally significant interaction, the interaction between HER and PSS might further increase cortisol stress reactivity. Norepinephrine secretion was predicted by both BP and HER. In addition, hypertensives with low social support show a higher epinephrine stress response, compared with normotensives and hypertensives with high social support that was independent of HER. Similar to cortisol, these group differences were significantly predicted by a psychological factor, namely PSS, suggesting a role for PSS in influencing epinephrine stress reactivity.

What are the potential implications of our study and how do they compare with the literature? Our findings of elevated stress reactivity of the sympathetic nervous system and HPA axis in hypertensives, compared with normotensives, corroborate previous findings (2, 5, 8, 24). We found that hypertensives and normotensives did not differ in cognitive anticipatory appraisal processes. Thus, it seems unlikely that the observed differences in physiological stress reactivity relate to differences in the cognitive appraisal of the stressful situation. Our findings suggest a possible role for emotional regulation and social support in moderating certain aspects of physiological stress reactivity. HER refers to a person's capability of regulating emotions in a hedonistic way, *i.e.* to intensify or maintain positive affect and practice mood repair when facing negative affect, *e.g.* to put oneself in surroundings that improve one's mood or think of something pleasant instead of intensifying or ruminating negative affect (40). Therefore, it is likely that HER provides one way of reducing tension, thereby facilitating stress recovery and stress protection. In line with such reasoning, hedonistic HER might simplify gaining of social support, which is also reflected by the positive correlation of the two constructs in our data. Low social support as a risk factor for hypertension development and lower social support in hypertensives and hypertension-prone subjects have already been reported in previous studies (38, 59, 60). A very recent study provides a possible explanation for the observed lower social support in hypertensives by evidencing possible underlying deficits in social competence and behavior measures in hypertensives (61). When confronted with anger-evoking role-play interactions, hypertensive patients showed less eye contact, used fewer positive assertive statements, and were rated as being less assertive than normotensive controls (61).

Our findings suggest associations between HER and PSS and stress reactivity of the HPA axis and sympathetic nervous system. The lower HER and the lower social support in hypertension, the higher the stress reactivity of certain physiological correlates. In other words, the higher HER or the higher social support, the lower HPA or sympathetic stress reactivity. Thus, one might assume a stress-protective role of these two psychological factors in hypertension. This notion seems even stronger, given that hypertensives with low HER or low social support showed the lowest values in HER or social support, whereas hypertensives with high HER and high social support had values in between normotensives with low and high values in HER or social support, respectively (Table 4). We thus may speculate that those hypertensives with low values exhibit some deficit in these psychological parameters, which, in turn, might account for the observed overall higher physiological stress reactivity in hypertensives. This reasoning might be of clinical importance because the roles of emotional regulation and social support in the development of hypertension have been previously discussed as potential causal factors (38, 39, 59, 60).

We mention several limitations of our study. First, our data are cross-sectional, so that causal interpretations of the observed associations remain speculative. For example, our data cannot prove whether the observed lower HER is a

cause, a consequence, or just a noncausal concomitant phenomenon of systemic hypertension and elevated stress reactivity. Second, our screening procedure to track subjects with systemic hypertension might embed a recruitment bias because we enrolled only male nonsmoking subjects who are not (yet) on antihypertensive medication and who are otherwise healthy. Also, although our analyses suggest that BMI did not substantially affect our findings, we did not match groups in terms of BMI. So the generalizability of our findings and implications to hypertensive patients in general or hypertensive patients with overt cardiovascular disease is questionable. Moreover, our subjects showed good health habits because we excluded those with alcohol or illicit drug abuse. Third, we cannot completely rule out the possibility that a white coat hypertension effect affected screening blood pressure and, as a consequence, some of the observed associations between psychological factors and heightened physiological stress reactivity. However, BP screenings were not performed in a clinical setting and continuous BP readings obtained while subjects were waiting alone in their room support our screening BP data (data not shown). We therefore feel that most of our hypertensive subjects were not diagnosed with systemic hypertension because they had white coat hypertension. Fourth, we determined our sample size to detect effects with a power of at least 85%. Thus, we cannot rule out the probability of type II error, *i.e.* to falsely not detect true effects. Therefore, the findings of nonsignificant effects, *e.g.* the interaction effects in regression analyses, cannot definitively rule out the possibility of existing interactions and should therefore be interpreted with caution.

In summary, our data suggest a role for the psychological factors HER and social support in physiological stress reactivity of persons with systemic hypertension. The clinical implications of our observations in health, systemic hypertension, and other cardiovascular disease remain to be demonstrated.

Acknowledgments

Received November 29, 2005. Accepted July 25, 2006.

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This work was supported by Research Grant 2003 from the University of Zurich (to P.H.W.).

Author disclosure: All authors have nothing to declare.

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