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Does Improving Mood in Depressed Patients Alter Factors That May Affect Cardiovascular Disease Risk?

C. Barr Taylor^{a,*}, Ansgar Conrad^{a,b}, Frank H. Wilhelm^c, Diane Strachowski^a, Anna Khaylis^a, Eric Neri^a, Janine Giese-Davis^a, Walton T Roth^{a,b}, John P. Cooke^a, Helena Kraemer^a, and David Spiegel^a

^aDepartment of Psychiatry and Behavioral Sciences, Stanford Medical Center, Stanford, California

^bDepartment of Veterans Affairs Palo Alto Health Care System, Palo Alto, CA ^cInstitute for Psychology, University of Basel, Basel, Switzerland

Abstract

To determine if improvement in mood would ameliorate autonomic dysregulation, HPA dysfunction, and typical risk factors and C-reactive protein in depressed patients with elevated cardiovascular disease risk (CVD), 48 depressed participants with elevated cardiovascular risk factors were randomized to a cognitive behavioral intervention (CBT) or a waiting list control (WLC) condition. Twenty non-depressed age and risk-matched controls were also recruited. Traditional risk factors (e.g., lipids, blood pressure) and C-reactive protein were assessed pre- and post-treatment six months later. Subjects also underwent a psychophysiological stress test while cardiovascular physiology was measured. Salivary cortisol was measured during the day and during the psychological stress test. At post-treatment, the CBT subjects were significantly less depressed than WLC subjects. There was no significant difference in change scores on any of the traditional risk factors or C-reactive protein, cortisol measures, or cardiovascular physiology, except for triglyceride levels and heart rate, which were significantly lower in treatment compared to control subjects. The normal controls exhibited no change in the variables measured during the same time. A significant improvement in mood may have little impact on most traditional or atypical risk factors, cortisol or cardiophysiology.

*Address correspondence to: C. Barr Taylor, M.D. Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Rd, Room 1316, Stanford, CA 94305-5722, USA. Tel.: (650) 725-5732; Fax: (650) 723- 9807; E-mail: btaylor@stanford.edu.

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Contributors: C. Barr Taylor oversaw all aspects of the study and wrote the final manuscript

Ansgar Conrad was responsible for psychophysiological assessment including data analysis and interpretation of data. He also was instrumental in writing the manuscript

Frank H. Wilhelm oversaw psychophysiological assessment and wrote data analyses programs

Diane Strachowski helped design and provide the intervention and helped with the manuscript preparation

Anna Khaylis provided the psychological stress testing, helped with data collection and analysis and with the manuscript preparation

Eric Neri was responsible for data analysis and helped with data interpretation Janine Giese-Davis designed and implemented the stress testing, helped with data analysis and write-up and helped obtain funding

Walton T Roth oversaw all aspects of physiological data collection and analyses

John P. Cooke oversaw the collection and interpretation of all data related to cardiovascular outcomes

Helena Kraemer provided guidance for all statistical analyses

David Spiegel helped obtain funding, manager the overall research project and helped with data analysis and write-up.

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Keywords

depression; CVD; cognitive behavioral therapy; risk factors

1. Introduction

Depression has a major impact on mortality, morbidity and functional recovery in patients with CVD (Aromaa et al., 1994; Carney et al., 2004; Frasure-Smith et al., 1995). A number of mechanisms have been proposed to explain how depression might increase CVD risk. Most recent attention has focused on HPA axis regulation, autonomic cardiovascular regulation and inflammation although other mechanisms have been proposed (Musselman et al 1998, Howren et al., 2009). In a previous study of older patients with elevated CVD risk and depression we found significantly less respiratory variation in sinus rhythm adjusted for respiratory variables (RSA_{TF}), a measure of autonomic control of the CV system, higher plasma levels of C-reactive protein and reduced levels of cortisol in response to psychological stress in depressed patients compared to a non-depressed control group (Taylor et al., 2006).

The argument for focusing on autonomic nervous system dysregulation as a possible explanation for the higher morbidity and mortality in depressed patients begins with observations that patients with greater CVD reactivity and dysregulation are at heightened risk for developing cardiovascular disease and for accelerated disease progression (Strike & Steptoe, 2003). Depression has effects on the autonomic control of the cardiovascular system. The respiratory sinus arrhythmia (RSA) is one measure of this regulation (Katona & Jih, 1975). Peripheral control of RSA is achieved mainly via the parasympathetic cholinergic vagus nerve. A high degree of RSA is observed in normal hearts with good cardiac function, whereas RSA can be significantly decreased in patients with severe CAD or heart failure (Dalack & Roose, 1990). The relative risk of sudden death after acute MI is significantly higher in patients with decreased RSA (Kleiger et al., 1987). Depression is associated with reduced RSA variability (Licht et al., 2008).

Abnormal HPA axis function may contribute to CVD risk through a variety of related risk factors, including elevated BP, high lipid levels, insulin resistance, and abdominal obesity, defined as the metabolic syndrome (Musselman et al., 1998; Brown et al., 2004). Although the conventional wisdom is that depression is associated with abnormal HPA axis function manifest as hypercortisolemia, this may only be the case in severely depressed patients, particularly those with psychotic features and melancholia. Patients with less severe depression and atypical features may show a reduced cortisol response to stress and have low or normal ambulatory measures of cortisol (Taylor et al., 2006; Gold & Chrousos., 2002; Stewart et al., 2005). For instance, in a meta-analysis of 7 studies that examined the association between depression and cortisol responses to psychological stressors. Burke et al. (2005a) found that MDD patients had blunted reactivity and impaired recovery to stress reactivity. In a study of 1100 low-income women, Burke et al. (2005b) also found that women with very high levels of depressive symptoms exhibit blunted cortisol responses to a naturalistic psychological stressor.

There is substantial evidence that inflammation plays an important role in atherogenesis (Moreno, 2004). Clinical depression is associated with marked increases in systematic inflammation as evidence by elevations in circulating concentrations of C-reactive protein and other inflammatory markers (Miller et al., 2005; Howren et al., 2009).

One way to examine the relationship between depression and potential CVD risk factors, is to determine if treating depression improves them. Changes in HPA activity have been observed

after pharmacologic treatments for depression, although generally in patients with more severe depression and the results have been inconsistent (Linkowski et al., 1987; Deusckle et al., 2003; Rota et al., 2005). These studies are complicated both by the immediate effects that antidepressants may have on the HPA axis and different HPA effects among antidepressants (Nemeroff & Owen, 2004). Other studies have examined the effects of treating depression on autonomic dysfunction. Tricyclic antidepressants tend to increase heart rate and decrease heart rate variability (HRV), presumably because of their anticholinergic side effects. Selective serotonin reuptake inhibitors (SSRIs) may also affect HRV (Bar et al 2004) but the results have been inconsistent (Carney et al., 2005). There is some evidence that the observed differences in RSA between depressed and non-depressed patients may be related to pharmacotherapy (Licht et al., 2009). To avoid medication confounds, Carney et al. (2000) examined the effects of cognitive behavioral therapy on HRV in fifty patients with stable CHD and co-morbid major depression. Heart rate was significantly lower following treatment and there was also a significant increase in a time-domain index of HRV during the daytime in the severely depressed group but not in the mildly depressed group, and there were no changes in 24-hour measures.

In summary, while some studies have examined the effects of medications on improving mood and in change in factors by which depression might increase CVD risk, little is known about the physiological effect of psychological interventions. Psychological interventions are effective treatments for depression and can avoid the multiple confounding effects of pharmacological therapies.

The purpose of this study was to determine the effects of reducing negative mood/improving depression in depressed, older patients with elevated CVD risk. Our hypotheses were that improved mood would be associated with improvement in two variables found to be different between depressed and non-depressed subjects in our previous study: cortisol dysregulation (as reflected by a hypocortisolemic response to stress testing), parasympathetic cardiovascular function (as reflected in higher RSA_{TF} activity). Our secondary analyses compared the effects of treating depression on ameliorating traditional risk factors (blood pressure, heart rate, lipids, triglycerides) and a measure of inflammation (C-reactive protein.)

2. Methods

2.1 Participants

The depressed patient sample consisted of 16 men and 32 women, aged 55 or older, at high risk for coronary artery disease. To be considered high risk, subjects needed to have a history of elevated BP and/or lipids, and to be taking medications to reduce BP and/or lipids as indicated. Subjects were excluded if they (a) currently smoked or (b) were taking any medications that might affect the HPA axis or autonomic nervous system (ANS) activity that could not be stopped during testing. Potential female subjects had to be post-menopausal or to be on stable doses of estrogen. A non-depressed sample consisted of 8 women and 12 men, matched for age and cardiovascular risk with the depressed sample. Patients and controls were recruited through advertisements and cardiovascular risk factor clinics. Most subjects (>75%) were recruited from the mass media. The study was approved by the Stanford IRB, and all subjects provided informed consent. The study was conducted from 6/1/02 through 5/31/05. The sample size (25 subjects/group at post-test) was based on having adequate power to detect an effect size of about 0.4 in the primary measures. A flowchart for subject recruitment, randomization and follow-up can be seen in Figure 1. The non-depressed control subjects were tested at baseline and again at six months. All measures were collected by research assistants blinded to the subjects randomization or depression status.

2.2 Measurements

2.2.1 Sociodemographic, Psychiatric and Medical Variables—Baseline demographics included education, ethnicity, and marital status. A structured clinical interview focusing on depression and modified to include the Hamilton Depression Interview was used (Freedland et al., 2002). All interviews and diagnoses were reviewed by a senior psychologist or psychiatrist. All subjects also completed the Beck Depression Inventory (BDI). Interviewers were blind to the participants randomization status at post-test.

A standard questionnaire assessing coronary risk factors, medications, and medical diagnoses was completed at baseline by all subjects. Subjects also underwent a physical examination by a cardiologist who reviewed and confirmed diagnoses related to CVD and CVD risk (e.g. hypercholesterolemia, hypertension.) A resting 12-lead electrocardiogram (ECG) was recorded. Subjects with significant abnormalities in their resting ECG (e.g. significant arrhythmia that would interfere with the physiological recordings) were excluded.

2.2.2 Cardiovascular Risk Factors—Baseline resting BP was measured in triplicate by auscultation using a mercury sphygmomanometer. Body weight (in kg) and height (in m) were obtained in a standing position, with shoes removed. These were used to calculate body mass index (BMI) (in kg/m²).

C-reactive protein was measured using a high-sensitivity assay (Dade, Behring, Marburg, Germany). (The final sample for the hsCRP assay was run on only 81% (35/43) of depressed subjects and 70% (14/20) control subjects because of a change to this assay method.) Fasting plasma levels of total cholesterol and triglycerides were measured using standard enzymatic procedures.

2.2.3 Cortisol—At baseline, each participant was scheduled to obtain saliva samples using cotton swabs in “salivette devices” at the time of waking, 30 minutes later, and then at 1200h, 1700h, and 2100h on each of two baseline saliva collection days. Saliva samples were obtained 10 times during the stress task. Salivary cortisols were assayed using luminescence immunoassay (LIA) reagents provided by Immuno-Biological Laboratories, Inc. Hamburg, Germany. Assay sensitivity was 0.015 microg/dl.

2.2.4 Psychological Stress Testing—A modified version of the Trier Social Stress Test (TSST) (Kirschbaum et al., 1993) was used in this study. The TSST is a standardized social and cognitive stressor composed of 5 minutes of anticipatory stress, followed by 5 minutes of public speaking (simulated job interview) and 5 minutes of mental arithmetic, both done before a panel of 2 evaluators. Subjects were sitting in a comfortable chair throughout the entire procedure.

2.2.5 Cardiovascular and Respiratory Physiology Data Recording and Analysis—Placement of electrodes/sensors, data recording, and data reduction followed conventions established for psychophysiological research and published guidelines (Wilhelm et al., 2004). A Finapres 2300 blood pressure monitor (Ohmeda, Inc., Madison, WI) obtained the continuous arterial pulse pressure waveform using the volume clamp method. Respiratory pattern data was measured using thoracic and abdominal bellows (Lafayette Instrument, Inc., Lafayette, IN) connected to pneumographic transducers (James Long Company, Inc., Caroga Lake, NY). In addition to these continuous measurements, an automatic blood pressure monitor (Dinamap 1846SX, Critikon & GE Healthcare, Chalfont St. Giles, UK) measured blood pressure with a cuff around the upper right arm. Inflation was triggered 2 minutes after onset of each test segment.

Physiological signals were analyzed and averaged for each 5-minute period using an integrated suite of biosignal analysis programs written in MATLAB (Mathworks, Inc., Natick, MA). Rate-pressure product was calculated as $HR \times SBP$. The impedance cardiogram dZ/dt -signal was ensemble averaged in alignment with the R-wave time over 5-minute periods. Characteristic points (B, Z, X) of the inverted dZ/dt signal of ensemble-averaged beats were identified automatically after exclusion of abnormal beats and edited when necessary. Pre-ejection period (PEP) (in ml) was calculated as the interval from the ECG Q-point to the ICG B-point. PEP is inversely related to left-ventricular contractility and beta-adrenergic sympathetic influences on the myocardium. Transfer function respiratory sinus arrhythmia (RSA_{TF}) was quantified by fast Fourier transform and the averaged periodogram method as the magnitude of the transfer function relating RR interval to lung volume oscillations at the prominent respiratory frequency (in ms/ml) (Wilhelm et al., 2004). Non-respiratory adjusted RSA, the high frequency (HF) power of heart period variability (in ms^2), was computed as the summed power spectral density of RR interval between 0.15-0.5 Hz for normative comparison. Similarly, spectral density of RR interval was summed over the low (LF, 0.07-0.15 Hz, in ms^2) and very low (VLF, 0.0033-0.07 Hz, in ms^2) frequency bands. HF, LF, and VLF power measurements were normalized by natural logarithmic transformation. As reported in the baseline paper, the TSST had a significant impact on HR, SBP, DBP, presystolic ejection period and cardiac output (Taylor et al., 2006). For instance, SBP increased by 32% for depressed patients and 40% for controls; HR increased by 22% and 18%. These results are comparable to what has been reported in other studies with similar populations and design (Strike & Steptoe, 2003).

2.3 Cognitive Behavior Therapy

The cognitive behavior therapy was based on the approach used in the ENRICH trial (Berkman et al., 2003) with several modifications to make it potentially more effective. First, weekly mood ratings, combined with activity and use of cognitive techniques, were used to determine activities over the ensuing week that might reduce depression. Second, telephone calls were made to patients when they were unable to attend sessions. Third, participants were provided a 50-page workbook with exercises, to be used between sessions. Participants needed to attend at least ten sessions to be considered treatment completers. All participants were instructed in the use of cognitive behavioral skills that include filling out dysfunctional thought records, overview of cognitive errors and the use of Socratic questioning in order to reframe negative thought. (For details of the effects of the intervention see Strachowski et al., 2008).

2.4 Data Analysis

For each dependent variable, a multiple regression analysis was computed with the change score as the dependent variable and the baseline score, group (CBT versus WLC) and interaction as factors in the model. Thus, the model was: $\text{Post-baseline} = c_{\text{baseline}} + c_{\text{Group}} + (c_{\text{baseline}} \times c_{\text{Group}})$, where “c” denotes centering. Centering was done to reduce collinearity (Kraemer & Blasey, 2004). The interaction term was included to avoid biased parameter estimates based on the assumption of equal slopes between groups for post-scores regressed on baseline scores. Analyses were done for completers and for intention-to-treat. TSST data was analyzed using an area under the curve analysis (AUC) (Pruessner et al., 2003). The baseline values were carried forward in case of missing post-data. A 5% two-tailed significance level was used for the primary hypotheses. A 1% two-tailed significance level was used for secondary hypotheses to reduce test-wise error.

3. Results

3.1 Participants

The depressed sample was primarily Caucasian (see Table 1). There were no differences in the demographic variables between the CBT and WLC groups. The demographics of the non-depressed control group are provided for purposes of comparison. For the 22 WLC subjects present at both baseline and post, 37% were on lipid lowering agents, 46% on antihypertensive medications, 14% on glucose altering medications and 23% on none of these agents. At post there was a net change in one less subject taking lipid lowering medication and one less taking an antihypertensive agent. For the 21 CBT subjects, at baseline, 19% were on lipid lowering agents 57% on antihypertensive medications, none were taking glucose altering meds and 14% were on none of these agents. At post test, 3 more subjects had started on lipid lowering medications and one on antihypertensive medications. For the non-depressed controls, 35% were on lipid lowering agents at baseline, 65% were on antihypertensive medications and 23% were on none of these. Thirty-six percent of WLC patients were on antidepressants at the beginning as were 43% of CBT patients. There was a net change of 2 patients starting antidepressants in the WLC group and no net change in the CBT group.

3.2 CBT Treatment Effects

Attendance of the CBT sessions was extremely high, dropping below 90% for only one week. All subjects completed therapy based on our criteria (>10 sessions attended); the mean number of sessions was 15.1 (range: 12-16). Nine sessions in total were conducted by telephone. The therapy was extremely effective (Strachoswki et al 2008). Scores on the Hamilton Depression Inventory and the Beck Depression Inventory were significantly reduced in the CBT group compared to the WLC group, post-treatment (see Table 2). With missing subjects considered non-responders, 57% (13/23) of subjects in the CBT treatment were considered to be in remission compared to only 4% (1/25) in the WLC group (Chi square [df=1]=9.0, $p=0.003$).

3.3 Cortisol

As seen in Table 3, there were no significant differences in waking, waking plus 30 minutes or daytime cortisol slopes between CBT or WLC with either the completer or intention-to-treat analyses.

3.4 Typical and CVD Risk Factors and C-reactive protein

On the basis of completer analyses there were no differences in atypical risk factors pre- and post-treatment. There was a significant reduction in triglyceride levels in the CBT compared to WLC group ($F = 7.9$, $p = .01$, $ES = 0.69$) and in heart rate ($F = 10.0$, $p = .003$, $ES = 0.32$). With the intention-to-treat analyses, there was also a significant reduction in triglycerides in the CBT group compared to the WLC group ($F = 5.4$, $p = .02$) and also in heart rate ($F = 6.7$, $p = 0.01$). There was no significant differences in C-reactive protein levels.

3.5 Psychological Stress Test Variables

There was no significant difference in change scores in any of the stress test data, by completer analysis or by intention-to-treat. Cortisol levels remained low for both CBT and WLC groups.

3.6 Non-depressed control group

As an exploratory analysis we compared pre and post differences between the combined CBT and WLC groups and the non-depressed group (NTC) on the variables that had been shown to be significantly different at baseline (Taylor et al., 2006). Differences between the two groups (depressed and controls combined and NTC) remained very similar at post with control subjects

having higher AUC RSA_{TF} and lower AUC cortisol on the TSST and lower C-reactive protein levels compared to the combined CBT and WLC subjects.

4. Discussion

Contrary to our hypotheses, there were no changes in the primary outcome variables, RSA_{TF}, and cortisol response during stress testing following a significant and robust improvement in mood produced by cognitive-behavioral therapy. However, there was a significant reduction in triglycerides and the triglyceride/HDL index in both the completer and intention-to-treat analyses. There was also a significant reduction in heart rate, in the treatment compared to no-treatment group. The magnitude of differences in the three variables, AUC RSA_{TF}, AUC cortisol and C-reactive protein found to be significantly different at baseline (Taylor et al., 2006) between non-depressed and depressed subjects were similar at pre and post test.

The examination of our primary hypotheses required a significant improvement in depression. Fortunately, the therapy was effective, both in the continuous measures (with effect sizes of the Hamilton of 1.8 and on the BDI of 0.85) and in percent of subjects improved: 57% in treatment compared to 4% in the wait-list control. The percentage of subjects in remission is similar to that found in other studies of CBT and comparable to the effect sizes of most pharmacological interventions (Gloaguen et al., 1998; DeRubeis et al., 2005).

To the extent that depression might cause changes in RSA_{TF} (and other heart rate variability measures) improvement in depression would be expected to be associated with improvement in these variables. In fact, Carney et al., (2000) did find improvement in HRV following CBT, although the study was uncontrolled, the findings were only significant during the day, and HRV was not adjusted for respiratory confounds. Our data also suggests that changing HPA activity through psychological interventions may be difficult.

The overall lack of change in the primary biological and physiological variables, and the sustained difference between WLC or CBT and normal controls at post suggests that these variables are quite stable and not amenable to change through psychological intervention or affected by change in mood, at least in the short run. The reasons for the persistence of a difference in the physiological differences, despite the improvement in mood, remains to be determined. In the ENRICH trial (Berkman et al., 2003), which had short-term CBT/no-treatment effects similar to those reported here, there were no differences in CVD morbidity and mortality, although this was confounded by continued improvement in the non-treatment control group. Alternatively, it may be that there is an unknown third factor leading to both depression and biological changes, with no direct causal link between depression and the physiological changes. In that case, changing the third factor would produce concomitant changes in depression and physiology.

The nature of this design adds important information on the possible impaired cortisol response to stress in depressed individuals. As cortisol is important to reduce cytokine response to stress, a lower level of cortisol might increase risk (Miller et al., 2005). To the extent that a normal cortisol response is necessary to reduce proinflammatory response to acute stress (Dhabhar et al., 1996), and the cortisol response remained suppressed, it would not be surprising to see no change in C-reactive protein levels, a non-specific measure of inflammation.

The large change in triglycerides was unexpected. The triglyceride/HDL ratio is significantly related to the metabolic syndrome (e.g. McLaughlin et al., 2003), which, in turn, is related to elevated CVD depending on population and criteria. However, these results need to be interpreted with caution as this was an exploratory analysis. We do not have measures of patients' diets but they were not explicitly encouraged to change diet or to lose weight. The

spearman correlation between changes in BMI and changes in triglycerides was not significant, suggesting that changes in BMI do not account for reduction in triglycerides. We also do not measure alcohol intake or have measures of serum glucose, both of which can affect TG levels. The observation of the change in triglycerides with improved mood finding to be replicated in larger samples, followed for longer time with more thorough measures of metabolic risk.

The changes in heart rate were very close to those reported by Carney et al. (2000) who found a difference of about 5 bpm in his study, compared to the change of 6.5 in this one. However, the WLC also had a reduction of 3.8 bpm and had a lower baseline heart rate. While the change in HR between the two groups may reflect a reduction in sympathetic tone, there were no significant changes in other psychophysiological variables affected by sympathetic tone. Thus, this finding needs to be confirmed in a larger sample.

There are a number of limitations of the study. The sample size was small, and there were relatively few men. Changes were examined only over a six-month period. Detailed measures of diet and exercise would have been helpful. Kraemer et al. (2001) have noted that the term “risk factor” is often used imprecisely, sometimes referring to a factor that increases the probability of an outcome or being associated (correlated) with the outcome or both being associated with the outcome and preceding it. It is often assumed that the risk factor is causally related to the outcome but this can only be shown by demonstrating that a change in the risk factor changes the outcome.

In summary, with the exception of changes in triglycerides and heart rate, there were no significant changes with improved mood on a number of other biological and physiological variables measured. Clinicians must ensure that typical and atypical cardiovascular risk factors are adequately treated with lifestyle and pharmacologic therapy, as appropriate. The changes in triglycerides, which may reflect improvement in the metabolic syndrome, are intriguing need to be confirmed in larger samples whose metabolic syndrome status is better characterized. Finally the intervention proved very robust and was extremely well received by the participants.

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Figure 1.

Table 1
Demographics of Participants Randomly Assigned to Treatment Groups

Variable ^a	CBT (n=23)	WLC (n=25)	Control group (n = 20)
Age in years			
M	62.4	62.1	62.5
SD	7.1	5.7	6.0
Years of education (%)			
Trade school	4	0	5
Some college	17	16	15
Bachelor's degree	4	28	45
Some Graduate	13	12	10
School	39	36	20
MS, Ph.D., M.D., and/or J.D.	22	8	5
Gender (%) Men	39	28	60
Ethnicity (%) White	91	100	80
Married Status (%)			
Single	9	8	10
Married	48	60	60
Separated	4	0	5
Divorced	35	20	10
Widowed	4	0	10
Separated/Widowed	0	0	5
Domestic partner	0	0	0
Employment Status (%)			
Full-time	61	68	65
Part-time	13	4	20
Not employed/retired	26	28	15

Table 2

Change in depression and risk and other factors, pre- to post-treatment for the CBT and WLC groups (completer sample)

Variable	CBT				WLC				F	P		
	N	Pre	SD	Post	N	Pre	SD	Post				
HRSD	19	18.3	6.4	5.1	4.2	22	18.4	5.3	15.5	6.0	52.8	<.0001
BDI	19	25.3	8.4	9.8	6.5	21	26.4	10.1	18.2	7.0	17.1	<.001
SBP (mmHG)	20	127.2	16.0	121.8	14.4	21	120.8	19.6	120.7	22.6	0.6	0.45
DBP (mmHG)	20	74.8	10.7	72.7	11.9	21	68.1	13.3	69.8	11.0	0.04	0.83
HR (bpm)	20	72.7	14.8	66.2	7.2	21	77.8	11.8	75.0	9.2	10.0	0.003
Total Cholesterol (mg/dL)	21	209.2	51.0	210.2	38.3	22	226.1	56.5	223.0	53.1	0.01	0.94
LDL (mg/dL)	20	131.9	43.1	128.9	25.3	20	138.8	44.9	138.1	47.6	0.4	0.55
HDL (mg/dL)	21	63.0	33.9	61.6	22.0	22	59.0	17.1	59.4	16.2	0.004	0.95
Triglycerides (mg/dL)	21	139.2	73.5	108.6	52.0	22	141.4	71.4	138.4	72.1	7.9	0.01
Trigly/HDL ratio	21	2.6	1.8	2.0	1.3	22	2.7	2.0	2.7	2.0	5.6	0.02
BMI (kg/m ²)	17	27.1	3.5	27.0	3.8	20	30.6	7.1	30.9	7.4	0.5	0.48
C-reactive protein (mg/L)	21	1.8	2.3	2.5	3.0	21	2.4	2.3	3.9	7.1	0.4	0.54

CBT = cognitive behavior therapy; WLC = wait list control; HRSD = Hamilton Rating Scale for Depression; BDI = Beck depression inventory.

Table 3
Change in cortisol variables, pre- to post-treatment for the CBT and WLC groups (completer sample)

Variable	CBT			WLC		
	N	Pre	Post	N	Pre	Post
Log 2-day cortisol slope	21	-0.2	0.1	0.1	0.1	0.2
Waking cortisol	21	-0.7	1.0	-0.7	0.7	2.2
Cortisol rise after waking	21	0.3	0.5	0.3	0.5	1.0

CBT = cognitive behavior therapy; WLC = wait list control

Table 4

Change in Trier Social Stress Test variables, pre- to post-treatment for the CBT and WLC groups (completer sample)

Variable	CBT				WLC				F	p	
	n	Pre	SD	Post	n	Pre	SD	Post			
AUC RSA _{TF}	140	0.25	0.15	0.29	0.14	200	0.21	0.14	0.26	0.02	0.90
AUC PPP	164	438.4	119.1	425.1	103.7	214.0	72.1	420.7	136.6	424.6	116.5
AUC LogHF	141	19.9	3.9	21.2	4.8	201	18.8	5.3	19.4	6.2	0.4
AUC LogVLF	152	5.1	4.3	26.8	2.6	202	3.4	4.5	24.4	4.3	2.0
AUC Cort	194	2.1	1.1	2.1	0.8	211	2.2	0.7	2.4	1.0	0.3

CBT = cognitive behavior therapy; WLC = wait list control; AUC = area under the curve; RSA_{TF} = respiratory sinus arrhythmia, transformed for respiratory variables; PEP = Presystolic ejection period

Table 5

Pre and post-test means in selected variables for the CBT and WLC (combined) and non-depressed groups

Variable	Depressed (n=42*)		Controls (n=16*)	
	Mean	SD	Mean	SD
AUCRSA _{TF}	Pre 0.23	0.14	0.33	0.27
	Post 0.27	0.22	0.42	0.23
AUC _{Cortisol}	Pre -2.13	0.89	-1.26	0.92
	Post -2.25	0.88	-1.42	0.89
C-reactive protein	Pre 2.10	2.28	0.74	0.65
	Post 3.16	5.42	1.48	1.38

CBT = cognitive behavior therapy; WLC = wait list control; AUC = area under the curve; RSA_{TF} = respiratory sinus arrhythmia, transformed for respiratory variables