Depression Is Associated With Decreased Blood Pressure, but Antidepressant Use Increases the Risk for Hypertension

Carmilla M.M. Licht, Eco J.C. de Geus, Adrie Seldenrijk, Hein P.J. van Hout, Frans G. Zitman, Richard van Dyck, Brenda W.J.H. Penninx

Abstract—The present study compared blood pressure levels between subjects with clinical anxiety and depressive disorders with healthy controls. Cross-sectional data were obtained in a large cohort study, the Netherlands Study of Depression and Anxiety (N=2981). Participants were classified as controls (N=590) or currently or remittedly depressed or anxious subjects (N=2028), of which 1384 were not and 644 were using antidepressants. Regression analyses calculated the contributions of anxiety and depressive disorders and antidepressant use to diastolic and systolic blood pressures, after controlling for multiple covariates. Heart rate and heart rate variability measures were subsequently added to test whether effects of anxiety/depression or medication were mediated by vagal control over the heart. Higher mean diastolic blood pressure was found among the current anxious subjects (β=0.932; P=0.03), although anxiety was not significantly related to hypertension risk. Remitted and current depressed subjects had a lower mean systolic blood pressure (β=−1.74, P=0.04 and β=−2.35, P=0.004, respectively) and were significantly less likely to have isolated systolic hypertension than controls. Users of tricyclic antidepressants had higher mean systolic and diastolic blood pressures and were more likely to have hypertension stage 1 (odds ratio: 1.90; 95% CI: 0.94 to 3.84; P=0.07) and stage 2 (odds ratio: 3.19; 95% CI: 1.35 to 7.59; P=0.008). Users of noradrenergic and serotonergic working antidepressants were more likely to have hypertension stage 1. This study shows that depressive disorder is associated with low systolic blood pressure and less hypertension, whereas the use of certain antidepressants is associated with both high diastolic and systolic blood pressures and hypertension. **(*Hypertension*. 2009;53:631-638.)**

Key Words: depression ■ anxiety disorder ■ blood pressure ■ hypertension ■ autonomic nervous system ■ antidepressants

High blood pressure (BP) is an important risk factor for cardiovascular disease (CVD)[1,2] and may be more prevalent in persons with psychopathology.[3–6] This has led to the hypothesis that BP can explain part of the well-known association between psychopathology and CVD.[7] However, studies investigating the association between BP and psychopathology have not produced consistent results, particularly for the 2 major classes of psychiatric ailments, anxiety disorders and major depressive disorder. Some studies observed increased BP or hypertension among persons with depressive[8,9] and anxiety disorders,[4,10] whereas others found no association[4,11,12] or even a decreased BP in depressed or anxious patients.[10,13,14] For example, a study of Hildrum et al[13] observed a significant lower BP in persons with depressive or anxiety disorders and additionally reported that symptoms of anxiety and depression predict low BP over time.[14]

This lower BP in anxious and depressed subjects is enigmatic and contrasts with the hypothesis that BP can explain part of the well-known association between psychopathology and CVD.[7] It is also hard to reconcile with the low cardiac vagal control (CVC) observed in anxious and depressed patients,[15–17] because low BP is typically accompanied by high CVC.[18,19] A possible explanation for the current state of affairs is that antidepressant use acts to confound the relationship between psychopathology and BP. In 2 recent studies in a large cohort of 2179 depressed and anxious patients compared with 616 controls,[16,17] it was found that the association between CVC and depression and anxiety was largely driven by the use of antidepressants. Significant decreases in CVC were observed in users of tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and noradrenergic and serotonergic (NS) working antidepressants. The largest effects were seen in TCA users, who also had a significant increase in heart rate (HR), which is in line with the conclusions from a recent review on the autonomic effects of antidepressants.[20]

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From the Department of Psychiatry (C.M.M.L., E.J.C.d.G., A.S., H.P.J.v.H., R.v.D., B.W.J.H.P.), Vrije Universiteit Medical Center, EMGO Institute and Neurocampus, Amsterdam; Department of Psychiatry (F.G.Z., B.W.J.H.P.), Leiden University Medical Center, Leiden; Department of Psychiatry (B.W.J.H.P.), University Medical Center Groningen, Groningen; and Department of Biological Psychology (E.J.C.d.G.), Vrije Universiteit, Amsterdam, The Netherlands.

Correspondence to Carmilla M.M. Licht, Vrije Universiteit Medical Center, Department of Psychiatry, AJ Ernststraat 887, 1081 HL, Amsterdam, The Netherlands. E-mail C.Licht@vumc.nl

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The present study addresses the important clinical question of whether anxiety and depressive disorders are associated with BP, either by themselves or when combined with the use of antidepressant medication.

Methods

Subjects

Subjects participating in the present study came from the Netherlands Study of Depression and Anxiety, an ongoing cohort study among 2981 adult subjects (18 to 65 years) to examine the course of depressive and anxiety disorders. Methods and recruitment strategy have been described elsewhere.[21] The Netherlands Study of Depression and Anxiety sample consists of 652 persons without depressive or anxiety disorders and 2329 with a (remitted or current) diagnosis of depressive or anxiety disorder. To represent various settings and stages of psychopathology, depressed or anxious subjects were recruited in different settings: community, primary care, and mental health care organizations. Community-based subjects had been identified previously in a population-based study; primary care subjects were identified through a 3-stage screening procedure (involving the K10[22] and the short-form Composite International Diagnostic Interview by telephone) conducted among patients of 65 general practitioners, and mental health care patients were recruited when newly enrolled at 1 of the 17 participating mental health organization locations.

Subjects were assessed between September 2004 and February 2007 during a 4-hour clinic site visit in which the presence of depressive and anxiety disorders was ascertained using the lifetime version of the Composite International Diagnostic Interview psychiatric interview (World Health Organization version 2.1). The Composite International Diagnostic Interview establishes diagnoses according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* criteria[23] and has shown high interrater and test-retest reliability and high validity for depressive and anxiety disorders.[24]

To test whether main sample and BP characteristics differed between persons with and without psychopathology and using and not using medication, 3 clearly distinct groups were created for the present study. The first group consisted of 590 control subjects with no lifetime history of anxiety or depressive disorders and not using an antidepressant. The second group consisted of 1348 persons with a major depressive disorder (MDD) or an anxiety disorder diagnosis (panic, social phobia, or generalized anxiety disorder) who did not take antidepressants. The third group consisted of 644 persons with a Composite International Diagnostic Interview–confirmed MDD or anxiety disorder who did use an antidepressant (see below). The remaining 363 Netherlands Study of Depression and Anxiety subjects were excluded from the analyses: 184 patients had a CVD (self-reported diagnosis of coronary disease, cardiac arrhythmia, angina, heart failure, or myocardial infarction, confirmed with the use of cardiovascular medication) or underwent an operation for heart or coronary problems and were excluded for analyses because of the possible interfering, confounding effects of CVD; 61 subjects did not meet the group criteria (eg, persons with minor depression or controls using an antidepressant); 8 persons had missing BP data; and 112 persons had missing physiological data because of equipment failure during assessment or poor ECG quality.

For additional analyses on the importance of specific psychopathology characteristics, an indicator was created to differentiate persons with a remitted MDD or anxiety diagnosis (lifetime diagnosis not present in the last 6 months) and those with a current MDD or anxiety diagnosis (present in the last 6 months). The use of medication was determined by copying medicine names from the containers brought in by all of the participants. Frequently used medications (>50% of all days in past month) were classified using the World Health Organization Anatomic Therapeutic Chemical (ATC) classification.[25] We distinguished SSRIs (ATC code N06AB), TCAs (ATC code N06AA), and other NS working antidepressants (antidepressants classified as N06AX: selective serotonin and noradrenalin reuptake inhibitors and noradrenergic and specific serotonergic antidepressants).

Measurements

The clinic visit consisted of a blood draw, a medical examination including BP measurements, a psychiatric interview, and administration of several written questionnaires concerning, eg, mood state, lifestyle, and medical history. The study protocol was approved by the ethical review board of participating centers, and all of the participants signed informed consent.

BP and Hypertension

BP was registered by the OMRON IntelliSense Professional Digital Blood Pressure Monitor, HEM-907XL (Omron Healthcare, Inc). Systolic BP (SBP) and diastolic BP (DBP) were measured twice during supine rest on the right arm and were averaged over the 2 measurements. A correction was made for all of the individuals on hypertensive medication, which was considered as being used if subjects frequently (>50% of days in last month) used antihypertensives (ATC code C02), diuretics (ATC code C03), β-blocking agents (ATC code C07), or calcium channel blockers (ATC code C08). In accordance with earlier studies and based on the efficacy of antihypertensive drugs in randomized trials,[26,27] we added 10 mm Hg to SBP and 5 mm Hg to DBP for subjects who used antihypertensives.

In addition to these continuous SBP and DBP variables, we also created a 5-category hypertension indicator following American Heart Association guidelines[28,29] ranging from no hypertension (medication-corrected SBP <140 mm Hg and medication-corrected DBP <90 mm Hg), isolated systolic hypertension (SBP ≥140 mm Hg and DBP <90 mm Hg), isolated diastolic hypertension (SBP <140 mm Hg and DBP ≥90 mm Hg), and hypertension stage 1 (SBP ≥140 mm Hg and DBP ≥90 mm Hg) to hypertension stage 2 (SBP ≥160 mm Hg and DBP ≥100 mm Hg).

Autonomic Nervous System Function

HR was extracted from a 3-lead ECG signal that was measured using the Vrije Universiteit Ambulatory Monitoring System. The Vrije Universiteit Ambulatory Monitoring System is a lightweight ambulatory device recording the ECG and changes in thorax impedance from 6 electrodes placed at chest and back of the subjects.[30,31] CVC was assessed by HR variability in the respiratory frequency range, known as respiratory sinus arrhythmia (RSA) by peak-valley estimation, using the combined ECG and thorax impedance signals to obtain the differences between the shortest beat during inspiration and the longest beat during expiration.[32] RSA by peak-valley estimation is highly correlated with high-frequency power of the internal beat interval (IBI) time series as obtained by Fourier or Wavelet analysis, but the advantage of RSA by peak-valley estimation assessments is that these additionally consider respiration rate and, consequently, do not suffer from potential confounding by individual differences in respiratory behavior.[32,33]

Subjects were wearing the monitoring device during the clinic visit. Movement registration through vertical accelerometry was used to excise periods where subjects were nonstationary and when subjects changed interview condition. For congruency, only the RSA by peak-valley estimation and HR data recorded during the period of BP recording were used in the analyses (average registration: 9.7 minutes).

Covariates

Sociodemographics included age, sex, and education in years. In addition, various health indicators were considered as covariates, because these have been linked to both hypertension and psychopathology. Body mass index was determined as measured weight in kilograms divided by the square of the measured height in meters. Physical activity was measured using the International Physical Activity Questionnaire[34] and expressed in the multiple of one's resting metabolic rate times minutes of physical activity per week. Smoking status was categorized as nonsmoker versus smoker, and alcohol use was defined as the number of alcoholic consumptions a

Table 1. Main Sample Characteristics for Controls, Individuals With Psychopathology not Using Antidepressants, and Individuals With Psychopathology Using Antidepressants

Characteristics	Control (N=590)	Psychopathology Without Antidepressant (N=1384)	Psychopathology Using Antidepressant (N=644)	*P**
Demographics				
Age, mean±SD, y	40.4±14.6	40.6±12.9	42.0±11.3	0.03
Sex, % female	62.5	69.8	68.6	0.006
Education, mean±SD, y	12.9±3.2	12.2±3.2	11.7±3.4	<0.001
Lifestyle and health factors				
BMI, mean±SD, kg/m^2	24.9±4.5	25.2±4.7	26.1±5.7	<0.001
Physical activity, mean±SD, 1000 METmin/wk	3.9±3.1	3.8±3.0	3.4±3.2	0.009
Smoking, % yes	26.2	39.6	46.7	<0.001
Alcohol, mean±SD, No. of consumptions per day	1.0±1.3	1.0±1.5	0.9±1.5	0.03
Antihypertensives, % yes	11.4	9.0	11.2	0.15
Chronic diseases, mean±SD, n	0.98±1.0	1.26±1.2	1.29±1.3	<0.001
Antidepressant use				
TCA, % yes	0	0	10.4	<0.001
SSRI, % yes	0	0	68.6	<0.001
NS working antidepressants, % yes	0	0	21.0	<0.001
Psychopathology†				
Current MDD, % yes	0	40.7	66.9	<0.001
Remitted MDD, % yes	0	39.7	24.7	<0.001
Current anxiety disorder, % yes)	0	46.7	65.1	<0.001
Remitted anxiety disorder, % yes	0	21.8	14.4	<0.001
Autonomic nervous system activity				
HR, mean±SD, bpm	72.3±8.9	71.9±9.4	73.0±10.3	0.05
RSA, mean±SD, ms	48.9±31.2	48.0±25.3	36.6±20.4	<0.001
Blood pressure				
SBP, mean±SD, mm Hg	136.3±19.6	133.9±18.9	136.2±19.0	0.008
DBP, mean±SD, mm Hg	80.4±11.2	80.5±10.8	82.7±11.2	<0.001

MET indicates multiple of the resting metabolic rate.
*Comparison was performed using ANOVA analyses (continuous variables) and χ^2 statistics (categorical variable).
†Percentages of MDD and anxiety disorder do not add up because of comorbidity.

day. Self-reports were used for the ascertainment of the presence of chronic conditions (epilepsy, diabetes mellitus, osteoarthritis, stroke, cancer, lung disease, thyroid disease, liver disease, chronic fatigue syndrome, intestinal disorders, or ulcer).

Statistical Analyses

Data were analyzed using SPSS 15.0. Characteristics across the 3 psychopathology-medication groups (controls, MDD or anxiety disorder without medication, and MDD or anxiety disorder on medication) were compared using ANOVA and χ^2 statistics. ANOVA was conducted to compare SBP and DBP between the further divided remitted and current specific psychopathology groups. Effect sizes were calculated with Cohen's *d*, defined as the difference in the mean SBP or DBP between groups, divided by the pooled SD of these groups.

To examine whether psychopathology and antidepressant use were associated with BP, we conducted linear regression analyses with the normally distributed continuous SBP and DBP variables as outcomes. First, we entered current and remitted MDD and anxiety and antidepressant use; in 3 additional steps, we further entered the covariates, and then RSA and HR, to explore whether observed associations were because of autonomic nervous system effects. Finally, we conducted multinomial regression analyses with the clinical hypertension groups as outcome, using the group without hypertension as a reference and dichotomous variables for psychopathology and antidepressant use as interest variables, in which we also adjusted for covariates.

Results

The mean age of the study sample (N=2618) was 40.9 years (SD: 13.0), 67.9% were women, and 49.0% had <12 years of education. Table 1 shows the demographic characteristics, lifestyle and health factors, antidepressant use, psychopathology, autonomic nervous system activity measures, and mean BP according to psychopathology/medication status. Compared with controls, subjects with psychopathology were a little older, more often female, lower educated, had a higher body mass index, were less physically active, were more often smokers but drank less, and had more diseases. Of the subjects with psychopathology using medication, 67 used a TCA, 442 used an SSRI (no TCA), and 135 used an NS working antidepressant (no TCA or SSRI). There were no differences in the prevalence of antihypertensive medication

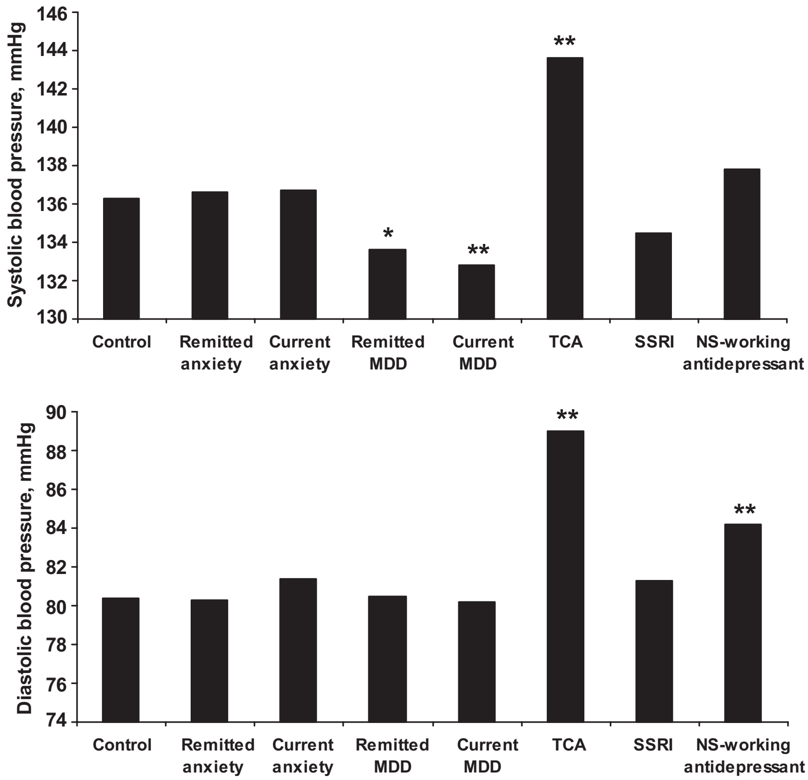

Figure. Mean systolic and diastolic blood pressure per psychopathology and medication group. *P* values are based on comparison with the control group; *$P<0.05$; **$P<0.01$.

across the 3 psychopathology/medication groups (overall prevalence: 10.1%).

The Figure presents the results of the unadjusted ANOVA analyses on SBP and DBP as a function of psychopathology and antidepressants use. Results show that SBP and DBP did not differ between subjects with anxiety disorders and controls. Subjects with MDD, however, had significantly lower SBP than controls (remitted diagnosis: $P=0.02$ and Cohen's $d=0.155$; current diagnosis: $P=0.002$ and Cohen's $d=0.184$). No depression-related differences in DBP were found. In addition, the Figure clearly shows that subjects using a TCA had a higher SBP ($P=0.003$; $d=0.388$) and DBP ($P<0.001$; $d=0.794$), and those using an NS working antidepressant had a higher DBP ($P<0.001$; $d=0.348$).

Table 2 presents the results of the linear regression analyses. The unadjusted model generally shows the same results as the ANOVA analyses reported in the Figure, with the exception that NS working antidepressants are also associated with increased SBP. Adjusting for covariates did not change the overall pattern of results, but the effects of NS working antidepressants on SBP disappeared, and a positive association between current anxiety and DBP appeared. Additional adjustment for RSA and HR removed the effect of NS working antidepressants on DBP and the effect of TCAs on SBP and greatly reduced their effects on DBP (β decreased from 5.47 to 3.06). This suggests that the effects of TCA and NS working antidepressants on BP are mediated in part by lowered CVC over HR.

Importantly, the final models show that both remitted ($\beta=-1.74$; $P=0.04$) and current ($\beta=-2.35$; $P=0.004$) MDDs remain associated with a lower SBP value even after correcting for antidepressant use, RSA, and HR. In addition, current anxiety disorder remained significantly associated with higher DBP ($\beta=0.93$; $P=0.03$). Both results remained intact in secondary analyses that excluded the subjects using antihypertensive medication.

Table 3 shows the results of the multinominal logistic regression analysis using hypertensive status as the outcome measure. Of the total sample, 36.3% (N=950) met the definition of hypertension; 15.8% had an isolated systolic hypertension, 2.7% an isolated diastolic hypertension, 13.1% a hypertension stage 1, and 4.7% a hypertension stage 2. Subjects with MDD were less often in the isolated systolic group (remitted: 14.3%; current: 13.6% versus 18.3% in controls) and less likely to have an isolated systolic hypertension (remitted: odds ratio [OR]: 0.72, 95% CI: 0.53 to 0.98, $P=0.03$; current: OR: 0.60; 95% CI: 0.44 to 0.82; $P=0.001$). Anxious subjects were not significantly more likely to have any kind of hypertension. In addition, subjects using a TCA had more often isolated diastolic hypertension (6.0%), hypertension stage 1 (20.9%), or hypertension stage 2 (13.4%) compared with nonmedicated subjects (3.1%, 12.2%, and 5.1%, respectively). TCA users were more likely to have hypertension stage 1 (OR: 1.90; 95% CI: 0.94 to 3.84; $P=0.07$) and hypertension stage 2 (OR: 3.19; 95% CI: 1.35 to 7.55; $P=0.008$). Finally, Table 3 shows that subjects using an NS working antidepressant were more likely to have hypertension stage 1 (OR: 1.72; 95% CI: 1.04 to 2.84; $P=0.03$). Leaving out subjects using antihypertensives from the analyses (remaining: N=2355) yielded very similar results.

Discussion

This large-scale cohort study showed that, when compared with healthy controls, subjects with MDD have a significantly

Table 2. Results of Regression Analyses Associating Depression, Anxiety, and Antidepressant Use With SBP and DBP

	Unadjusted			Adjusted for Lifestyle and Health Factors			Additionally Adjusted for RSA			Additionally Adjusted for HR		
Variable	B	*P*	R^2	B	*P*	R^2	B	*P*	R^2	B	*P*	R^2
SBP, mm Hg												
Model			0.011			0.304			0.306			0.316
Current MDD	−3.052	0.002		−2.452	0.003		−2.491	0.003		−2.350	0.004	
Remitted MDD	−1.842	0.06		−1.827	0.03		−1.913	0.02		−1.740	0.04	
Current anxiety disorder	−0.833	0.34		0.475	0.52		0.449	0.55		0.466	0.53	
Remitted anxiety disorder	−0.661	0.56		−0.765	0.43		−0.743	0.44		−0.730	0.45	
Use of a TCA, yes vs no	10.093	<0.001		5.388	0.008		4.845	0.02		3.173	0.12	
Use of an SSRI, yes vs no	1.136	0.29		−0.142	0.87		−0.459	0.61		−0.023	0.98	
Use of NS working antidepressant, yes vs no	3.607	0.03		1.287	0.36		0.866	0.54		0.570	0.69	
Age, per 1-y increase				0.512	<0.001		0.475	<0.001		0.535	<0.001	
Sex, female vs male				−9.567	<0.001		−9.356	<0.001		−10.256	<0.001	
Education, per 1-y increase				−0.310	0.002		−0.314	0.002		−0.285	0.005	
PA, per 1000 MET-min/wk increase				0.010	0.92		0.014	0.89		0.046	0.66	
BMI, per 1 kg/m^2 increase				0.754	<0.001		0.736	<0.001		0.685	<0.001	
Alcohol, per 1 consumption increase a day				1.470	<0.001		1.482	<0.001		1.464	<0.001	
Smoking, yes vs no				−1.654	0.02		−1.645	0.02		−1.789	0.008	
Chronic disease, per 1 disease increase				−0.216	0.44		−0.196	0.48		−0.218	0.43	
RSA, per 1 ms increase							−0.032	0.009		0.005	0.73	
HR, per 1 bpm increase										0.234	<0.001	
DBP												
Model			0.020			0.265			0.277			0.307
Current MDD	−0.541	0.33		−0.384	0.43		−0.441	0.36		−0.306	0.52	
Remitted MDD	0.258	0.65		−0.050	0.92		−0.178	0.72		−0.011	0.98	
Current anxiety disorder	0.368	0.47		0.953	0.03		0.915	0.04		0.932	0.03	
Remitted anxiety disorder	0.436	0.51		0.148	0.80		0.180	0.75		0.193	0.73	
Use of a TCA, yes vs no	8.453	<0.001		5.468	<0.001		4.666	<0.001		3.058	0.009	
Use of an SSRI, yes vs no	0.779	0.20		−0.095	0.53		−0.564	0.29		−0.144	0.78	
Use of NS working antidepressant, yes vs no	3.347	0.001		2.052	0.01		1.430	0.09		1.144	0.16	
Age, per 1-y increase				0.288	<0.001		0.234	<0.001		0.291	<0.001	
Sex, female vs male				−1.961	<0.001		−1.650	<0.001		−2.516	<0.001	
Education, per 1-y increase				−0.113	0.06		−0.118	0.05		−0.091	0.12	
PA, per 1000 MET-min/wk increase				−0.124	0.04		−0.118	0.05		−0.088	0.14	
BMI, per 1 kg/m^2 increase				0.551	<0.001		0.524	<0.001		0.476	<0.001	
Alcohol, per 1 consumption increase a day				0.722	<0.001		0.739	<0.001		0.722	<0.001	
Smoking, yes vs no				−0.324	0.42		−0.311	0.44		−0.450	0.25	
Chronic disease, per 1 disease increase				−0.172	0.30		−0.142	0.39		−0.163	0.31	
RSA, per 1 ms increase							−0.047	<0.001		−0.012	0.12	
HR, per 1 bpm increase										0.225	<0.001	

PA indicates physical activity; BMI, body mass index.

Table 3. Association of Different Stages of Hypertension With MDD and Anxiety With and Without Antidepressants Estimated With a Multinomial Logistic Regression Model

Psychopathology Variable	Isolated Systolic Hypertension*			Isolated Diastolic Hypertension†			Hypertension Stage 1‡			Hypertension Stage 2§		
	%	OR (95% CI)	*P*	%	OR (95% CI)	*P*	%	OR (95% CI)	*P*	%	OR (95% CI)	*P*
Current MDD												
No	17.1			2.7			12.6			5.1		
Yes	13.6	0.60 (0.44 to 0.82)	0.001	2.7	0.83 (0.44 to 1.55)	0.56	13.9	0.96 (0.68 to 1.35)	0.81	3.9	0.92 (0.53 to 1.60)	0.77
Remitted MDD												
No	16.4			2.7			13.3			4.1		
Yes	14.3	0.72 (0.53 to 0.98)	0.03	2.7	0.84 (0.44 to 1.58)	0.58	12.6	0.86 (0.61 to 1.22)	0.41	6.2	1.41 (0.85 to 2.33)	0.19
Current anxiety disorder												
No	15.9			2.5			13.5			4.8		
Yes	15.7	1.18 (0.90 to 1.55)	0.24	3.1	1.56 (0.87 to 2.79)	0.14	12.5	0.91 (0.67 to 1.23)	0.54	4.5	1.22 (0.76 to 1.97)	0.41
Remitted anxiety disorder												
No	16.1			2.6			13.2			4.7		
Yes	14.0	0.88 (0.61 to 1.26)	0.47	3.3	1.43 (0.70 to 2.91)	0.33	12.7	0.81 (0.55 to 1.19)	0.29	4.3	0.70 (0.38 to 1.30)	0.26
Use of a TCA												
No	15.8			2.6			12.9			4.4		
Yes	16.4	1.43 (0.68 to 3.00)	0.34	6.0	2.12 (0.69 to 6.49)	0.19	20.9	1.90 (0.94 to 3.84)	0.07	13.4	3.19 (1.35 to 7.55)	0.008
Use of an SSRI												
No	16.2			2.9			12.6			5.0		
Yes	14.2	0.94 (0.67 to 1.32)	0.71	2.0	0.57 (0.27 to 1.22)	0.15	15.7	1.23 (0.87 to 1.74)	0.25	3.1	0.59 (0.31 to 1.12)	0.10
Use of NS working AD												
No	15.8			2.8			12.7			4.6		
Yes	16.9	1.24 (0.75 to 2.07)	0.40	2.0	0.68 (0.20 to 2.28)	0.53	19.6	1.72 (1.04 to 2.84)	0.03	5.4	1.41 (0.61 to 3.23)	0.42

AD indicates antidepressant. Data were adjusted for age, sex, education, body mass index, physical activity, smoking, alcohol use, and chronic diseases.
*Isolated systolic hypertension: SBP ≥140 mm Hg and DBP <90 mm Hg.
†Isolated DBP: SBP <140 mm Hg and DBP ≥90 mm Hg.
‡Hypertension stage 1: SBP ≥140 mm Hg and DBP ≥90 mm Hg.
§Hypertension stage 2: SBP ≥160 mm Hg and DBP ≥100 mm Hg.

lower mean SBP and are less likely to have isolated systolic hypertension. Currently anxious subjects had a significantly higher mean DBP (but not SBP) compared with controls, although in our study it did not result in a significantly higher risk of (isolated diastolic) hypertension. Patients using a TCA had significantly higher SBP and DBP compared with controls and nonmedicated patients and a clearly higher risk of being clinically hypertensive (stage 1 or 2). The increase in SBP was largely accounted for by the anticholinergic effects of TCAs on vagal control over the heart. However, for DBP, the effect of TCAs remained significant even after correcting for RSA and HR, suggesting additional vascular effects of TCAs. In addition, the use of NS working antidepressants also increased DBP, and these subjects were more often diagnosed as stage 1 hypertensive. These effects, however, were fully accounted for by RSA and HR.

A review of Rutledge and Hogan[8] reported an overall increased hypertension risk among anxious subjects, which is in line with our observed elevated DBP risk in anxious individuals, although the hypertension risk did not reach significance. However, they found an increased risk for hypertension for the depressed subjects as well, where we found a decreased risk. Our results also differ from Yan et al[11] and Shinn et al,[12] who found no association between anxiety and depression with BP and hypertension risk. Our results are in line, however, with those of Paterniti et al,[10] who found high BP in anxious subjects but low BP in depressed subjects. Low BP in depressed subjects was also found by Hildrum et al.[13,14]

Several possible mechanisms for low BP in depression have been hypothesized. First, depressed subjects may more often use antihypertensive drugs and suffer from heart failure, which may both reflect in lower BP levels. However, our study did not find more antihypertensive users in the psychopathology group than in the control group, and leaving out antihypertensive users from the analyses did not change our findings. In addition, subjects with known CVD, including heart failure, were excluded from the analyses. Therefore, it is not likely that heart failure or antihypertensive use is the explanation for the low SBP found in depressive subjects in this study.

A second explanation for the observed association is that chronic low BP itself causes depression, eg, through somatic symptoms and fatigue. This possibility was addressed in recent longitudinal studies, although with inconsistent results:

some report that low BP at baseline is predictive for depressive symptoms at follow-up but not the other way around,[35] whereas others found the opposite to be true.[14]

A final explanation for the observed association does not assume causality but instead assumes a common underlying factor that independently increases the risk for depression, as well as the likelihood to maintain a low BP level. The central monoamine system may be a possible source of this common factor.[36,37] Depression and anxiety are characterized by altered levels of neuropeptide Y, an important modulator of norepinephrine signaling. The same alterations in neuropeptide Y may suppress sympathetic activity and decrease BP.[38,39] More research is needed to unravel the underlying mechanisms involved in the low BP in depressed subjects.

The higher DBP in anxious individuals could reflect a chronic state of psychological arousal in these subjects, which is typically accompanied by increased sympathetic nervous activity and decreased parasympathetic activity. At the cardiac level, the shift in sympathovagal balance leads to an increase in cardiac output; at the vascular level, the increased norepinephrinergic drive may further increase the peripheral resistance. Both effects can, in principle, explain the increase in DBP. Correcting for HR, a major indicator of cardiac output, did not remove the association between current anxiety disorder and DBP. Our analyses suggest, therefore, that anxiety mainly acts through vascular effects. The association between the use of TCA or NS working antidepressants and high BP was found earlier by several small studies.[40–43]

Because our results are based on cross-sectional data, we cannot make any assumptions on causality in these relations. Whether low BP predicts depression, whether anxiety predicts high BP or the other way around, and whether the start of antidepressant use causes high BP or finishing antidepressant use ceases the risk on hypertension remain to be studied with longitudinal analyses. In addition, we were unable to investigate whether the found associations between certain antidepressants and BP and hypertension were mediated by sympathetic control over the heart, because a measure for pure sympathetic activity was missing. These study limitations were balanced by strong points: our study sample was large and included both medicated and nonmedicated subjects with psychopathology, as well as healthy controls. We were able to study continuous BP, as well as a more clinic categorical hypertension measure, and could examine the additional contribution of CVC measures.

Perspectives

Our results provide no support for the hypothesis that the association between depression and cardiac diseases partly derives from an effect of depression on BP. Depression is associated with lower, not higher, BP. However, our results do partly support this hypothesis for the association with anxiety disorders. These findings have consequences for BP research, because it seems clearly meaningful to take the specific psychopathological status of participants into account when testing determinants of interindividual variation in BP. Our findings also have consequences for the pharmacological treatment of depressive and anxiety disorders. TCAs (and, to a lower degree, NS working antidepressants) have a detrimental effect on BP, partly through their effect on vagal control over the heart. When treating depressive or anxiety disorders, especially in patients with comorbid CVD, SSRIs may be the most likely choice. If these fail to show clinical efficacy, TCA and NS working antidepressant use should be paired to careful BP monitoring in these patients.

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Disclosures

None.

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