

Anxiety and Hostility Are Associated With Reduced Baroreflex Sensitivity and Increased Beat-to-Beat Blood Pressure Variability

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Objective: The purpose of this study was to determine whether psychological factors are associated with heart rate variability (HRV), blood pressure variability (BPV), and baroreflex sensitivity (BRS) among healthy middle-aged men and women. **Methods:** A population-based sample of 71 men and 79 women (35–64 years of age) was studied. Five-minute supine recordings of ECG and beat-to-beat photoplethysmographic finger systolic arterial pressure and diastolic arterial pressure were obtained during paced breathing. Power spectra were computed using a fast Fourier transform for low-frequency (0.04–0.15 Hz) and high-frequency (0.15–0.40 Hz) powers. BRS was calculated by cross-spectral analysis of R-R interval and systolic arterial pressure variabilities. Psychological factors were evaluated by three self-report questionnaires: the Brief Symptom Inventory, the shortened version of the Spielberger State-Trait Anger Expression Inventory, and the Toronto Alexithymia Scale. **Results:** Psychological factors were not related to HRV. Anxiety was associated with decreased BRS ($p = 0.001$) and higher low-frequency ($p = 0.002$) power of systolic arterial pressure variability. These associations were independent of age, gender, other psychological factors, heart rate, and systolic and diastolic blood pressures. Hostility was an independent correlate of increased low-frequency power of diastolic arterial pressure ($p = 0.001$) and increased high-frequency power of systolic arterial pressure ($p = 0.033$) variability. **Conclusions:** Anxiety and hostility are related to reduced BRS and increased low-frequency power of BPV. Reduced BRS reflects decreased parasympathetic outflow to the heart and may increase BPV through an increased sympathetic predominance. **Key words:** heart rate variability, blood pressure variability, baroreflex sensitivity, Brief Symptom Inventory, Spielberger State-Trait Anger Expression Inventory, Toronto Alexithymia Scale.

BPV = blood pressure variability; **BRS** = baroreflex sensitivity; **BSI-37** = shortened 37-item version of the Brief Symptom Inventory; **HRV** = heart rate variability; **STAXI** = Spielberger State-Trait Anger Expression Inventory; **TAS-26** = Toronto Alexithymia Scale.

INTRODUCTION

Power spectral analysis of HRV has been used to assess whether sympathetic and parasympathetic modulation of the heart rate is associated with cardiovascular morbidity, psychological distress, and psychiatric disorders. While the high-frequency power of HRV is an indicator of parasympathetic cardiac modulation, the low-frequency power of HRV reflects both sympathetic and parasympathetic modulation (1). In the general population, low HRV is associated with increased risk of death from several causes (2–4) and with increased risk of cardiac events (5, 6).

Previous studies of associations between psychological factors and HRV have been carried out predominantly with selected groups of subjects suffering from psychiatric disorders (7–11) or with apparently healthy volunteers (12–16). Although reduced HRV based on 24-hour recording of the heart rate is associated with depression in patients with coronary artery disease (17, 18), short-term HRV measured at supine rest does not differentiate depressive patients from their healthy controls (9, 19, 20). No data exist of the relationship between HRV and depression in the general population. In apparently healthy volunteers, anxiety has been associated with decreased total, low-frequency, and high-

frequency powers of HRV (12, 13). Hostility has been linked to decreased high-frequency power of HRV (15). Some data suggest that alexithymic individuals have sympathetic overactivity (16). To the best of our knowledge, no population-based study exists on the effects of anxiety, hostility, or alexithymia on the power spectral components of HRV.

Suppressed anger and hostility (21, 22), alexithymia (23, 24), anxiety (22, 25, 26), and depression (26) have been associated with hypertension. Negative affects composed of anxiety, anger, or sadness increase blood pressure temporarily (27) and may thereby also increase 24-hour BPV. Increased daytime systolic BPV in turn is associated with increased cardiovascular mortality (28). To date, no prognostic data are available from the short-term BPV. The power spectrum of beat-to-beat BPV is composed basically of the same spectral components as that of HRV. Changes in the low-frequency power of BPV have been suggested to reflect changes of central sympathetic nervous control (29, 30). However, the high-frequency power of BPV is determined largely by mechanical effects of respiration on intrathoracic pressure and cardiac filling (30). Thus, exploring the beat-to-beat BPV could give additional information from autonomic nervous function because association of psychological factor with an increased low-frequency power of BPV might indicate increased sympathetic modulation. Concurrently with this assumption, anxiety has been related to increased low-frequency power of systolic BPV (13).

BRS reflects vagal modulation of heart rate by the arterial baroreceptors. A low BRS predicts increased cardiovascular mortality (31). Only a paucity of data are available concerning the effects of psychological factors on BRS. Previous studies suggest that BRS correlates inversely with higher levels of anxiety (10, 14, 32).

The impact of psychological factors on BPV and BRS is largely obscure. There is also insufficient data concerning the relation of psychological factors to HRV in healthy subjects

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representing the general population. Therefore, we wanted to study whether psychological factors, namely, somatization, depression, anxiety, hostility, phobicity, anger expression, and alexithymia, are associated with HRV, BRS, and beat-to-beat BPV in healthy middle-aged subjects of the general population. We expected that these factors would be associated with reduced HRV, increased beat-to-beat BPV, and diminished BRS.

METHODS

Subjects

An age- and gender-stratified random sample consisting of 45 subjects of each gender and each 10-year age group (35–44, 45–54, and 55–64 years) was drawn from the national population register of inhabitants residing in the vicinity of Turku in southwestern Finland. Medical history, clinical examination, routine biochemical tests, exercise ECG, and echocardiographic examination were used to exclude subjects with any disease known to influence the autonomic nervous system. Therefore, we excluded subjects with diabetes mellitus, coronary artery disease, congestive heart failure, previous cerebrovascular events, claudication, hemodynamically significant valvular disease, significant anemia (hemoglobin <110 g/l for men and <100 g/l for women), chronic alcoholism, antihypertensive medication, anti-ischemic agents, or other confounding medication (β -blocker eye drops, teophyllamine, β_2 -sympathomimetics, antidepressants, neuroleptics and previous or prevailing anti-neoplastic medication). From 269 subjects, 72 were excluded because of these criteria. Power spectra could not be computed reliably in 47 of the remaining subjects because of ventricular or atrial arrhythmias or technical artifacts. The final analyses included data from 150 subjects (79 women and 71 men). The study was conducted following the Second Declaration of Helsinki and was approved by the ethical committee of the Social Insurance Institution of Finland. All subjects gave their informed written consent.

Procedures

Evaluation of Psychological Factors

For the evaluation of psychological factors, three self-report questionnaires were used: a shortened 37-item version (BSI-37) of the original 53-item Brief Symptom Inventory (33), the shortened version of the Spielberger State-Trait Anger Expression Inventory (STAXI) (34), and the Toronto Alexithymia Scale (TAS-26) (35). The BSI-37, validated in a Finnish population study, does not cover psychotic symptoms (36). The total score of the BSI-37 divided by the number of items, known as general severity index, was used as an indicator of psychological distress. Symptom dimensions for somatization, depression, anxiety, hostility, and phobicity were derived from the BSI-37. The total score of the TAS-26 was used as an indicator of alexithymia. The TAS-26 consists of four factors, which describe difficulty in identifying and distinguishing between feelings and bodily sensations (Factor 1), difficulty in describing feelings (Factor 2), reduced daydreaming (Factor 3), and externally oriented thinking (Factor 4). The STAXI consists of 31 items, which reflect the intensity of feelings of anger (state anger), the disposition to experience anger (trait anger), behaviorally expressed anger (anger-out), suppressed anger (anger-in), and self-control of anger behavior (anger control).

Cardiovascular Measurements

Blood pressure and heart rate were estimated by a trained nurse and averaged over 4 duplicate measures (24). Blood pressure was recorded in seated posture with a mercury sphygmomanometer, always between 8 and 10 AM according to the guidelines of the American Society of Hypertension (37). ECG and beat-to-beat blood pressure recordings for the assessment of HRV, BPV, and BRS were carried out between 8:30 AM and 12 noon in an isolated examination room at a stable temperature between 20°C and 22°C. The subjects were requested to avoid coffee, tea, cola drinks, and smoking for 12 hours and alcoholic beverages for 24 hours before investigations. A light breakfast was allowed not later than 2 hours before these investigations.

ECG was recorded after 10-minute supine rest for 5 minutes while

subjects were resting in a supine position and breathing with a controlled frequency of 15 per minute (0.25 Hz). R-R intervals were measured from the precordial leads V_1 – V_6 of a standard 12-lead ECG. Simultaneous beat-to-beat blood pressure recording was obtained by the photoplethysmographic technique (Finapres 2300, Ohmeda, Eaglewood, CO, USA) from the middle phalanx of the left middle finger held at the heart level. The automatic servo-adjustment option of the device was disabled during the recording. The method has been found to provide an accurate estimate of BPV (38, 39). Beat-to-beat ECG and blood pressure signals were digitized and fed into a personal computer. Subjects with time series showing unstationarity, artifacts, or arrhythmias, even a single precocious beat, making it impossible to obtain a minimum of 4-minute continuous recording, were discarded from the analyses. The time series were detrended, linearly interpolated, resampled at 5 Hz, and subjected to a Parzen window. The power density spectra of HRV, systolic arterial pressure, and diastolic arterial pressure variabilities were then computed over low-frequency (0.04–0.15 Hz) and high-frequency (0.15–0.4 Hz) bands using a fast Fourier transform algorithm and triangular smoothing.

BRS was calculated by cross-spectral analysis (40, 41) between the R-R interval and systolic arterial pressure variabilities in the low-frequency band, provided that the coefficient of coherence was >0.50 and that the phase between variabilities was negative. Data of seven subjects did not meet the coherence and phase criteria but were used to calculate the power spectra of HRV, systolic arterial pressure, and diastolic arterial pressure variabilities. Spectral analyses were performed with CPRS 2.41 software (CardioPulmonary Research Software, Absolute Aliens Ay, Turku, Finland).

Statistical Analyses

Before statistical analyses, the skewed distributions of the measures of HRV, BPV, and BRS were transformed logarithmically. The summary statistics are given as mean (SD). Interrelations between psychological factors and univariate associations between psychological factors and measures of HRV, BPV, and BRS were studied with Pearson's correlation coefficients. Multivariate associations of psychological factors with the measures of HRV, BPV, and BRS were evaluated with a single linear regression analysis for each dependent variable. In this analysis, age and gender were forced to control their effects, and psychological factors were tested in a stepwise manner. Finally, heart rate and systolic and diastolic blood pressures were forced in the model to evaluate whether the possible associations of psychological factors with dependent variable result from their associations with heart rate or blood pressures. Statistical analyses were performed with SPSS 10.0 software (SPSS Inc., Chicago, IL). *p* values <0.05 were considered as statistically significant.

RESULTS

The demographic characteristics, psychological measures, and measures of HRV, BPV, and BRS of the study subjects are presented in Tables 1 and 2. Psychological measures were interrelated. Particularly, symptom dimensions of the BSI-37 were related to each other (correlation coefficients, *r*, ranging from 0.41 to 0.68). Anxiety and hostility scores of the BSI-37 correlated with anger-out (*r* = 0.24 and *r* = 0.41, respectively), state anger (*r* = 0.45 and *r* = 0.29), and trait anger (*r* = 0.37 and *r* = 0.49) scores of the STAXI. The total score of the TAS-26 correlated with the score of anxiety of the BSI-37 (*r* = 0.32).

Psychological Correlates of HRV

Increased behaviorally expressed anger (anger-out) correlated with increased low-frequency power of HRV (*r* = 0.18, *p* = 0.032). None of the psychological factors predicted HRV according to the multivariate regression analyses.

PSYCHOLOGICAL FACTORS AND AUTONOMIC ACTIVITY

TABLE 1. Characteristics and psychological measures of the study subjects

	Men (N = 71)	Women (N = 79)
Age (yr)	47.3 (7.8)	48.2 (8.1)
Systolic blood pressure (mm Hg)	123.3 (13.8)	118.1 (12.4)
Diastolic blood pressure (mm Hg)	76.7 (9.6)	74.3 (8.1)
Heart rate (beats/min)	69.3 (9.0)	71.7 (6.7)
BSI-37		
Somatization, 0–4	0.61 (0.46)	0.88 (0.64)
Depression, 0–4	0.62 (0.62)	0.72 (0.77)
Anxiety, 0–4	0.59 (0.46)	0.73 (0.51)
Hostility, 0–4	0.53 (0.38)	0.62 (0.45)
Phobicity, 0–4	0.34 (0.41)	0.35 (0.48)
General severity index, 0–4	0.63 (0.40)	0.77 (0.47)
TAS-26		
Total score, 26–130	64.8 (9.6)	60.9 (11.2)
Factor 1, 11–55	24.9 (6.0)	23.2 (7.6)
Factor 2, 7–35	18.4 (3.6)	16.6 (5.2)
Factor 3, 5–25	14.5 (4.2)	13.9 (4.3)
Factor 4, 6–30	15.1 (2.9)	14.5 (3.5)
STAXI		
State anger, 0–21	5.0 (3.3)	5.1 (4.0)
Trait anger, 0–18	5.0 (2.5)	5.4 (2.6)
Anger-out, 0–18	4.6 (2.7)	4.8 (3.1)
Anger-in, 0–18	6.3 (2.6)	6.6 (3.1)
Anger control, 0–18	11.7 (3.5)	10.7 (4.0)

Values are mean (SD). BSI-37 = shortened 37-item version of the Brief Symptom Inventory; STAXI = Spielberger State-Trait Anger Expression Inventory; TAS-26 = Toronto Alexithymia Scale.

TABLE 2. Frequency domain measures of HRV, BPV, and BRS

	Men (N = 71)*	Women (N = 79)*
LF power of HRV [(ms) ²]	400 (446)	258 (289)
HF power of HRV [(ms) ²]	357 (626)	435 (559)
LF power of SAP variability [(mm Hg) ²]	9.1 (8.2)	9.5 (9.3)
HF power of SAP variability [(mm Hg) ²]	3.0 (3.2)	2.9 (2.0)
LF power of DAP variability [(mm Hg) ²]	2.6 (1.9)	3.0 (2.2)
HF power of DAP variability [(mm Hg) ²]	0.5 (0.5)	0.5 (0.4)
BRS (ms/mm Hg)	8.3 (4.8)	7.2 (6.0)

Values are mean (SD). BRS = baroreceptor reflex sensitivity; DAP = diastolic arterial pressure; HF = high frequency; HRV = heart rate variability; LF = low frequency; SAP = systolic arterial pressure.

* BRS analyzed from 67 men and 76 women.

Psychological Correlates of BPV

Higher scores of somatization, depression, anxiety, hostility, phobicity, the general severity index of the BSI-37, and state anger of the STAXI were associated with higher low-frequency power of BPV (range of Pearson's r from 0.16 to 0.31). According to the multivariate regression analyses, increased anxiety was associated with increased low-frequency power of systolic arterial pressure variability ($p = 0.001$, model $R^2 = 0.11$) and increased hostility with increased low-frequency power of diastolic arterial pressure variability ($p < 0.001$, model $R^2 = 0.09$), independently from age, gender, and other psychological factors. Associations between

anxiety and the low-frequency power of systolic arterial pressure variability and between hostility and the low-frequency power of diastolic arterial pressure variability remained essentially unchanged after heart rate and systolic and diastolic blood pressures were added to the model (Table 3).

A higher score of somatization ($r = 0.23$) and a lower score of anger-in ($r = -0.16$) were associated with increased high-frequency power of systolic arterial pressure variability. According to the multivariate analysis, reduced anger-in ($p = 0.020$) and increased hostility ($p = 0.033$) were associated with increased high-frequency power of systolic arterial pressure variability independently from age, gender, other psychological factors, heart rate, and systolic and diastolic blood pressures. None of the psychological variables was associated with the high-frequency power of diastolic arterial pressure variability.

Psychological Correlates of BRS

Higher scores of somatization, depression, anxiety, hostility, phobicity, and the general severity index of the BSI-37 were associated with reduced BRS (range of Pearson's r from -0.19 to -0.29). According to the multivariate regression analysis, higher age ($p < 0.001$), higher anxiety ($p < 0.001$), and a lower total score of the TAS-26 ($p = 0.050$) were associated with reduced BRS independently from age, gender, and other psychological factors (model $R^2 = 0.25$). The association between a higher score of anxiety and lower BRS remained unchanged, but the association between the total score of the TAS-26 and BRS disappeared after heart rate and systolic and diastolic blood pressures were added to the model (Table 3).

DISCUSSION

Our study demonstrates that, in the middle-aged men and women of the general population, psychological factors are associated with increased BPV and reduced BRS independently of age, gender, blood pressure, and heart rate. The psychological measures correlate strongly with each other. Among them, increased anxiety and hostility seem to be the strongest determinants of increased low-frequency power of BPV and reduced BRS.

Psychological Factors and HRV

The relations of psychological factors to HRV have usually been examined in small case-control studies with patients suffering from various psychiatric disorders (8–11, 19) or in apparently healthy volunteers (12–15). Results from these studies suggest that panic disorder or increased anxiety (8, 11–14, 19) and increased hostility (15) are associated with decreased HRV, especially when measured in upright posture. Results concerning depression are inconsistent (17–19). Although reduced HRV based on 24-hour heart rate recording has been linked to depression in patients with coronary artery disease (17, 18), short-term HRV has not been found to differentiate patients with major depression from their healthy controls (19). Our findings suggest that the low-frequency and

TABLE 3. Final multivariate regression models of LF powers of BPV and BRS

	LF Power of SAP ln[(mm Hg) ²] (N = 150)	LF Power of DAP ln[(mm Hg) ²] (N = 150)	BRS ln[ms/mm Hg] (N = 143)
Age (yr)	0.13 (0.106)	-0.08 (0.364)	-0.36 (<0.001)
Gender (1 = men, 2 = women)	-0.02 (0.797)	0.05 (0.595)	-0.09 (0.233)
Anxiety	0.25 (0.002)	—	-0.27 (0.001)
Hostility	—	0.29 (0.001)	—
Heart rate (beats/min)	0.03 (0.699)	0.02 (0.836)	-0.18 (0.031)
Systolic blood pressure (mm Hg)	0.23 (0.088)	0.09 (0.626)	-0.05 (0.655)
Diastolic blood pressure (mm Hg)	-0.01 (0.963)	0.05 (0.381)	-0.14 (0.250)
Model R ²	0.16	0.11	0.34
Model <i>p</i>	<0.001	0.010	<0.001

Variable values are $\beta(p)$; β = regression coefficient corresponding standardized variable, p = significance of the variable in the model. R² = model R square; DAP = diastolic arterial pressure variability; SAP = systolic arterial pressure variability; BRS = baroreceptor reflex sensitivity; HF = high frequency; LF = low frequency.

high-frequency powers of short-term HRV under supine resting conditions do not reflect symptoms of anxiety, hostility, and depression of middle-aged healthy men and women.

Several factors may explain our negative findings in regard to the association between psychological factors and HRV. We used population-based setup and excluded subjects using antidepressants and neuroleptics known to influence on the autonomic nervous system. Thus, patients with major depression and panic disorder were not included. A population-based setup and exclusion of medicated patients with psychiatric disorders may decrease variability in the psychological measures and thereby dampen the possible associations between HRV, anxiety, hostility, and depression. We measured HRV from short-term recordings acquired under controlled laboratory conditions while subjects were resting in a supine position. However, the effects of psychological symptoms, such as hostility, on HRV may only be revealed in recordings that are sufficiently long to produce transactions between individuals and their environments (15). Posture may also modify results during short-term recordings, as persons with panic disorder or anxiety have been found to have altered HRV only in the standing position and not at supine rest (8, 9, 11, 19).

Psychological Factors and Increased BPV

Anxiety, hostility, and depression have been proposed to be associated with diminished autonomic control of the heart, which may disinhibit pathogenic BPV and thereby increase the risk of coronary artery disease (42). However, the literature of the relations of BPV and psychological factors is limited. Higher anxiety symptom scores were related with increased low-frequency power of BPV in 117 apparently healthy adults recruited from an outpatient clinic (13). In a small study with 25 unmedicated subjects, behaviorally expressed anger was associated with increased low-frequency power of systolic BPV (43). Adolescents with high systolic BPV have been found to be characterized by type A behavior and also by high levels of hostility (44).

We found that a higher score of state anger and higher symptom scores of depression, somatization, anxiety, hostil-

ity, and phobicity were related to increased low-frequency power of BPV. Anxiety and hostility were the strongest determinants of increased low-frequency powers of systolic arterial pressure and diastolic arterial pressure variabilities, and they explained BPV over age, gender, heart rate, and blood pressure. Our multivariate models explained only a small fraction of the variation in the low-frequency power of BPV. Thus, the vast majority of the short-term spontaneous variation in the low-frequency power of BPV is explained by other factors not examined in this study. Our findings of increased low-frequency power of BPV in association with increased anxiety and hostility suggest a link between psychological distress and increased sympathetic modulation. Psychological factors were not associated with the high-frequency power of diastolic arterial pressure variability, and the associations between the high-frequency power of systolic arterial pressure and anger-in or hostility were only weak. This finding is logical because the high-frequency power of BPV reflects principally rhythmic changes of intrathoracic pressure owing to respiratory mechanics (30).

Numerous population-based studies suggest a relationship between anxiety and depression and the development of coronary artery disease (45). Some prospective studies relate increased hostility to increased coronary artery disease incidence (46–50), whereas negative findings have also been reported (51, 52). Large-scale prospective studies are needed to explore whether increased low-frequency power of BPV explains increased coronary artery disease risk in association with anxiety and hostility.

Psychological Factors and Reduced BRS

We found that depression, increased anxiety, hostility, phobicity, and the general severity index of the BSI-37 were related with decreased BRS but not with HRV. Anxiety was the strongest psychological determinant of decreased BRS, independently from age, gender, the other psychological factors, heart rate, and blood pressures. Our finding of decreased BRS in association with increased psychological distress is consistent with recent studies. Watkins et al. found that de-

PSYCHOLOGICAL FACTORS AND AUTONOMIC ACTIVITY

creased BRS was associated with higher levels of anxiety in healthy volunteers (14) and in subjects with depression (10) or acute myocardial infarction (32). Furthermore, anxiety was not associated with the high-frequency power of HRV (10) or was only modestly associated with reduced respiratory sinus arrhythmia (14). Thus, our study and the previous studies (10, 14) suggest that BRS reflects more sensitively than HRV effects of psychological factors on autonomic nervous function, when the short-term measurements are made at supine rest.

Causality

Because of the cross-sectional nature of our study, we cannot draw definitive conclusions concerning the causality between psychological factors, BPV, and BRS. Previous studies have shown that parasympathetic blockade with atropine increases BPV (53). According to experimental animal studies, removal of baroreceptor control by lesions of the nucleus tractus solitarius increases blood pressure as well as blood pressure reactivity to behavioral, emotional, and environmental stimuli (54–56). Thus, decreased baroreceptor control of the heart in association with increased anxiety and hostility may reflect decreased vagal flow to the heart, which in turn may result to increased BPV through increased sympathovagal balance. Alternatively, these psychological stressors may primarily increase BPV, which in turn may lead to increased baroreceptor loading and decreased BRS. Further studies are needed to explore the mechanisms by which psychological factors are associated with decreased BRS and increased BPV.

Limitations

Effects of psychological factors on autonomic activity may depend on age (15). Thus, our findings may be limited to subjects in an age group of 35 to 64 years. A short-term recording in supine rest may lead to an underestimation of the relations between psychological factors and HRV. The confounding effects of antidepressants and neuroleptics on autonomic nervous function were controlled by excluding subjects using such medications. This procedure decreases variability in depression scores among the study subjects and may thus dampen the association between depression, HRV, BPV, and BRS.

CONCLUSION

Psychological factors, particularly increased hostility and anxiety, are related to reduced BRS and increased low-frequency power of BPV. Our findings suggest that decreased parasympathetic outflow to the heart and increased sympathetic predominance may at least partly explain increased cardiovascular morbidity and mortality in association with increased anxiety and hostility. However, further studies are needed to test this hypothesis and to explore the exact mechanisms by which psychological factors are associated with decreased BRS and increased BPV.

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