NEGATIVE AFFECTIVITY: A MODEL OF UNDERSTANDING PSYCHOSOCIAL RISK FOR IMPAIRMENT IN CARDIAC AUTONOMIC FUNCTION

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The dispositional tendency to experience negative emotions may underlie correlated psychological risk factors for coronary heart disease (CHD). Here, we examined the relative contribution of variance shared by depression, anxiety, and anger (i.e. negative affect) and the variance unique to each negative affective disposition in predicting cardiac autonomic function as indexed by heart rate variability (HRV). The sample included 653 community volunteers (51.0% female; 15.8% Black) ages 30-54 (M= 43.8 $\pm$ 7.1). Latent constructs of depression, anxiety, and anger were each measured by three scales from well-validated self-report questionnaires. Indices of HRV were derived from a 5-minute segment of continuous ECG recording and included high frequency (HF-HRV), low frequency (LF-HRV), and the ratio of LF to HF (LF:HF-HRV) power components. Factor analysis/multiple regression and structural equation modeling analyses were employed with covariate-adjustment for age, sex, race, education, BMI, smoking status, SBP, and DBP. At the single-trait level of analysis, examination of depression, anxiety, and anger individually showed depression to predict reduced HF-HRV and LF-HRV and increased LF:HF-HRV, anxiety to predict reduced HF-HRV and LF-HRV, and anger to be unrelated to any HRV index. However, a more complex pattern of relations emerged when the common (i.e. negative affect) and unique effects of depression, anxiety, and anger on HRV were evaluated simultaneously. First, the relation of depression to HRV indices was partially accounted for by negative affect, though variance unique to depression also predicted

HF-HRV independently. Secondly, the relation of anxiety to HRV indices was fully accounted for by negative affect. Thirdly, anger emerged as an independent predictor of *increased* HF-HRV, suggesting the variance that anger shares with depression and anxiety predicts reduced HF-HRV and the variance that is unique to anger predicts increased HF-HRV. In sum, negative affect explains the common effects of psychosocial risk factors for CHD on cardiac autonomic function with unique aspects of depression and anger related independently to reduced and increased vagal modulation of heart rate, respectively. These findings underscore the importance of examining multiple negative affective dispositions in the same analysis to differentiate the elements of these traits that are specifically cardiotoxic.

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PREFACE

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1.0 INTRODUCTION

1.1 Overview

Diagnostic categories of mood and anxiety-related disorders (e.g. major depressive disorder [MDD], generalized anxiety disorder [GAD]), as well as self-reported symptoms of depression, anxiety, and anger have been shown to co-occur in both psychiatric and non-clinical samples (e.g. Blumberg & Hokanson, 1983; Gotlib & Robinson, 1982; Merikangas, et al., 1996; Mineka, Watson, & Clark, 1998; Newman, Gray, & Fuqua, 1999; Thomas & Atakan, 1993). This observation has led investigators to postulate that discrete classifications of psychiatric disorders and normative variation in psychiatric symptomatology may reflect an underlying diathesis or dispositional tendency to experience negative emotions (e.g. Krueger, Caspi, Moffit, Silva, & McGee, 1996; Trull & Sher, 1994). In fact, structural data analyses (e.g. confirmatory factor analysis) show a single latent factor to account for a substantial portion of variance common to these mood, anxiety, and anger-related facets of both psychiatric disorders and personality traits, variably but interchangeably termed "neuroticism", "negative emotionality", and "negative affect" (e.g. Watson, Clark, & Carey, 1988; Watson, Clark, & Tellegen, 1984). In epidemiological studies, these same mood and anxiety-related diagnostic categories and self-reported symptoms (i.e. depression, anxiety, and anger), collectively labeled "psychosocial risk factors", have been shown to predict incident cardiac events in healthy and patient populations (e.g. Anda et al., 1993; Barefoot & Schroll, 1996; Frasure-Smith, Lesperance, & Talajic, 1995; Hearn, Murray, & Luepker, 1989; Kawachi et al., 1994; Koskenvuo et al., 1988). In parallel, it may be postulated that these psychosocial risk factors for coronary heart disease (CHD) also reflect a common underlying component of trait negative affect. Thus, competing, yet largely untested, hypotheses may suggest that psychosocial factors confer risk for CHD through (1)

variance unique to an individual factor (e.g. depression), (2) variance common across psychosocial factors (e.g. negative affect), or (3) a combination of both unique and shared variation (e.g. depression and negative affect).

One pathway by which psychosocial factors are related to risk for CHD is the autonomic nervous system (ANS). Because the ANS, through its sympathetic (SNS) and parasympathetic (PNS) branches, modulates heart rate (HR), this system figures prominently among numerous physiological correlates of depression, anxiety, and anger. One noninvasive method of measuring autonomic nervous system control of HR is "heart rate variability" (HRV). HRV refers to the beat-to-beat variation in HR derived from electrocardiographic (ECG) recordings over a specific interval of time. Alterations in HRV (e.g. decrements in vagal activation) have been related to cardiac mortality in normal populations, prognosis among survivors of acute myocardial infarction (MI), and extent of atherosclerosis in patients with coronary artery disease (CAD) (e.g. Bigger, Fleiss, Rolnitzky, & Steinman, 1993; Hayano et al., 1990; Liao et al., 1997). Evidence also shows depression, anxiety, and anger to be correlated with HRV indices (e.g. Carney, Saunders, Freedland, Stein, Rich, & Jaffe, 1995; Cohen, Kotler, Matar, Kaplan, Miodownik, & Cassuto, 1997; Sloan et al., 1994) though the precise nature and relative strength of association between each psychosocial dimension and HRV is not well understood. Few studies have included multiple psychosocial factors in the same analysis to determine whether depression, anxiety, and anger are related to HRV independently of one another, or rather that variance shared across factors (i.e. negative affect) accounts for the observed associations.

The purpose of the study proposed herein is to assess psychosocial risk factors for CHD (depression, anxiety, anger), as well as the variance that these factors may share (negative affect), in relation to autonomic modulation of HR as measured by indices of HRV in a community-based sample of men and women. Using a combined data analytical approach with factor analysis/multiple regression and structural equation modeling (SEM), we evaluated a

series of models designed to test the proposed hypotheses. First, the relationship of each psychosocial factor (depression, anxiety, anger) to HRV was assessed in three separate models in which each psychosocial factor was examined as an individual predictor of HRV. Next, the relative significance of individual psychosocial factors in predicting HRV was assessed in a model in which all three psychosocial factors are evaluated simultaneously. Negative affect was then added to this model to test the proposed hypothesis that negative affect (as a dimension common to all psychosocial factors) may better account for any observed relationships between these factors and HRV. Finally, to determine whether any psychosocial factor may predict HRV in addition to the variance accounted for by negative affect, a model in which both direct pathways between the psychosocial factors and HRV and the indirect pathway by which negative affect may mediate the effects of individual psychosocial factors on HRV, was evaluated. In sum, models were compared to test (1) the relative significance of individual psychosocial factors in predicting HRV (model of unique variance), (2) the possibility that psychosocial factors are related to HRV by a common underlying dimension of negative affect (model of common variance), and finally (3) whether any psychosocial factor may predict HRV in addition to the variance accounted for by negative affect (model of unique and common variance).

1.2 Common dimension of negative affect

1.2.1 Psychiatric comorbidity.

In the psychiatric literature, it is well established that mental disorders commonly co-occur (e.g. Clark, Watson, & Reynolds, 1995; Kendall & Clarkin, 1992; Kessler, 1997), particularly among mood and anxiety diagnoses (e.g. Maser & Cloninger, 1990; Merikangas et al., 1996; Mineka, Watson, & Clark, 1998). For example, 72% of individuals who meet criteria for Major Depressive Disorder (MDD) in their lifetime, also meet criteria for at least one other disorder (Kessler et al., 2003), with more than half (range 51%-59%) meeting criteria for an anxiety

disorder specifically (Clark, 1989; Kessler et al., 2003). Among patients with anxiety disorders, rates of a secondary mood disorder diagnosis (i.e. MDD, dysthymia) are also high (50% on average), but have been shown to range considerably (20%-73%) due to increased heterogeneity in anxiety disorder classifications (Clark, 1989; Dealy, Ishiki, Avery, Wilson, & Dunner, 1982; Roth, Gurney, Garside, & Kerr, 1972). Although "anger" is not exclusively represented in any one diagnostic category within the DSM-IV (American Psychiatric Association, 1994), angry symptomatology, measured categorically (e.g. presence of anger attacks) and dimensionally (e.g. self-reported trait anger), has been documented in both mood and anxiety disorders. In Sayar et al. (2000), approximately 50% of MDD patients reported anger attacks; symptoms of depression and anxiety were greater among these patients than in patients without anger attacks. Moreover, anger attacks and self-reported anger symptoms among several other psychiatric patient groups (e.g. alcohol use, binge eating disorder), have been shown to predict the presence of a mood or anxiety disorder and to correlate significantly with depressive and anxious symptoms (e.g. Fassino, Leombruni, Piero, Abbate-Daga, & Rovera, 2003; Mammen, et al., 1999; Moreno, Selby, Fuhriman, & Laver, 1994; Tivis, Parsons, & Nixon, 1998; Troisi & D'Argenio, 2004). Importantly, self-reported symptoms of depression, anxiety, and anger have also been shown to covary in non-clinical samples (Blumberg & Hokanson, 1983; Gotlib & Robinson, 1982; Newman, Gray, & Fuqua, 1999; Thomas & Atakan, 1993).

1.2.2 Psychopathology and personality traits.

The relation of diagnostic classifications of psychiatric illness to trait dimensions of personality, including psychiatric symptoms of depression, anxiety, and anger (e.g. neuroticism, trait anxiety), has been the focus of much research. Interestingly, it has been hypothesized that features of psychopathology and personality may not describe distinct phenomena but rather reflect common variation along a continuum of increasing symptom severity (e.g. Krueger,

1999). In Trull and Sher (1994), the presence of an MDD or anxiety disorder diagnosis was related to higher Neuroticism and lower Extraversion scores on the NEO-PI (Costa & McCrae, 1985). Similar findings were reported in a longitudinal investigation of adolescents in which the Negative Emotionality factor from the Multidimensional Personality Questionnaire (MPQ) (Tellegen, 1982) predicted mood and anxiety disorders over a 3-year period (age 21), after controlling for psychiatric disorders at the initial assessment (age 18) (Krueger, 1999; Krueger, Caspi, Moffit, Silva, & McGee, 1996). In sum, cross-sectional and prospective evidence indicates dimensional variability in personality traits is related to diagnostic categories of psychiatric illness, with some evidence suggesting that personality traits (e.g. elevated neuroticism) predispose one to psychopathology and that these same traits persist after psychiatric symptoms remit (e.g. Clark et al., 1994; Hirschfeld et al., 1983; Krueger et al., 1996; Trull & Sher, 1992).

1.2.3 Negative affect.

A variety of terms have been used to describe the variance that is common to personality tendencies toward negative emotions and mood and anxiety-related psychiatric disorders, including "neuroticism", "negative emotionality", and "negative affect". These terms are largely interchangeable as all refer to individual differences in the tendency to experience emotional distress, including specific states of fear, sadness, anger, guilt, contempt, and disgust (Tellegen, 1985; Watson & Clark, 1997; Watson & Tellegen, 1985). From structural data analyses (e.g. confirmatory factor analysis), a single dimension reflecting negative affect has emerged repeatedly, accounting for a sizable portion of variance common to numerous measures of personality traits and psychiatric symptoms/diagnoses (Krueger, 1999; Watson, 1988; Watson, Clark, & Tellegen, 1984). Moreover, evidence suggests this factor may reflect a higher order dimension under which sub-classifications of negative affect may be made (e.g. "anxious

misery") (Diener, Smith, & Fujita, 1995; Krueger et al., 1998; Watson & Clark, 1992a, 1992b). In this regard, several integrated models have been proposed in which a nonspecific factor of negative affect is identified in conjunction with separate factors reflecting variance unique to mood and anxiety disorder diagnoses (Barlow, Chorpita, & Turovsky, 1996; Chorpita, Albano, & Barlow, 1997; Clark & Watson, 1991). Notably, a comprehensive model with considerable empirical support has been posited in which negative affect reflects a higher order factor (i.e. variance common to all psychiatric diagnoses) and *each* psychiatric disorder a second order factor (i.e. variance unique to that disorder alone) (Brown, Chorpita, & Barlow, 1998; Mineka, Watson, & Clark, 1998; Zinbarg & Barlow, 1996). Finally, findings from the behavioral genetics literature further substantiate that personality tendencies to experience negative emotions, as well as mood and anxiety-related psychiatric disorders, may share a common underlying dimension of trait negative affect as all have been shown to share common genetic variance, including measures of neuroticism specifically (Kendler, 1996; Kendler, Heath, Martin, & Eaves, 1987; Kendler, Neale, Kessler, Heath, & Eaves, 1992; Kendler, Neale, Kessler, Heath, & Eaves, 1993a; Kendler, Neale, Kessler, Heath, & Eaves, 1993b; Jardine, Martin, & Henderson, 1984; Roy, Neale, Pedersen, Mathe, & Kendler, 1995).

1.3 Psychosocial risk factors for CHD

As described above, psychiatric disorders and self-reported psychiatric symptomatology, assessed in both clinical and non-clinical samples, share considerable variance, including a common genetic component (e.g. Kendler et al., 1996; Krueger, 1999; Watson, Clark, & Tellegen, 1984). Because these measures are largely identical to categorical and continuously measured dimensions labeled "psychosocial factors" in the epidemiological literature, this term will be used throughout the remainder of this thesis. To be clear, however, we use "psychosocial factors" in reference to only to those factors reflecting dispositional biases to experience negative

emotions (i.e. depression, anxiety, anger), rather than constructs that may be related but not integral conceptually to our interest in the role of negative emotionality in CHD (e.g. social support, job stress, socioeconomic status).

1.3.1 Depression.

Several population-based investigations have shown depression, including diagnoses of major and minor depressive disorder and depressive symptomatology, to predict incident myocardial infarction (MI), as well as cardiac-specific and all-cause mortality (Anda et al., 1993; Aromaa et al., 1994; Barefoot & Schroll, 1996; Ford et al., 1998; Penninx et al., 2001; Pratt et al., 1996; Wasserthal-Smoller et al., 1996). Depression has also been shown to predict coronary events among patients with documented myocardial infarction (MI), coronary artery disease (CAD), and cardiac arrhythmias (Barefoot, Helms, & Mark, 1996; Carney et al., 1988; Frasure-Smith, Lesperance, Talajic, & Bourassa, 1995; Kennedy, Hofer, Choen, Shindledecker, & Fisher, 1987). Importantly, results across studies show depression to confer risk for CHD independently of common confounding variables (e.g. socioeconomic status, smoking, alcohol, blood pressure, body mass index) and that the severity of depression relates to risk for coronary events in a graded fashion.

1.3.2 Anxiety.

Evidence suggests that anxiety may similarly predict incident coronary events among initially healthy individuals. Study findings vary, however, according to the type of anxiety measured, as well as the specific coronary outcome under investigation. For example, anxiety symptoms, including *phobic* anxiety, have been shown to predict coronary death, as well as sudden death specifically, but not nonfatal MI or angina (Kawachi et al., 1994; Kawachi, Sparrow, Vokonas, & Weiss, 1994; Haines, Imeson, & Meade, 1987). Notably, results from two other prospective

studies, however, show increased risk for MI among panic disorder patients and subjects who endorse tendencies to worry (Kubzansky et al., 1997; Weissman, Markowitz, Ouellete, Greenwald, & Kahn, 1990), suggesting that the type of anxiety under investigation may partially account for differential associations with CHD endpoints. Among post MI patients, those with greater anxiety had more in-hospital complications, including reinfarction, new onset ischemia, ventricular fibrillation, sustained ventricular tachycardia, and in-hospital death, compared to patients with lower levels of anxiety (Moser & Dracup, 1996).

1.3.3 Anger/Hostility.

Among initially healthy individuals, studies have shown baseline measures of hostility, as well as anger, to predict incident coronary events and mortality (Barefoot, Dahlstrom, & Williams, 1983; Barefoot, Larson, Lieth, & Chroll, 1995; Kawachi, Sparrow, Spiro, Vokonas, & Weiss, 1996; Shekelle, Gale, Ostfeld, & Paul, 1983), though null findings have also been reported (Everson et al., 1997; Hearn, Murray, & Luepker, 1989; Leon, Finn, Murray, & Bailey, 1988; Maruta et al., 1993; McCranie, Watkins, Brandsma, & Sisson, 1986). Among CAD patients, the hostility component of the Type A behavior pattern predicted incident coronary events and coronary death among cases (Type A) compared to controls (Dembroski, MacDougall, Costa, & Grandits, 1989; Hecker, Chesney, Blacks, & Frautschi, 1988; Dembroski et al. 1989). Also among CAD patients, measures of both hostility and anger predicted incident coronary events, as well as the progression of CAD (Angerer et al., 2000; Koskenvuo et al., 1988; Mendes de Leon, Kop, de Swart, Far, & Appels, 1996).

1.3.4 Multiple psychosocial risk factors.

Several studies have examined depression, anxiety, and anger, as well as related psychosocial factors (e.g. Type A behavior pattern, and self-reported tendencies toward irritability or

particular styles of emotional expression [anger expressed outwardly]) in the same analysis in an effort to differentiate the roles that each may play in conferring risk for incident coronary disease in healthy individuals. For example, anxiety and anger, as well as depression-related (i.e. loneliness) and anxiety-related (i.e. tension) constructs, were evaluated in association with 20-year incident MI and coronary death in women; among these factors, anxiety, loneliness, and tension (in homemakers), and tension (in working women) predicted CHD events (Eaker et al., 1992). In contrast, Haynes et al. (1980) reported Type A behavior and suppressed hostility (defined as an unwillingness to show or discuss anger), but *not* anxiety, to predict CHD events in a population-based sample of both men and women.

Concurrent examination of these same psychosocial factors has been conducted in relation to coronary outcomes among individuals with prevalent CHD. For example, depression predicted cardiac-specific and all-cause mortality 10 years following first MI; psychosocial factors unrelated to mortality included anxiety, anger-in, irritability, and Type A behavior (Welin, Lappas, & Wilhelmsen, 2000). In contrast, Strik, Denollet, Lousberg, & Honig (2003) reported only anxiety to predict cardiac events (fatal MI, nonfatal MI, cardiac re-hospitalization, frequent visits to the outpatient clinic) when depression, anxiety, and hostility were examined in multivariate analysis. Furthermore, in Frasure-Smith et al. (1995), *both* depression and anxiety predicted incident cardiac events (unstable angina admission, fatal, and nonfatal MI) among numerous psychosocial factors including styles of anger expression (i.e. anger-in, anger-out). Finally, varying patterns of association between psychosocial factors and cardiac outcomes have also been reported, with higher state anxiety and lower anger-out related to mortality and higher depression related to risk of cardiac arrest and death (Ahern et al., 1990; Thomas et al., 1997). Null findings have been reported in MI patients, in which depression, anxiety, and hostility were all unrelated to cardiac-specific or all-cause mortality (Kaufmann et al., 1999; Lane, Carroll, Ring, Beevers, & Lip, 2002; Mayou et al., 2000).

Two studies are highlighted here because each also examines variance that is shared across psychosocial factors (i.e. negative affect) in predicting coronary outcomes. In Frasure-Smith & Lesperance (2003), only depression predicted cardiac death in MI patients at 5-years follow-up among measures also including anxiety and anger. Factor analysis of these psychosocial dimensions produced three factors, among them one labeled "negative affect". Upon re-analysis, each factor score was also entered into the multivariate model, showing both depression *and* negative affect to predict cardiac-specific mortality. Similarly, Denollet & Brutsaert (1998) assessed depression, anxiety, and anger, as well as the "Type D personality", defined as a "distressed" personality style. In this analysis, depression, anxiety, and anger initially predicted cardiac death and nonfatal MI. When Type D personality was entered into the multivariate model, however, these associations were attenuated. Interestingly, findings from Frasure-Smith & Lesperance (2003) suggest depression contributes to prognosis post MI independently of the variance it shares with negative affect, whereas findings from Denollet & Brutsaert (1998) suggest that the Type D personality style may subsume the common variance (i.e. negative affect) that might otherwise drive associations between these factors and incident coronary events.

1.4 Autonomic pathway: Linking psychosocial factors to CHD

Dysregulated autonomic control of heart rate (HR) and cardiac contractility is one pathway by which psychosocial factors are hypothesized to promote premature cardiovascular morbidity and mortality. The autonomic nervous system (ANS), through its sympathetic (SNS) and parasympathetic (PNS) branches, can exert a coactive, reciprocal, or independent influence over HR and cardiac contractility (Jalife & Michaels, 1994). The exact nature of this relationship is predicated on contextual factors such as the state (i.e. basal versus stress) of the individual. Under conditions of emotional or physical stress, SNS activation is related to increased HR and

increased cardiac contractility. The degree to which these changes occur, however, is partially dependent on the concurrent inhibitory action of the PNS, such that PNS activation slows, and PNS withdrawal increases, HR. Conversely, under resting conditions, the PNS is the predominant influence on HR and cardiac contractility (Levy, 1971); its action is mediated by acetylcholine release from the vagus nerve which then binds to receptors of the sinoatrial (SA) node, slowing HR through the atrioventricular (AV) node. Thus, ANS activity at the SA node influences beat-to-beat variation in HR over time, known as "heart rate variability (HRV)" (Chess, Tam, & Calaresu, 1975). The capacity of the ANS to vary the length of the interval between consecutive heart beats is considered adaptive relative to reductions in HRV that may render the individual less physiologically responsive to internally-driven perturbations, as well as environmentally-based stimuli. Importantly, such tendencies in ANS responsivity in the modulation of HR as measured by HRV has been shown to be stable across time and samples (Bigger, Fleiss, Rolnitzsky, & Steinman, 1992; Kleiger et al., 1991; Van Hoogenhuyze et al., 1991).

HRV has been recognized as a noninvasive marker of autonomic modulation of HR by The European Society of Cardiology and the North American Society of Pacing and Electrophysiology Task Force (1996). Although there are various methods of measuring HRV, two prominent strategies, both derived from continuous electrocardiogram (ECG) recordings, include time and frequency domain indices. Time domain indices of HRV are considered to be the most simple approach to HRV assessment. Within a specified recording segment, "normal-to-normal" intervals (i.e. intervals between QRS complexes that result from depolarization of the sinus node) are identified and used to estimate cycle components underlying HRV. Overall measures (e.g. standard deviation of NN intervals [SDNN]) estimate total variability in HR, long term measures (e.g. standard deviation of the average NN interval over 5 minutes [SDANN]) estimate low frequency variations in HR, and short term measures (e.g. square root of the mean

squared differences of successive NN intervals [RMSSD]) estimate high frequency variations in HR. Frequency domain indices of HRV are derived from power spectral analysis in which HR variance, distributed as a function of frequency, can be partitioned into components. The power spectral components are identified and labeled according to frequency band width, including very low frequency (VLF), low frequency (LF), and high frequency (HF) power. Power components are usually expressed in absolute values (ms^2), but may also be normalized to the total power estimate.

Much research has been conducted in an effort to elucidate the physiological processes that underlie HRV components. HF HRV has been shown to reflect vagal activity as demonstrated by experimental studies in which the HF component was diminished after pharmacological blockade of the parasympathetic nervous system (Akselrod et al., 1981; Malliani, Pagani, Lombardi, & Cerutti, 1991; Pomeranz et al., 1985; Saul et al., 1991). On the other hand, because LF HRV is diminished with both parasympathetic and sympathetic receptor blockade, this component is thought to be influenced by both autonomic branches (Akselrod et al., 1981; Pomeranz et al. 1985; Saul, Berger, Chen, & Cohen, 1989; Saul et al., 1991). Though controversial, sympathetic tone has been estimated using LF/total power ratio (Pagani et al., 1981; Pagani et al., 1986), and sympathovagal balance by the LF/HF ratio (Malliani, Lombardi, & Pagani, 1994). HRV frequency components correspond with time domain measures; notably RMSSD, PNN50, and HF power are highly correlated.

1.5 HRV and CHD risk

1.5.1 Healthy samples.

Population-based studies of initially healthy subjects have examined indices of HRV in relation to risk for incident CHD and death in order to evaluate the predictive power of HRV beyond that of traditional risk factors (e.g. blood pressure, smoking). In one population-based investigation of

both healthy men and women, Dekker et al. (2000) utilized a time domain index of HRV to predict incident CHD, cardiac-specific, and all-cause mortality. HRV analyzed by tertiles, showed subjects in the lowest tertile to have poorer relative cardiovascular risk profiles. Independent of such risk factors, however, low HRV was related to increased risk of incident CHD and all-cause mortality, but did not predict cause-specific death. Similarly, in a population-based sample of men only, low overall HRV (comparing men < 20 ms to men 20-39 ms) predicted 5-year incident death from all causes but was not reliably related to CHD mortality (Dekker et al., 1997). In the Framingham Heart study, (Tsuji et al., 1994) both time and frequency domain measures of HRV, derived from 2 hours of ambulatory ECG recording, predicted all-cause mortality at 5 year follow-up. In multivariate analysis, however, only the LF power component remained significant after covariate adjustment, with 1 standard deviation decrease in LF power related to 1.7 times increased risk for death. In a subsequent analysis of the same data, Tsuji et al. (1996a) reported that all indices of HRV (except the LF/HF ratio) predicted CHD events, with decrements in HRV related to increased risk for CHD death as well as congestive heart failure, myocardial infarction, and angina pectoris. Findings from several other large-scale investigations have largely substantiated the link between reduced HRV and risk for combined incident CHD events (MI, fatal CHD, non-CHD mortality, cardiac revascularization procedures) (Carnethon et al., 2002; Liao et al., 1997), and CHD death alone (Kikuya et al., 2000) but with some important exceptions. For example, in de Bruyne et al. (1999) elderly men and women in both the lowest and highest quartiles of HRV were at increased risk for CHD mortality. In Gerritsen et al. (2001), low HRV predicted CHD mortality but only among subjects with previously diagnosed diabetes or hypertension. Finally, in Molgaard, Sorensen, & Bjerregaard (1991) a trend was observed between low HRV and sudden death only.

1.5.2 MI patients.

Alterations in HRV have been examined in patients following myocardial infarction in order to better characterize risk for subsequent cardiac events, including re-infarction and cardiac mortality. In Bigger, Fleiss, Rolnitzky, & Steinman (1993), HRV was assessed 2 weeks post MI by frequency domain indices derived from 24 hour ambulatory monitoring, as well as shorter segments of measurement extracted from day and nighttime periods within the 24 hour time interval. Importantly, long and short measurement segments were highly correlated and both predicted all-cause, cardiac, and sudden death at 31 months follow-up. Numerous studies have replicated this finding, showing indices of HRV, of both time and frequency domain measures and of both long (24 hour) and short (1 to 5 min) measurement segments, to predict all-cause and cardiac mortality, as well as incident cardiac events (e.g. re-infarction, revascularization procedures, sustained ventricular tachycardia) over follow-up periods ranging in duration from 8 months to 3 years (Bigger et al., 1992; Copie et al., 1996; Cripps, Malik, Farrell, & Camm, 1991; Fei, Copie, Malik, & Camm, 1996; Kleiger, Miller, Bigger, & Moss, 1987; Quintana, Storck, Lindblad, Lindvall, & Ericson, 1997; Vaishnav et al., 1994). Additionally, all studies included statistical correction for appropriate covariates, typically including demographics, indices of disease severity, cardiovascular risk factors, as well as indices of post infarction risk specifically (i.e. age, New York Heart Association functional class, rales in the coronary care unit, left ventricular ejection fraction, and ventricular arrhythmias detected in a 24-hour Holter ECG recording). Interestingly, in contrast to the majority of studies in which HRV assessment occurred within 1 to 2 weeks post MI, Bigger, Fleiss, Rolnitzky, & Steinman (1993) examined 24-hour frequency domain indices of HRV 1 year following MI to determine whether alterations in HRV, thought to largely stabilize within 3 months after MI, would continue to predict mortality. Results indicate that, in fact, independent of relevant demographic information and markers of disease severity, low HRV predicted risk of death from all causes, further

substantiating the important prognostic value of HRV assessment (both short and long term) among post MI patients.

1.5.3 CAD patients.

Indices of HRV have also been related to disease severity among patients with CAD determined by angiographic assessment. Hayano et al. (1991) reported reduced vagal activity in relation to coronary atherosclerosis and stenosis, after statistical adjustment for prevalent disease (i.e. previous MI, left ventricular function). When standard cardiovascular risk factors were entered into multivariate analysis, the relationship of vagal activity to atherosclerosis, but not stenosis, remained statistically significant. Findings from Hayano et al. (1990) further substantiate that decrements in vagal function correspond to increasing CAD severity assessed by angiography in a heteogeneous patient sample (i.e. subjects with normal vessel, single vessel, and multi-vessel disease). Among the remaining studies to examine HRV in CAD samples, reductions in HRV were related to increase disease severity (Wennerblom, Lurje, Tygeson, Vahisalo, & Hjalmarson, 2000), mortality following elective angiography in a sample without history of MI (Rich et al., 1988), and disease progression over time (Huikuri et al., 1999). In contrast to these findings, Nolan et al. (1994) reported no association between parasympathetic activity and disease.

1.6 Depression and HRV

1.6.1 Psychiatric samples.

The relation of depression to cardiac autonomic function has been evaluated by comparing HRV between depressed and non-depressed subjects. Study findings have shown indices of overall HRV (e.g. SDNN) (Agelink Boz, Ullrich, & Andrich, 2002; Imaoka et al., 1985; Rechlin, Weis, & Kaschka, 1995; Van Der Kooy et al., 2006), as well as vagally-mediated components of HRV (e.g. HF) (Agelink et al., 2002; Guinjoan, Bernabo, & Cardinali, 1995; Rechlin et al., 1995;

Rechlin, Weis, Spitzer, & Kaschka, 1994) to be lower among patients diagnosed with major depressive disorder (MDD) than non-depressed controls. With respect to non-psychiatric samples, depressive symptomatology was assessed in one case-control study in which indices of HRV were compared between subjects scoring high (16+) versus low ($\leq$4) on the Beck Depression Inventory (BDI) (Thayer, Smith, Rossy, Sollers, & Friedman, 1998). Results showed the association of depressive symptoms with HRV to vary significantly by gender; depressed men had lower vagal activity than non-depressed men and depressed women had *higher* vagal activity than non-depressed women. That parasympathetic activation was greater among depressed than non-depressed women was unanticipated and contrasts with study findings showing significant negative correlations between vagal function and depressive symptoms (O'connor, Allen, & Kaszniak, 2002), as well as depressive episode duration (Moser et al., 1998). Notably, several studies have reported *no* differences in HRV indices between cases and controls (Lehofer et al., 1997; Moser et al., 1998; O'connor et al., 2002; Tulen et al., 1996; Yeragani et al., 1991), nor any association between vagal activity and depressive symptom severity (Watkins & Grossman, 1999). In sum, study findings are not entirely consistent with results showing reduced overall and vagally-mediated indices of HRV among depressed versus non-depressed subjects in several (Agelink et al., 2002; Guinjoan et al., 1995; Imaoka et al., 1985; Rechlin et al., 1995; Rechlin et al., 1994) but not all (Lehofer et al., 1997; Moser et al., 1998; O'connor et al., 2002; Tulen et al., 1996; Yeragani et al., 1992) studies. Similarly, evidence suggesting parasympathetic activity to covary with depressive symptomatology remains preliminary with reports of both significant (Moser et al., 1998; O'connor et al., 2002) and nonsignificant (Watkins et al., 1999) associations.

1.6.2 Cardiac samples.

Indices of HRV, assessed by 24 hour ambulatory monitoring, have also been compared between depressed and non-depressed patients with prevalent cardiovascular disease, including recent ($\leq$ 28 days) myocardial infarction (MI) and angiographically determined coronary artery disease (CAD). Study findings show consistently that patients meeting criteria for major depressive disorder (MDD) exhibit lower HRV than non-depressed patients by both time (Carney et al., 1995; Carney et al., 1988; Stein et al., 2000) and frequency (Carney et al., 2001; de Guevara et al., 2004; Guinjoan et al., 2004; Stein et al., 2000) domain measurement, including indices of vagal activation specifically (e.g. RMSSD, HF). Two additional studies of cardiac patients examined depressive symptomatology by psychometric assessment using the Depression Scale of the MMPI (Krittayaphong et al., 1997) and Zung's Self-Rating Depression Scale (Pitzalis et al., 2001). Both studies reported reduced overall HRV (i.e. SDNN) by time domain assessment among the low versus high depressive groups as well as significant negative correlations between the depression scales and overall HRV. Notably, these associations persisted after statistical correction for possible confounding factors (e.g. age, gender, BMI, beta-blocker use), including symptoms of anxiety (Krittayaphong et al., 1997; Pitzalis et al., 2001). In contrast to these findings, one recent report found no relation between depression and HRV in a large sample (N=873) of individuals with stable CHD (Gehi, Mangano, Pipkin, Browner, & Whooley, 2005). With one notable exception (i.e. Gehi et al., 2005), study findings among cardiac patients are largely consistent, showing patients with clinically diagnosed MDD or greater self-reported depressive symptoms to exhibit reduced HRV, including indices of vagal function, relative to controls without MDD or with fewer depressive symptoms (Carney et al., 2001; Carney et al., 1995; Carney et al., 1988; Krittayaphong et al., 1997; Pitzalis et al., 2001; Stein et al., 2000). Furthermore, significant negative associations were reported between depressive symptoms and

HRV indices (Carney et al., 2001; Krittayaphong et al., 1997; Pitzalis et al., 2001), substantiating the linearity of this relationship.

1.6.3 Healthy samples.

In addition to studies of psychiatric and cardiac patients, the potential link between depressive symptoms and cardiac autonomic function has been evaluated among non-depressed individuals without known physical disease. In so far as depressive symptoms are associated with impaired autonomic control of HR among healthy individuals, study findings may clarify whether depressive symptomatology is a risk factor for cardiovascular disease in the population more generally. In one population-based sample of healthy women, subjects who endorsed at least one depressive symptom showed lower sympathetic relative to parasympathetic activation (LF/HF ratio) than women with no depressive symptoms, independent of common confounding factors (i.e. age, smoking, hypertension, exercise, menopausal status, BMI, education) (Horsten et al., 1999). Notably, this sample was considered representative as these women reported similar demographic characteristics and health behaviors to a population registry of 2500 women. In a large sample of postmenopausal women without CAD (N=2,627), subjects with depressive symptoms had lower HRV than subjects with depressive symptoms (Kim et al., 2005). In a comparatively small sample, also of healthy women, those scoring in the highest quartile of the Beck Depression Inventory (BDI) showed lower vagal activity (i.e. MSD) than those in the lowest quartile during both baseline and stress tasks (Light, Kothandapani, & Allen, 1998). In contrast to the above findings, HRV, including indices of vagal function, did not differ between high and low depressive groups in two studies of both healthy men and women (Hughes & Stoney, 2000; Virtanen et al., 2003). In sum, evidence that depressive symptomatology is related to HRV by review of only those studies including physically and psychologically healthy subjects (Horsten et al., 1999; Hughes et al., 2000; Kim et al., 2005; Light et al., 1998; Virtanen

et al., 2003) remains equivocal. While relative sympathetic activity (LF/HF ratio) was lower among women with at least one depressive symptom than women with no symptoms (Horsten et al., 1999) and vagal activity and overall HRV lower among women with depressive symptoms (Kim et al., 2005; Light et al., 1998), two other large studies of significant design and methodological quality produced null findings (Hughes et al., 2000; Virtanen et al., 2003).

1.7 Anxiety and HRV

1.7.1 Psychiatric samples.

In parallel to the depression literature, the relationship of anxiety to cardiac autonomic function has been similarly evaluated by comparing HRV between anxious and non-anxious subjects. Unlike the depression literature, however, in which variability in diagnoses is limited to major depression, minor depression, and dysthymia, 'anxious' subjects include individuals from diverse patient populations. Such patient groups have included individuals meeting criteria for post-traumatic stress disorder (PTSD), panic disorder, specific phobia, and generalized anxiety disorder (GAD). In the only study of PTSD patients, results show reduced vagal modulation of heart rate in patients compared to controls, as well as greater sympathetic activity (i.e. LF%, LF/HF ratio) (Cohen et al., 1997). Interestingly, this finding suggests that vagal activity may be diminished among PTSD patients relative to controls, as was demonstrated among depressed patients, but that sympathetic activity may also be elevated among anxious patients specifically. Modest support for this observation is evident among panic disorder patients in which study findings have also shown vagally-mediated indices of HRV to be lower (Yeragani et al., 1991; Friedman & Thayer, 1998) and sympathetic relative to parasympathetic activity (LF/HF ratio) to be higher (Tucker et al., 1997; Friedman & Thayer, 1998) among panic patients than controls. Additional reports, however, show inconsistencies. For example, only overall HRV (SDNN) and LF power were lower among panic disorder patients than controls (Rechlin et al., 1994; Yeragani

et al., 1993; Yeragani et al., 1990), while no differences were observed between patients and controls in Stein & Asmundson (1994). Finally, evidence also shows diminished vagal activity among GAD patients compared to controls (Kollai & Kollai, 1992; Lyonfields, Borkovec, & Thayer, 1995; Thayer, Friedman, & Borkovec, 1996), as well as children presenting with a variety of anxiety diagnoses (e.g. separation anxiety, over-anxious disorder, panic disorder/panic attacks, social phobia) compared to healthy counterparts (Monk et al., 2001). In sum, psychiatric samples of anxious patients, though diverse symptomatically, show lower overall HRV (e.g. Yeragani et al., 1993), as well as lower vagally-mediated HRV indices (e.g. Thayer et al., 1996) than controls, with some evidence showing concomitant increases in sympathetic modulation of HR (e.g. Friedman & Thayer, 1998).

1.7.2 Cardiac samples.

Few studies have examined the relation of anxiety to autonomic function among cardiac patients. In Pitzalis et al. (2001), Zung's Self-Rating Anxiety Scale was used to divide the sample into those reporting high ($\geq$50) versus low (<50) anxiety symptoms. Although HRV did not differ between groups, overall HRV (SDNN) correlated negatively with anxiety symptoms. In multivariate analysis, however, when both depressive and anxiety symptoms were entered as predictors, only depressive symptoms predicted HRV significantly. Additionally, in a sample of patients with CAD, those with panic disorder exhibited lower LF:HF HRV relative to non-panic disorder patients (Lavoie et al., 2004). Thus, findings, though preliminary, do not support a role for anxiety in explaining impairments in autonomic function among cardiac patients.

1.7.3 Healthy samples.

In addition to studies of psychiatric and cardiac patients, the potential link between anxiety symptoms and cardiac autonomic function has been evaluated among healthy individuals,

typically screened to exclude individuals with psychiatric or known physical illness. For example, in a sample of women, vagal activity was diminished among "repressors" (those with low trait anxiety [MAS] but high social desirability) compared to women in the high and low trait anxiety groups; vagal activity was also significantly lower among those in the high versus low trait anxiety group (Fuller, 1992). Similarly, in a sample of men only, higher phobic anxiety (Crown-Crisp Index) was related to lower overall and vagally-mediated HRV (Kawachi, Sparrow, Vokonas, & Weiss, 1995). Finally, among both men and women, vagal activity was lower among those in the highest compared to the lowest quartile of trait anxiety (STAI); a significant negative correlation was reported between trait anxiety and vagal activity (Watkins, Grossman, Krishnan, & Sherwood, 1998). These reports contrast with several studies of null findings. For example, Hughes et al. (2000) reported no differences in vagal activity between subjects scoring above and below the median split on state and trait anxiety symptoms (STAI). In Dishman et al. (2000) both trait anxiety (Bendig's short form of the Taylor Manifest Anxiety Scale [MAS]) and stress (Cohen's Perceived Stress Scale) were included as predictors in multivariate analysis. Only stress, however, was related independently to lower vagal activity. In addition to these findings, other reports have similarly found anxiety symptoms unrelated to indices of HRV (Ramaekers, Ector, Demyttenaere, Rubens, & Van de Werf, 1998; Virtanen et al., 2003). In sum, the relation of anxiety to HRV in healthy samples remains equivocal. Null findings (Hughes et al., 2000; Dishman et al., 2000; Ramaekers et al., 1998; Virtanen et al., 2003) have been reported as commonly as those studies suggesting parasympathetic activity to be reduced among individuals with greater levels of trait anxiety (Fuller, 1992; Kawachi et al., 1995; Watkins et al., 1998).

1.8 Anger and HRV

1.8.1 Healthy samples.

Among healthy women, HRV indices (SDNN, VLF, LF) were significantly lower in subjects who reported not discussing their anger (Framingham Anger Scales) compared to individuals who, when angered, were more willing to discuss angry feelings with family and friends (Horsten et al., 1999). Though this scale has been conceptualized as a measure of "suppressed" anger, it is noteworthy that the "anger-in" scale was not similarly related to HRV indices, nor were the "anger symptoms" and "anger-out" scales. In a large age- and sex-stratified population-based sample, univariate analyses showed the "anger-out" expression scale of Spielberger's State-Trait Anger Expression Inventory (STAXI) to correlate modestly with the LF power component of HRV. However, multivariate analyses of several psychosocial dimensions, including hostility and anger, as well as modes of anger expression, showed no significant associations with HRV indices (HF, LF) (Virtanen et al., 2003). In Ramaekers et al. (1998), examination of coping styles in relation to HRV showed the "expression of negative emotions or anger" dimension of coping associated with higher RMSSD, HF, and LF, but only in men. This suggests that at least among men, the tendency to express negative emotions or anger may be accompanied by heightened autonomic arousal of both the sympathetic and parasympathetic branches. Among women, however, coping style was unrelated to HRV.

Using 24-hour ambulatory assessment of HRV, hostility measured by the Cook-Medley Hostility Inventory, did not predict vagal activity or relative sympathetic to parasympathetic activation (LF/HF ratio) after age was covaried (Sloan et al., 1994a). A significant interaction between age and hostility, however, was detected in the prediction of HF and the LF/HF ratio during the daytime hours. Follow-up analysis showed hostility to correlate inversely with HF and positively with LF/HF ratio among younger men (<40 years) while no relationship was observed among men 40 years of age and older. Importantly, these findings were strongest during daytime

measurement, weakened when overall (i.e. 24 hour) recordings were analyzed, and diminished entirely at night. Sloan et al. (1994a) have concluded that tendencies toward hostility predict a pattern of vagal decrement and relative sympathetic activation during the day when men are most likely to encounter environmental triggers for hostile responding. In the same sample, Sloan et al. (1994b) further reported that a composite measure of "stress" created from mood ratings including feelings of anger, irritability, and tension, predicted higher LF/HF ratio after statistical adjustment for physical position. In a laboratory study of shorter measurement segments of HRV, parasympathetic indices (HF, RMSSD) as well as LF power were inversely related to hostility at rest and during stress tasks (i.e. mental arithmetic, stroop, orthostatic challenge), controlling for respiration among both men and women (Sloan et al., 2001).

In sum, studies of healthy subjects in which a trait measure of anger or hostility was included, showed HRV related to anger, but with varying directions of association across studies. With respect to modes of anger expression, the tendency to inhibit discussion of angry feelings in women was related *inversely* to HRV indices (SDNN, VLF, LF) (Horsten et al., 1999), while in men the outward expression of anger was related *positively* to both parasympathetic (RMSSD, HF) and sympathetic (LF) components of HRV (Ramaekers et al., 1998; Virtanen et al., 2003). Among younger men (<40 years) dispositional hostility (assessed by the CMHI) was both negatively associated with parasympathetic (HF) and positively associated with sympathetic (LF/HF ratio) activity (Sloan et al., 1994a), while all indices of HRV (RMSSD, HF, LF) were inversely related to hostility (CMHI) in Sloan et al. (2001). In conclusion, evidence supports a link between anger/hostility and HRV, in some instances of decreased parasympathetic and increased sympathetic activity, though the direction of this relationship remains unclear and may depend on the precise nature of the anger variable under investigation (e.g. anger inhibition versus expression), as well as the characteristics of the sample itself (e.g. differences between men and women).

1.9 Summary and statement of problem

Because mood and anxiety disorders, as well as psychiatric symptomatology (i.e. depression, anxiety, and anger) are highly comorbid in both psychiatric and non-clinical samples (e.g. Blumberg & Hokanson, 1983; Mineka, Watson, & Clark, 1998; Newman, Gray, & Fuqua, 1999; Thomas & Atakan, 1993), a common diathesis or dispositional tendency to experience negative emotions has been postulated to underlie these diagnoses/symptoms (e.g. Krueger, Caspi, Moffit, Silva, & McGee, 1996; Trull & Sher, 1994). In fact, structural data analyses confirm that a single latent factor accounts for a substantial portion of variance common to these mood, anxiety, and anger-related facets of both psychiatric disorders and personality traits, referred to as "negative affect" (e.g. Watson, 1988; Watson, Clark, & Tellegen, 1984). In epidemiological studies, these same dimensions (i.e. depression, anxiety, and anger), measured both categorically and continuously, are commonly labeled "psychosocial risk factors", and have been shown to predict incident cardiac events in healthy and patient populations (e.g. Anda et al., 1993; Barefoot et al., 1996; Frasure-Smith et al., 1995; Kawachi et al., 1996; Kawachi et al., 1994). In parallel, it may be postulated that these psychosocial risk factors for coronary heart disease (CHD) also reflect a common underlying component of trait negative affect.

One pathway by which psychosocial factors are related to risk for CHD is the autonomic nervous system (ANS). HRV refers to one noninvasive method of measuring autonomic nervous system control of HR. Alterations in HRV (e.g. decrements in vagal activation) have been related to cardiac mortality in normal populations, prognosis among survivors of acute myocardial infarction (MI), and extent of atherosclerosis in patients with coronary artery disease (CAD) (e.g. Bigger et al., 1993; Hayano et al., 1990; Liao et al., 1997). Evidence also shows depression, anxiety, and anger to be correlated with HRV indices (e.g. Carney et al., 1995; Cohen et al., 1997; Sloan et al., 1994). The precise nature and relative significance of each psychosocial dimension in relation to HRV, however, is not well understood, leaving unanswered questions

regarding the (1) relative significance of individual psychosocial factors in predicting HRV (model of unique variance), (2) the possibility that psychosocial factors are related to HRV by a common underlying dimension of negative affect (model of common variance), and finally, (3) whether any psychosocial factor may predict HRV in addition to the variance accounted for by negative affect (model of unique and common variance).

The purpose of the study proposed herein was to assess psychosocial risk factors for CHD (depression, anxiety, anger), as well as the variance that these factors may share (negative affect), in relation to autonomic modulation of HR as measured by indices of HRV in a community-based sample of men and women. Using a combined data analytical approach with factor analysis/multiple regression and structural equation modeling (SEM), we evaluated a series of models designed to test the proposed hypotheses. First, models including depression, anxiety, and anger as predictors were assessed to determine how much variance in HRV is explained by each factor individually (Figures 1, 5, 9). Next, a model including all factors simultaneously was assessed to determine how much variance in HRV is explained by each factor relative to the others (Figure 15). Third, a model including all factors, as well as negative affect as a predictor, was assessed to determine how much variance in HRV is explained by negative affect specifically (Figure 18). Finally, a model including direct pathways between each factor and HRV, as well as a mediated pathway by which effects are transmitted through negative affect were assessed to determine how much variance in HRV is explained both by the individual factors (depression, anxiety, and anger) and negative affect (Figure 22). In sum, within the full model were nested models by which the proposed hypotheses were tested, including (1) a model of unique variance, (2) a model of common variance, and finally, (3) a model of unique and common variance.

2.0 METHOD

Data included in the present analysis were derived from the Adult Health and Behavior (AHAB) project, a community-based registry of behavioral and biological phenotypes established under the University of Pittsburgh Initiative for Neurobehavioral Genetics. The primary objective of the AHAB registry is to permit identification of genetic correlates of normative variation in measured phenotypes, as obtained on men and women of European-American and African-American descent. The parent data collection of AHAB includes a broad array of questionnaire, interview, and instrumented assessments relating to personality, psychopathology, cognitive abilities, lifestyle-associated risk factors for chronic disease, and various physiological processes. Among these measures, self-reported depressive symptoms, trait anxiety, and anger-related personality traits will be employed in this study, along with electrocardiogram-derived indices of HRV. The study was approved by the University of Pittsburgh Biomedical Institutional Review Board and informed written consent was obtained from all study participants.

2.1 Participants

Participants from the AHAB registry included 820 men and women (50.0% female; 19.5% Black) ages 30-54 (M= 43.8 $\pm$ 7.0) recruited from Southwestern Pennsylvania (Allegheny County) by mass-mail solicitation. Participants were excluded based on the following criteria: self-reported clinical history of severe or chronic diseases affecting general health (e.g. myocardial infarction or cancer within the past year, chronic kidney or liver disease, and neurological disorders); psychotic disorders (e.g. schizophrenia); current use of certain cardiovascular, psychotropic, glucocorticoid, diabetic, or weight-loss medications; and

pregnancy. Thus, participants in the AHAB study, though community-based, were selected to be in better general health physically and mentally than participants in representative samples in which study participation is unrestricted.

In the present analysis, additional exclusionary criteria were imposed to limit potential confounding influences of significant clinical disease (e.g. history of myocardial infarction) or medications affecting autonomic function (e.g. beta-blockers) on measures of HRV. These criteria included the following: past history of atherosclerotic disease (myocardial infarction, stroke); angina pectoris or claudication; coronary, carotid, or peripheral revascularization procedures; anti-hypertensive medications (diuretics, beta-blockers, calcium channel blockers, ace- inhibitors, central sympatholytics, and vasodilators); and cold or allergy medications taken within 12 hours of the laboratory session.

2.2 Psychometric measures

Participants completed several psychometric instruments selected to assess self-reported dimensional variability in three psychological domains: depression, anxiety, and anger. Specifically, three scales were chosen to measure each domain. Depression was measured by (1) the total score of the Beck Depression Inventory (BDI), (2) the total score of the Center for Epidemiological Studies Depression Scale (CES-D), and (3) the Depression facet scale score of the revised NEO Personality Inventory (NEO PI-R). Anxiety was measured by (1) the Trait Anxiety scale score of the State-Trait Anxiety Inventory (STAI), (2) the Anxiety facet scale score of the NEO PI-R, and (3) the Harm Avoidance scale score of the Temperament and Character Inventory (TCI). Finally, anger was measured by (1) the Trait Anger scale score of the State-Trait Anger Expression Inventory (STAXI), (2) the Anger-Out scale score of the STAXI,

and (3) the Anger facet scale score of the NEO PI-R. The inclusion of multiple scale scores for each domain was required for planned statistical analyses (i.e. factor analysis and structural equation modeling).

2.2.1 Beck Depression Inventory (BDI).

The BDI (Beck, Rush, Shaw, & Emery, 1979) measures the presence and severity of depressive symptoms over the past week. The BDI is a 21-item self-report questionnaire with each item scored on a 0-3 point scale. Questionnaire items are summed; overall scores range from 0 to 63 with higher scores indicating more depressive symptoms. Original item construction was designed to evaluate specific components of depression, including 11 items reflecting cognitive, 2 affective, 2 behavioral, 1 interpersonal, and 5 somatic-related symptoms. Good internal consistency has been demonstrated in both psychiatric and non-psychiatric samples with split-half reliability coefficients ranging from 0.73 to 0.95 (Beck, Steer, & Garbin, 1988). Similarly, test-retest reliability has been adequate to good with coefficients ranging from 0.48 to 0.86 among psychiatric and 0.60 to 0.83 among non-psychiatric patients (Beck et al., 1988). The validity of the BDI has been established by its correspondence with clinician ratings of depression, as well as significant correlations with other psychometric and interview-based methods of depression assessment, including the Hamilton Rating Scale for Depression, the Zung self-reported depression scale, and the MMPI depression scale (Beck et al., 1988).

2.2.2 Center for Epidemiological Studies Depression Scale (CES-D).

The CES-D (Radloff, 1977; Weissman, Scholomskas, Pottenger, Prusoff, & Locke, 1977) also measures depressive symptomatology over the past week. The CES-D is a 20-item self-report

questionnaire developed for use in the general population. Each item is scored on a 0-3 point scale. Response choices indicate the frequency with which each symptom (or item) is experienced, ranging from "rarely or none of the time (< 1 day)" scored 0 to "most or all of the time (5-7 days)" scored 3. Items are summed to produce a total score (ranging from 0 to 60), as well as 4 sub-scale scores. Sub-scales include: depressed affect, positive affect, somatic and retarded activity, and interpersonal difficulties (Hertzog, Van Alstine, Usala, Hultsch, & Dixon, 1990; Knight, Williams, McGee, & Olaman, 1997; Radloff, 1977; Weissman et al., 1977). Higher values on the total and sub-scales reflect more depressive symptoms. High internal consistency has been demonstrated in psychiatric and non-psychiatric samples, reliability coefficients 0.90 and 0.85, respectively (Nunnally, 1967; Radloff & Teri, 1986). Additionally, validity of the CES-D is well-established; it has been shown to distinguish patient from non-patient samples, correlate with clinician ratings of depression, fluctuate in accordance with treatment for depression, and correlate with alternative measures of depression (Blazer, Landerman, Hays, Simonsick, & Saunders, 1998; Clark, Aneshensel, Freirichs, & Morgan, 1981; Hertzog et al., 1990; Knight et al., 1997; Radloff et al., 1986; Weissman et al., 1977).

2.2.3 Revised NEO Personality Inventory (NEO PI-R).

The NEO PI-R (Costa & McCrae, 1992) assesses normative variation in personality traits. On a 5-point scale, respondents indicate their level of agreement (1=strongly disagree, 2=disagree, 3=neutral, 4=agree, 5=strongly agree) with each of 240 statements. Items are summed to yield total scores. Based on the five-factor model of personality (Digman, 1990), the NEO PI-R measures five domains of personality (Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness) and 30 sub-scales (facets). The Depression, Anxiety, and Angry Hostility

facets of the Neuroticism domain (i.e. tendency to experience negative emotions) include 8 items each. Example items from these facet scales include “Sometimes I feel completely worthless” (Depression), “I often worry about things that might go wrong” (Anxiety), and “I am known as hot-blooded and quick tempered” (Angry Hostility). Good internal structure of this instrument has been demonstrated (reliability coefficients ranging 0.89-0.95) (Costa, McCrae, & Dye, 1991); instrument validity has been established by its association with similar constructs, convergence with observer reports, and relationship to psychopathology (McCrae & Costa, 1987; Miller, 1991).

2.2.4 State-Trait Anxiety Inventory (STAI).

The State-Trait Anxiety Inventory (STAI) (Spielberger, 1983) measures symptoms of anxiety. The STAI consists of two scales: Trait Anxiety (T-Anxiety) and State Anxiety (S-Anxiety). State Anxiety refers to transient emotions of anxiety experienced by an individual in a given situation, whereas Trait Anxiety refers to an individual’s disposition to respond to perceived threats with states of anxiety. The T-Anxiety scale includes 20 items for which participants are requested to indicate how they “generally feel” by rating the frequency of their feelings on a 4-point scale (1=almost never, 2=sometimes, 3=often, 4=almost always). The S-Anxiety scale includes 20 items for which participants are requested to indicate how they feel “right now, at this moment” by rating the intensity of their feelings on a 4-point scale (1=not at all, 2=somewhat, 3=moderately so, 4=very much so). Items are summed with overall scores for each scale ranging from 20 to 80; higher scores indicate more anxiety symptoms. Internal consistency of the STAI is excellent with reliability coefficients ranging from 0.89 to 0.91 across various samples; additionally, validity has been well established by data showing the STAI to discriminate

between psychiatric and non-psychiatric samples, to correlate with other measures of anxiety, and to be associated with related constructs (i.e. aspects of psychological adjustment, stress) (Spielberger, 1983).

2.2.5 Temperament and Character Inventory (TCI).

The TCI (Cloninger, Svrakic, & Przybeck, 1993; Cloninger, Svrakic, & Przybeck, 1991) assesses four dimensions of temperament, including Novelty Seeking, Harm Avoidance, Reward Dependence, and Persistence. Each dimension measures a pattern of emotional/behavioral responding to perceived environmental stimuli. Evidence supports the stability of these patterns throughout an individual's life (Sigvardsson, Bohman, & Cloninger, 1987) as well as their heritability (Heath, Cloninger, & Martin, 1994). Specifically the Harm Avoidance (HA) dimension describes an individual's tendency to inhibit behavior in response to cues of punishment. Individuals high in HA are fearful, pessimistic, socially inhibited, and easily tired; individuals low in HA are carefree, optimistic, outgoing, and energetic. The HA dimension consists of 35 items from four subscales, including Pessimism versus Uninhibited Optimism, Fear of Uncertainty, Shyness with Strangers, and Fatigability and Asthenia. Response choices are in true/false format. An example item is "I often feel tense and worried in unfamiliar situations, even when others feel there is little to worry about". Internal consistency reliability for the scales is high, ranging from .76 to .87 (Cloninger et al., 1993). Construct validity is evidenced by studies showing consistency in the factor structure of these scales as well as correlations with neurobiological processes hypothesized to underlie differences in temperament (Cloninger, 1987; Cloninger et al., 1993)

2.2.6 State-Trait Anger Expression Inventory (STAXI).

The STAXI assesses dispositional (trait) anger and habitual modes of anger expression (Spielberger, 1991). The Trait Anger scale includes two component subscales: Angry Temperament and Angry Reaction. Angry Temperament reflects quick-temperedness, or the tendency to experience anger on minimal provocation, whereas Angry Reaction denotes the tendency to become angered in response to criticism or mistreatment by others. The anger expression dimensions reflect the tendency for angry feelings to be expressed outwardly toward people or objects in the environment (Anger-Out), suppressed (Anger-In), or controlled (Anger Control). The STAXI contains 34 items each rated by the participant according to the intensity or frequency with which they experience or express anger (1=never, 2=sometimes, 3=often, and 4=almost always). Responses are summed to yield a score for each anger dimension. Internal consistency and test-retest reliability of the trait anger and anger expression scales are all satisfactory, with reliability coefficients ranging from 0.70 to 0.89 across multiple samples (Spielberger, 1991). Additionally, convergent validity is evident by associations of Trait Anger with the Buss Durkee Hostility Inventory (BDHI) (r=.66-.73), and the hostility (r=.43-.59), and overt hostility (r=.27-.32) scales on the MMPI (Buss & Durkee, 1957; Cook & Medley, 1954). Notably, despite substantial correlations with hostility, factor analysis of multiple questionnaires indicates that anger and hostility items load on separate factors (Spielberger, 1991).

2.3 Heart rate variability (HRV)

Electrocardiographic (ECG) recordings were obtained on a single occasion as part of a laboratory protocol in which basal-level physiological parameters (i.e. electricocortical activation, blood pressure, energy expenditure) and anthropomorphic indices (i.e. height, weight,

waist-to-hip ratio, percent body fat) were assessed. Prior to this laboratory session, participants were requested to abstain from alcohol (24 hours), exercise (12 hours), cold and allergy medications (12 hours), food (8 hours), and nicotine (1 hour). Participants were seated in a relaxed upright position and silver-silver chloride electrodes placed bilaterally to the wrists. ECG recordings were obtained continuously over two five-minute segments. In the first segment, breathing was paced by auditory tones cueing participants to inhale and exhale at a mean breathing rate of 11 breaths per minute. In the second segment, breathing was unpaced allowing participants to breathe spontaneously. Instructions for paced and unpaced breathing segments were counterbalanced to eliminate possible order effects. Additionally, respiration rate was measured by thoracic strain-gauge to ensure compliance with paced breathing instructions and to estimate the high frequency (HF) HRV power component (Grossman & Kollai, 1990; Hirsch & Bishop, 1981).

The ECG signal, sampled at 1000 Hz, was digitized and stored for off-line processing using MATLAB and PSPAT software (Weber, Molenaar, & van der Molen, 1988). A time series of interbeat intervals (IBI's) was generated, reflecting the time in milliseconds between consecutive R spikes in the ECG waveform. Errors in signal detection were inspected visually and by an automated detection program; identified artifacts were corrected manually. Spectral power analysis was used to derive frequency component power estimates (ms2/Hz) of these time series segments using a Point Process statistical method (Weber et al., 1988). The high frequency (HF-HRV) power estimate was defined in the respiration frequency +/- 0.015 Hz bandwidth and the low frequency (LF-HRV) power estimate in the 0.09 - 0.12 Hz bandwidth (Task Force, 1996). An index of sympathovagal balance was also derived by taking the ratio of LF-HRV to

HF-HRV power estimates (LF/HF ratio) as has been recommended in the literature (Malliani, Lombardi, & Pagani, 1994; Pagani et al., 1986).

2.4 Data analysis

In sum, the present study sought to evaluate six primary hypotheses. In Hypotheses 1-3, depression, anxiety, and anger were examined individually in relation to each dependent measure of interest (HF-HRV, LF-HRV, and LF:HF-HRV). In Hypothesis 4, these relationships were then examined simultaneously to determine whether depression, anxiety, or anger predicted HRV independently of one another. Next, in Hypothesis 5, negative affect (conceptualized as the variance common to depression, anxiety, and anger) was examined in relation to HRV. Finally, in Hypothesis 6, negative affect, as well as depression, anxiety, and anger, were examined simultaneously in relation to HRV to determine whether depression, anxiety, or anger added to the prediction of HRV beyond negative affect.

Each hypothesis was evaluated from two different data analytical perspectives. In the first approach, a combination of factor analyses and multiple regression analyses were employed. This analytical strategy was planned to allow comparison of study results to findings in relevant research literatures. Currently, the vast majority of studies use similar statistical methods with a focus on testing the statistical significance of relationships between variables. In the second approach, structural equation modeling (SEM) techniques were used. SEM differs from non-modeling approaches because of its focus on the quality or "goodness of fit" of the proposed model overall versus assessment of the strength of associations between individual variables. Notably, in SEM, path coefficients may be examined but are only meaningful in the context of an adequately fitting model. SEM is growing in popularity as it offers several advantages to more

conventional approaches, including its ability to incorporate both measured and unmeasured (latent) variables (Herschberger, 2003).

2.4.1 Factor analysis/multiple regression.

Factor analysis is used to characterize a set of measured variables according to a smaller set of underlying latent factors that "cause" or produce the measured variables. Among the various methods of factor extraction, principal axis factoring was chosen because it extracts only the variance that is common to the measured variables while removing unique and error variance from the variables. This approach differs from other data reduction strategies such as principal components analysis in which factors are *composites* of the measured variables, representing both their common and unique variance. In the present study, four factor analyses using principal axis factoring were performed to identify factors underlying questionnaire measures of depression (BDI, CES-D, NEO-DEP), anxiety (STAI-T, NEO-ANX, TCI-HA), anger (STAXI-T, STAXI-OUT, NEO-ANG) separately, as well as all nine questionnaire measures examined together (BDI, CES-D, NEO-DEP, STAI-T, NEO-ANX, TCI-HA, STAXI-T, STAXI-OUT, NEO-ANG). Factor scores were calculated by the regression method and entered as independent variables in multiple regression analyses. Multiple regression analyses were employed to evaluate the relationships between these psychological constructs (represented by factor scores) and HRV. Independent variables were entered in a hierarchical fashion when the step-wise contribution of the independent variables to the prediction of HRV was of interest, allowing statistical adjustment for variables entered on earlier steps.

2.4.2 Structural equation modeling (SEM).

Structural equation modeling (SEM) refers to a group of statistical techniques used to assess complex relationships between variables. SEM encompasses confirmatory factor analytic techniques used to assess latent factors reflecting variance common across observed variables, structural analytic techniques used to assess directional relationships between both latent and observed variables, and hybrid approaches in which factor *and* structural analytic techniques are employed. The primary goal of SEM is to explain relations among correlated variables by a proposed model. Specifically, model parameter estimates reflecting hypothesized associations between variables are used to estimate the population covariance matrix which is then compared to the sample (observed) covariance matrix to determine whether the proposed model is consistent with the data. In other words, if the model is satisfactory, the estimated population covariance matrix and sample covariance matrix will be similar. If the model is not an adequate fit to the data, however, the model may be rejected or modified and re-evaluated.

The proposed hypotheses are depicted by SEM conceptual models in Figures 1, 5, 9, 13, 15, 16, 18, and 22. By convention, rectangles represent measured variables, circles represent latent variables, lines with single-headed arrows represent direct, unidirectional relationships between variables (i.e. regression coefficients), and lines with double-headed arrows represent covariances between pairs of variables (i.e. correlations). Measurement error terms are depicted for observed variables and residual error terms depicted for the prediction of latent dependent variables from latent independent variables. The latent constructs of depression, anxiety, and anger were measured by three indicators each, using the same questionnaire measures described above. Each model was adequately identified by ensuring that the number of measured variables exceeded the number of unknown parameters to be estimated. Covariance matrices of all models

were analyzed using the maximum likelihood (ML) method. The ML assumption of multivariate normality was evaluated according to skewness and kurtosis values of univariate distributions as well as the Mahalanobis D statistic used to identify individual multivariate outliers. On several occasions, multivariate outliers were identified and removed. Because the results did not change, however, these subjects were retained in the final analyses. Additionally, tolerance values (1-R^2_{smc}) were examined to evaluate multicollinearity and parameter estimates were reviewed to identify Heywood cases, nonsensical values (e.g. negative error variances) usually caused by problems with the model such as model misspecification.

Model fit indices were used to measure the degree to which the hypothesized models correspond with the sample data. Fit indices reported in the present study were selected according to recommendations from several sources (e.g. Hu & Bentler, 1998, Kline, 2005). Indices included the chi-square test statistic (χ^2), the normed chi-square test statistic (χ^2/df), the root mean square error of approximation (RMSEA; Steiger, 1990; Steiger & Lind, 1980), the comparative fit index (CFI; Bentler, 1990), the Akaike information criterion (AIC; Akaike, 1987), and the chi-square difference test ($\chi^2_{difference}$). The χ^2 is commonly reported in the SEM literature. Poor model fit is suggested by χ^2 values with p's <.05. The χ^2 is limited, however, due to its assumption of perfect model fit and its dependence on sample size. Thus, type II error (i.e. rejection of the null hypothesis when it is the true model) is likely to arise in large samples (Kline, 2005). Because of this, the χ^2 is commonly disregarded. The χ^2/df is reported as an alternative to the χ^2 because it is less sensitive to sample size; χ^2/df values below 5 are considered acceptable (Bollen, 1989). In contrast, the RMSEA and CFI are not influenced by sample size (Fan, Thompson, & Wang, 1999). The RMSEA assumes approximation of model fit and favors simpler models when multiple models explain equal amounts of variance; RMSEA

values $\leq$ .05 indicate close fit, .values 05-.08 indicate reasonable fit and values >.10 indicate poor fit (Brown & Cudeck, 1993). The CFI reflects the comparison of the hypothesized model to an independence model (i.e. assuming variables are unrelated); values greater than .95 indicate good fit (Hu & Bentler, 1999). The AIC is a predictive fit index used to compare nested as well as non-hierarchical models; there are no cut-off values to determine fit but rather smaller values reflect better fitting models. The $\chi^2_{difference}$ is used to test the statistical improvement in overall model fit when individual paths are added or removed. Finally, the standardized residual matrix was examined as a supplement to formal tests of model fit. Values deviating substantially from zero (i.e. perfect model fit) reflect discrepancies between the model-implied population and sample covariance matrices; values > 2.58 are considered "large" (Joreskog & Sorbom, 1988).

All models exhibited sufficient statistical power to detect relationships among variables in the hypothesized models. In the final model in which there were the largest number of unknown parameters to be estimated (63), the present sample size (N=653) exceeded the recommended minimum number of cases (i.e. 630), according to the guideline that the ratio of cases to free parameters be 10:1 (Kline, 2005).

2.4.3 Software program.

Statistical analyses were performed using Version 5 of Amos (Analysis of Moment Structures; Arbuckle, 2003). Among its many features, this model-fitting program allows the user to represent hypothesized models graphically. Symbols (e.g. circles to represent latent variables) and parameter specifications (e.g. whether parameter is fixed) are used to indicate the relationships between the variables from which the program generates the program code necessary to test the model.

3.0 RESULTS

3.1 Sample description

The present sample included 653 participants (51.0% female; 15.8% Black) ages 30-54 (M= 43.8 ± 7.1) derived from the AHAB project (N=820). Fifty-nine subjects were excluded due to use of medications affecting autonomic function, 57 were taking anti-hypertensives and 2 nitrates. Additionally, 76 subjects were excluded because of missing HRV data. These data were incomplete for several reasons, including noncompliance with instructions for the session (e.g. abstinence from cold and allergy medications), technical failures (e.g. inadequate ECG signal detection), and miscellaneous problems (e.g. scheduling conflicts). Finally, 32 participants without complete questionnaire data on 9 scales of primary interest (BDI, CES-D, NEO-DEP; STAI-T, NEO-ANX, TCI-HA; STAXI-T, STAXI-OUT, NEO-ANG) were also excluded.

Demographic data and cardiovascular risk factors are summarized in Table 1 and Table 1.1 for the full sample, as well as men and women separately and White and Black subjects separately. Overall, subjects averaged 44 years of age and 63% of the sample was married. On average, subjects had 4 years of post-secondary education and earned an annual income (before taxes) between $25,000 and $34,999. Subjects were overweight on average (BMI=27), 41% were current or former smokers, and SBP (115 mm Hg) and DBP (77 mm Hg) measurements fell within normal ranges. Comparison of men and women showed men to have higher individual income, BMI, and BP (all p's <.05). Comparison of White and Black subjects showed White subjects to have more education and higher income as well as healthier cardiovascular risk profiles, including lower BMI, less smoking, and lower BP (all p's <.05).

Table 1. Demographic characteristics and cardiovascular risk factors among all subjects and in men and women and White and Black subjects separately.

	Total (n=653)	Men (n=320)	Women (n=333)	Statistic	p	White (n=550)	Black (n=103)	Statistic	p
Race (% Black); Sex (% men)	15.8	15.0	16.5	$\chi^2 = .282$	.595	49.5	46.6	$\chi^2 = 0.282$	.595
Age (years)	43.8 (7.1)	43.4 (7.2)	44.2 (6.9)	$t_{651} = -1.32$	.189	44.0 (7.2)	42.8 (6.4)	$t_{651} = 1.51$	.132
Education (years)	16.1 (3.1)	16.1 (2.8)	16.1 (3.3)	$t_{651} = -0.01$	.992	16.5 (3.0)	14.4 (2.9)	$t_{651} = 6.28$	.000
Ind Income (coded 1-8*)	3.7 (2.2)	4.4 (2.1)	2.9 (1.9)	$t_{380} = 7.49$	.000	3.8 (2.1)	3.1 (2.0)	$t_{380} = 2.42$	.016
Fam Income (coded 1-8*)	5.3 (2.1)	5.3 (2.1)	5.4 (2.1)	$t_{647} = - 0.94$	.350	5.6 (2.0)	3.9 (2.1)	$t_{647} = 7.86$	.000
Marital Status (% married)	63.4	60.9	65.8	$\chi^2 = 1.639$	.200	67.3	42.7	$\chi^2 = 22.541$	.000
Body Mass Index	27.1 (5.7)	27.6 (4.6)	26.7 (6.5)	$t_{647} = 2.19$	.029	26.8 (5.3)	28.8 (6.9)	$t_{647} = -2.71$	.008
Smoking (% ever)	40.9	40.3	41.4	$\chi^2 = .086$	.769	37.8	57.3	$\chi^2 = 13.597$	.000
Systolic BP (mmHg)	115.4 (13.4)	119.3 (12.8)	111.5 (12.9	$t_{647} = 7.67$	.000	114.6 (13.3)	119.7 (13.2)	$t_{647} = -3.57$	.000
Diastolic BP (mmHg)	77.3 (9.0)	80.1 (8.8)	74.6 (8.5)	$t_{647} = 8.14$	.000	76.8 (8.9)	80.1 (9.3)	$t_{647} = -3.39$	.001

*Individual and family income: 1=<$10, 000, 2=$10,000-14,999, 3=$15,000-$24,999, 4=$25,000-$34,999, 5=$35,000-$49,999, 6=$50,000-$64,999, 7=$65,000-$80,000 8=>$80,000

Table 1.1. Demographic characteristics and cardiovascular risk factors among White and Black men and women.

	Men (n=320)		Statistic	p	Women (n=333)		Statistic	p
	White (n=272)	Black (n=48)			White (n=278)	Black (n=55)		
Age (years)	43.6 (7.3)	42.3 (7.0)	$t_{318} = 1.20$	.230	44.3 (7.1)	43.3 (5.8)	$t_{651} = -1.32$	.189
Education (years)	16.5 (2.6)	14.0 (2.8)	$t_{318} = 6.19$	.000	16.4 (3.3)	14.9 (3.0)	$t_{651} = -0.01$	.992
Ind Income (coded 1-8*)	4.7 (2.0)	2.7 (1.9)	$t_{201} = 5.23$	.000	2.8 (1.8)	3.6 (1.9)	$t_{380} = 7.49$	.000
Fam Income (coded 1-8*)	5.6 (2.0)	3.4 (2.0)	$t_{316} = 6.97$	.000	5.6 (2.0)	4.3 (2.1)	$t_{647} = - 0.94$	.350
Marital Status (% married)	64.0	43.8	$\chi^2 = 7.008$	.008	70.5	41.8	$\chi^2 = 16.781$	.000
Body Mass Index	27.5 (4.4)	28.3 (5.4)	$t_{318} = -1.11$	.270	26.2 (6.0)	29.3 (8.0)	$t_{647} = 2.19$	.029
Smoking (% ever)	63.2	39.6	$\chi^2 = 9.486$	.002	61.2	45.5	$\chi^2 = 4.662$	.031
Systolic BP (mmHg)	119.2 (12.8)	119.8 (12.8)	$t_{318} = -.318$	.751	110.0 (12.2)	119.6 (13.5)	$t_{647} = 7.67$	.000
Diastolic BP (mmHg)	79.9 (8.5)	80.9 (9.9)	$t_{318} = -.721$	.472	73.7 (8.1)	79.3 (8.6)	$t_{647} = 8.14$	.000

*Individual and family income: 1=<$10, 000, 2=$10,000-14,999, 3=$15,000-$24,999, 4=$25,000-$34,999, 5=$35,000-$49,999, 6=$50,000-$64,999, 7=$65,000-$80,000 8=>$80,000

Psychometric information for the psychosocial questionnaire measures is summarized in Table 2. Because distributions of the BDI, CES-D, STAI-T, and STAXI-T scales were skewed

Table 2. Psychometric description of self-reported psychosocial measures.

Measure	Mean (SD)	Median	Range	Skewness	Kurtosis	Cronbach α
Depression						
BDI*	4.1 (5.0)	3.0	0-44	.087	-1.023	.875
CES-D*	7.8 (7.5)	6.0	0-50	-.364	-.518	.900
NEO-DEP	11.5 (5.9)	11.0	0-31	.525	.000	.848
Anxiety						
STAI-T*	32.5 (9.1)	31.0	20-68	.322	-.554	.921
NEO-ANX	12.8 (5.3)	12.0	0-28	.299	-.246	.803
TCI-HA	10.9 (6.9)	9.0	0-32	.678	-.325	.890
Anger						
STAXI-T*	16.8 (4.1)	16.0	10-37	.191	.059	.814
STAXI-OUT	14.5 (3.6)	14.0	8-28	.684	.627	.789
NEO-ANG	11.5 (5.3)	11.0	0-30	.502	.253	.813

*Skewness and kurtosis values reported for measures following logarithmic transformation.

positively, these measures were normalized using logarithmic transformations. Following transformation, skewness and kurtosis values for all measures fell within acceptable ranges; absolute values of skewness >3 (Curran, West, & Finch, 1997) and kurtosis >10 (DeCarlo, 1997) are considered serious departures from normality. Internal consistency reliability of these measures was good to excellent according to Cronbach's coefficient alphas ranging between .79 and .92. Comparison of men and women (Table 3 and Table 3.1) showed men to have higher scores on the CES-D and NEO-DEP depression measures (all p's <.05). Conversely, women had higher scores on the NEO-ANX and TCI-HA anxiety measures (all p's <.05). Comparison of White and Black subjects (Table 3 and Table 3.1) showed differences only on the CES-D depression measure on which Black subjects scored higher than White subjects (p <. 01).

Table 3. Mean scores of psychosocial measures among all subjects and in men and women and White and Black subjects separately.

	Total (n=653)	Men (n=320)	Women (n=333)	Statistic	p	White (n=550)	Black (n=103)	Statistic	p
Depression									
• BDI*	4.1 (5.0)	4.3 (5.5)	3.9 (4.5)	$t_{651} = 0.09$	.929	3.9 (4.5)	5.3 (7.2)	$t_{651} = -1.65$	.099
• CES-D*	7.8 (7.5)	8.4 (7.8)	7.2 (7.1)	$t_{651} = 2.50$	.013	7.4 (7.1)	9.6 (9.3)	$t_{651} = -2.76$	.006
• NEO-DEP	11.5 (5.9)	12.0 (5.9)	11.0 (5.9)	$t_{651} = 2.29$	.022	11.5 (6.0)	11.5 (5.7)	$t_{651} = -0.08$	.939
Anxiety									
• STAI-T*	32.5 (9.1)	32.8 (9.0)	32.1 (9.2)	$t_{651} = 1.18$	.240	32.3 (9.0)	33.3 (9.5)	$t_{651} = -1.02$	.308
• NEO-ANX	12.8 (5.3)	12.3 (4.9)	13.3 (5.5)	$t_{651} = -2.56$	.011	12.8 (5.3)	12.7 (4.9)	$t_{651} = 0.10$	.921
• TCI-HA	10.9 (6.9)	10.0 (6.8)	11.7 (6.9)	$t_{651} = -3.15$	.002	10.8 (7.0)	11.6 (6.6)	$t_{651} = -1.10$	.270
Anger									
• STAXI-T*	16.8 (4.1)	16.9 (4.3)	16.7 (3.8)	$t_{651} = 0.52$	.603	16.9 (4.0)	16.6 (4.1)	$t_{651} = 0.81$	.421
• STAXI-OUT	14.5 (3.6)	14.6 (3.5)	14.5 (3.6)	$t_{651} = 0.22$	.827	14.6 (3.5)	13.9 (3.8)	$t_{651} = 1.95$	.051
• NEO-ANGER	11.5 (5.3)	11.8 (5.3)	11.1 (5.2)	$t_{651} = 1.80$	.073	11.3 (5.4)	12.1 (4.4)	$t_{651} = -1.65$	.101

*Test statistic and p-value reported on logarithmically-transformed measures

Table 3.1. Mean scores of psychosocial measures among White and Black men and women.

	Men (n=320)		Statistic	p	Women (n=333)		Statistic	p
	White (n=272)	Black (n=48)			White (n=278)	Black (n=55)		
Depression								
• BDI*	3.9 (4.7)	6.7 (8.6)	$t_{318} = -2.38$	.018	3.9 (4.2)	4.0 (5.4)	$t_{331} = 0.05$	.961
• CES-D*	7.9 (7.2)	11.0 (10.4)	$t_{318} = -2.27$	.024	6.9 (6.9)	8.4 (8.1)	$t_{331} = -1.75$	.081
• NEO-DEP	12.0 (6.0)	12.5 (5.4)	$t_{318} = -0.52$	.601	11.0 (5.9)	10.7 (5.8)	$t_{331} = 0.32$	.746
Anxiety								
• STAI-T*	32.5 (8.8)	34.8 (9.8)	$t_{318} = -1.53$	.127	32.2 (9.2)	32.1 (9.0)	$t_{331} = -0.01$	.989
• NEO-ANX	12.1 (5.1)	12.9 (4.2)	$t_{318} = -0.99$	.319	13.4 (5.5)	12.6 (5.5)	$t_{331} = 1.04$	.298
• TCI-HA	9.7 (6.8)	12.0 (6.5)	$t_{318} = -2.19$	.030	11.8 (7.0)	11.2 (6.6)	$t_{331} = 0.59$	.554
Anger								
• STAXI-T*	17.0 (4.3)	16.5 (4.4)	$t_{318} = 0.96$	.338	16.7 (3.8)	16.7 (3.8)	$t_{331} = 0.15$	.882
• STAXI-OUT	14.7 (3.5)	13.8 (3.5)	$t_{318} = 1.69$	.092	14.6 (3.5)	14.0 (4.1)	$t_{331} = 1.09$	.279
• NEO-ANGER	11.7 (5.4)	12.7 (4.4)	$t_{318} = -1.28$	.203	10.9 (5.4)	11.6 (4.4)	$t_{331} = -0.83$	.406

*Test statistic and p-value reported on logarithmically-transformed measures

Descriptive information for HF, LF, and LF:HF indices of heart rate variability are summarized in Table 4. All power estimates were normalized using logarithmic transformations.

Table 4. Mean scores of HRV measures among all subjects and in men and women and White and Black subjects.

	Total (n=653)	Men (n=320)	Women (n=333)	Statistic	p
HRV					
• HF-HRV*	8.91 (1.26)	8.64 (1.24)	9.19 (1.21)	$t_{651} = -5.73$	.000
• LF-HRV*	8.84 (1.15)	8.93 (1.13)	8.75 (1.16)	$t_{651} = 2.03$	.042
• LF:HF-HRV*	-0.08 (1.28)	0.30 (1.29)	-0.43 (1.17)	$t_{651} = 7.58$	.000
HRV					
		White (n=550)	Black (n=103)	Statistic	p
• HF-HRV*		8.86 (1.27)	9.23 (1.12)	$t_{651} = -2.76$	.006
• LF-HRV*		8.88 (1.17)	8.65 (1.01)	$t_{651} = 1.88$	.061
• LF:HF-HRV*		0.02 (1.27)	-0.58 (1.7)	$t_{651} = 4.42$	.000

*Test statistic and p-value reported on logarithmically-transformed measures

Statistically significant differences were found between men and women and White and Black subjects. Women exhibited higher HF-HRV and lower LF-HRV and LF:HF-HRV than men (all p's <.05). Similarly, Black subjects exhibited higher HF-HRV and lower LF-HRV and LF:HF-HRV than White subjects (all p's <.07).

3.2 Bivariate correlations

Univariate associations among the depression, anxiety, and anger-related psychosocial questionnaire measures are displayed in Table 5. Correlations were small to large in size, ranging between .20 and .74. All correlation coefficients were significant at the p <.001 level.

Table 5. Bivariate correlations among psychosocial measures of depression, anxiety, and anger.

	DEPRESSION			ANXIETY			ANGER		
	BDI*	CES-D*	NEO-DEP	STAI-T*	NEO-ANX	TCI-HA	STAXI-T*	STAXI-OUT	NEO-ANG
BDI*	-	.667 .000	.536 .000	.674 .000	.411 .000	.412 .000	.280 .000	.235 .000	.386 .000
CES-D*		-	.562 .000	.708 .000	.459 .000	.388 .000	.288 .000	.224 .000	.397 .000
NEO-DEP			-	.741 .000	.676 .000	.573 .000	.363 .000	.282 .000	.580 .000
STAI-T*				-	.637 .000	.598 .000	.431 .000	.328 .000	.565 .000
NEO-ANX					-	.614 .000	.330 .000	.217 .000	.490 .000
TCI-HA						-	.342 .000	.202 .000	.428 .000
STAXI-T*							-	.591 .000	.623 .000
STAXI-OUT								-	.533 .000
NEO-ANG									-

*Variables logarithmically-transformed.

Univariate associations between the psychosocial questionnaire measures and the demographic and cardiovascular risk factors and the indices of HRV are summarized in Table 6. Overall, lower education and income were related to higher depression, anxiety, and anger scale scores. Greater age was related to lower depression (NEO-DEP), anxiety (STAI-T), and anger (STAXI-T, STAXI-OUT, NEO-ANG) (p's <.05). Being married was also related to lower depression (BDI, CES-D, NEO-DEP), anxiety (STAI-T), and anger (NEO-ANG) (p's <.05) while current/past smoking was related to greater depression (BDI) and anger (STAXI-OUT) (p's <.05). With respect to HRV, higher HF-HRV was related to lower depression (BDI, CES-D, NEO-DEP) and anxiety (STAI-T) (p's <.01). Higher LF-HRV was related to lower depression (BDI, CES-D) only and higher LF:HF-HRV was related to higher anxiety (STAI-T) (p's <.05).

Table 6. Bivariate correlations between psychosocial measures of depression, anxiety, and anger and demographic and cardiovascular risk factors and HRV indices.

	DEPRESSION			ANXIETY			ANGER		
	BDI*	CES-D*	NEO-DEP	STAI-T*	NEO-ANX	TCI-HA	STAXI-T*	STAXI-OUT	NEO-ANG
Sex	-.004	-.097	-.089	-.046	.100	.123	-.020	-.009	-.070
	.929	.013	.022	.240	.011	.002	.602	.827	.073
Race	.065	.107	.003	.040	-.004	.043	-.032	-.076	.056
	.099	.006	.939	.308	.921	.270	.421	.051	.150
Age	.017	-.042	-.084	-.111	-.055	-.033	-.157	-.085	-.105
	.672	.279	.032	.004	.161	.401	.000	.030	.007
Education	-.099	-.092	-.051	-.078	-.064	-.108	.002	-.114	-.147
	.011	.019	.192	.046	.103	.006	.967	.004	.000
Individual Income	-.106	-.116	-.111	-.130	-.145	-.208	.015	-.100	-.054
	.038	.023	.029	.011	.005	.000	.773	.051	.289
Family Income	-.130	-.247	-.197	-.214	-.102	-.142	-.050	-.091	-.193
	.001	.000	.000	.000	.010	.000	.203	.021	.000
Marital Status	.115	.156	.112	.115	.024	-.009	.019	.041	.093
	.003	.000	.004	.003	.548	.811	.622	.295	.018
BMI	.133	.081	.055	.081	.009	.030	.101	.049	.070
	.001	.039	.163	.040	.815	.448	.010	.208	.074
Smoking	.097	.047	.014	.044	-.019	-.005	.006	.107	.066
	.013	.231	.729	.259	.627	.905	.873	.006	.093
SBP	-.016	.035	-.005	-.019	-.015	-.039	-.030	-.012	.039
	.679	.370	.896	.620	.707	.322	.445	.756	.321
DBP	.030	.068	.031	.016	-.007	.014	-.010	-.038	.066
	.442	.086	.426	.683	.868	.720	.793	.329	.092
HF-HRV*	-.168	-.149	-.104	-.111	-.054	-.021	.041	-.003	.026
	.000	.000	.008	.004	.169	.600	.301	.937	.512
LF-HRV*	-.099	-.080	-.037	-.026	-.061	-.034	.023	-.014	-.002
	.011	.042	.339	.510	.116	.388	.560	.726	.962
LF:HF-HRV*	.075	.075	.068	.086	-.002	-.010	-.019	-.009	-.027
	.055	.056	.082	.028	.953	.795	.624	.813	.494

*Variables logarithmically-transformed.
Sex coded 1=men, 2=women; Race coded 1=White, 2=Black; Individual and family income coded 1=<$10, 000, 2=$10,000-14,999, 3=$15,000-$24,999, 4=$25,000-$34,999, 5=$35,000-$49,999, 6=$50,000-$64,999, 7=$65,000-$80,000 8=>$80,000; Marital status coded 1=married, 2=other; Smoking coded 1=never smoked, 2=current/past smoking.

Univariate associations between the indices of HRV and the demographic and cardiovascular risk factors are summarized in Table 7. Women and Black subjects exhibited higher HF-HRV and lower LF-HRV and LF:HF-HRV (p's <.07). Greater age was related to HF-HRV and LF-HRV negatively and greater education was related to LF-HRV and LF:HF-HRV positively (p's <.05). Finally, higher SBP was related to lower HF-HRV and LF-HRV while higher DBP was related to lower HF-HRV and higher LF:HF-HRV (p's <.01).

Table 7. Bivariate correlations between indices of HRV (HF-HRV, LF-HRV, LF:HF-HRV) and demographic and cardiovascular risk factors.

	HF-HRV	LF-HRV	LF:HF-HRV
Sex (1=men, 2=women)	.219 .000	-.079 .042	-.285 .000
Race (1=White, 2=Black)	.107 .006	-.073 .061	-.171 .000
Age (years)	-.370 .000	-.379 .000	.023 .558
Education (in years)	-.038 .335	.101 .010	.128 .001
Ind Income (coded 1-8)*	-.078 .129	.008 .881	.082 .111
Fam Income (coded 1-8)*	-.052 .187	-.005 .906	.047 .235
Marital Status (1=married, 2=other)	-.072 .066	.000 .998	.070 .072
Body Mass Index (BMI)	-.013 .740	-.002 .960	.011 .778
Smoking (1=never, 2=current, past)	.011 .784	-.056 .152	-.061 .122
SBP (mm Hg)	-.127 .001	-.107 .006	.028 .478
DBP (mm Hg)	-.110 .005	.000 .999	.108 .006

*Individual and family income: 1=<$10, 000, 2=$10,000-14,999, 3=$15,000-$24,999, 4=$25,000-$34,999, 5=$35,000-$49,999, 6=$50,000-$64,999, 7=$65,000-$80,000 8=>$80,000

3.3 Hypothesis 1: Is depression related to variation in autonomic control of heart rate?

3.3.1 Factor analysis of depression scales.

As summarized in Table 8, factor analysis was performed on the full sample (n=653) to examine the factor structure underlying subjects' responses on three depression-related self-report questionnaires (BDI, CES-D, NEO-DEP). The total scores of each measure were entered

Table 8. Factor analysis of depression scales in full sample (N=653).

Items	Factor Loadings (h)	Communalities (h^2)	Variance Explained (%)
BDI*	.798	.637	
CES-D*	.835	.697	
NEO-DEP	.673	.453	
Depression Factor			59.5%

*Measure logarithmically transformed.

simultaneously into the analysis. Factor extraction was based on principal axis factoring methods. Results showed a single factor, labeled "depression factor", to account for 59.5% of the variance in the depression-related measures; the eigenvalue for this factor (2.178) well exceeded the convention of 1 for factor extraction. Evidence that a single factor solution best fits the data was provided by visual inspection of the scree plot (eigenvalues plotted against factors), as well as examination of the residual correlation matrix showing differences between the observed and reproduced correlations to approximate 0. Internal consistency of the factor was good and the factor well defined by its items as indicated by high correlations between the depression factor and each measure: BDI (r=.80), CES-D (r=.84), and NEO-DEP (r=.67). Moreover, communality estimates were high, showing the depression factor to account for 64% of the variance in BDI scores, 70% of the variance in CES-D scores, and 45% of the variance in NEO-DEP scores.

As summarized in Table 9 and Table 10, factor analysis of depression scales examined in men and women separately and in White and Black subjects separately produced a single factor structure similar to findings reported in the full sample. Because this factor structure was invariant across sex and race sub-samples, the depression factor score from the full sample was retained for use in subsequent analyses.

Table 9. Factor analysis of depression scales in men (n=320) and women (n=333) separately.

Items	Factor Loadings (h)		Communalities (h^2)		Variance Explained (%)	
	Men	Women	Men	Women	Men	Women
BDI*	.821	.789	.674	.623		
CES-D*	.798	.869	.637	.756		
NEO-DEP	.674	.664	.454	.440		
Depression Factor					58.8%	60.6%

*Measure logarithmically transformed.

Table 10. Factor analysis of depression scales in White (n=550) and Black (n=103) subjects separately.

Items	Factor Loadings (h)		Communalities (h^2)		Variance Explained (%)	
	White	Black	White	Black	White	Black
BDI*	.809	.731	.654	.534		
CES-D*	.835	.835	.697	.698		
NEO-DEP	.676	.677	.457	.458		
Depression Factor					60.3%	56.3%

*Measure logarithmically transformed.

3.3.2 Multiple regression.

As summarized in Table 11, a series of multiple regression analyses were performed to assess the relationship between the depression factor score, derived from factor analysis (see results above), and three frequency domain indices of heart rate variability (HF-HRV, LF-HRV, LF:HF-HRV).

Table 11. Multiple regression analyses assessing the relationship between depression (depression factor score) and HRV (HF-HRV, LF-HRV, LF:HF-HRV) in the full sample.

	β	p	R^{2b}	ΔR^{2b}	b	95% CI (b)	
DV: HF-HRV							
1. Depression F-score	-.169	.000	.029	-	-.233	-.338	-.129
After covariate-adjustment[a]:							
1. Covariates	-	-	.204	-	-	-	-
2. Depression F-score	-.182	.000	.236	.032	-.253	-.349	-.157
DV: LF-HRV							
1. Depression F-score	-.090	.021	.008	-	-.114	-.210	-.017
After covariate-adjustment[a]:							
1. Covariates	-	-	.171	-	-	-	-
2. Depression F-score	-.106	.004	.182	.011	-.133	-.223	-.043
DV: LF:HF-HRV							
1. Depression F-score	.085	.030	.007	-	.120	.012	.228
After covariate-adjustment[a]:							
1. Covariates	-	-	.123	-	-	-	-
2. Depression F-score	.085	.025	.130	.007	.120	.015	.224

[a]Covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) were entered on the first step of each regression equation.
[b]R^2 and ΔR^2 values are reported for the final model of each regression equation.

These associations were first examined alone and then with covariate-adjustment by entering covariates simultaneously on the first step of each regression equation. Covariates included the following demographic and cardiovascular risk factors: gender (1=men, 2=women), age (in years), race (1=White, 2=Black), education (years in school), smoking status (1=never, 2=ever/current), and body mass index, and systolic and diastolic blood pressure (mean of two separate clinic assessments).

Multiple regression analyses showed higher depression factor scores to predict lower HF-HRV ($\beta = -.169$, $t_{(1, 651)} = -4.384$, $p = .000$). This relationship persisted after covariates were entered into the model ($\beta = -.182$, $t_{(9, 643)} = -5.172$, $p = .000$). Demographic and cardiovascular risk factors accounted for 20.4% and depression factor scores an additional 3.2% of the variance

in HF-HRV; this addition to the model was statistically significant (F_{change} = 26.754, p = .000). Gender, age, and race correlated significantly with HF-HRV in the final model; women (β = .221) and Black subjects (β = .076) exhibited higher HF-HRV while advancing age (β = -.387) was associated with lower HF-HRV (all p's <.05). Similarly, higher depression factor scores were associated with lower LF-HRV (β = -.090, $t_{(1, 651)}$ = -2.312, p = .021). This relationship also persisted after covariate-adjustment (β = -.106, $t_{(9, 643)}$ = -2.898, p = .004). Demographic and cardiovascular risk factors accounted for 17.1% and depression factor scores an additional 1.1% of the variance in LF-HRV; this addition to the model was statistically significant (F_{change} = 8.401, p = .004). Age, SBP, and DBP correlated significantly with LF-HRV in the final model; older age (β = -.371) and higher SBP (β = -.180) were associated with lower LF-HRV and higher DBP (β = .172) was associated with higher LF-HRV (all p's <.01). In contrast, higher depression factors scores were associated with *higher* LF:HF-HRV both before (β = .085, $t_{(1, 651)}$ = 2.175, p = .030) and after covariate-adjustment (β = .085, $t_{(9, 643)}$ = 2.254, p = .025). Demographic and cardiovascular risk factors accounted for 12.3% and depression factor scores an additional 0.7% of the variance in LF:HF-HRV; this addition to the model was statistically significant (F_{change} = 5.082, p = .025). Women (β = -.268) and Black subjects (β = -.134) exhibited lower LF:HF-HRV; greater education (β = .106) and higher DBP (β = .147) were related to higher LF:HF-HRV while higher SBP (β = -.136) was related to lower LF:HF-HRV (all p's <.05).

3.3.3 Structural equation modeling.

The relationship between depression and HRV was reexamined using structural equation modeling. The conceptual model representing Hypothesis 1 is depicted in Figure 1.

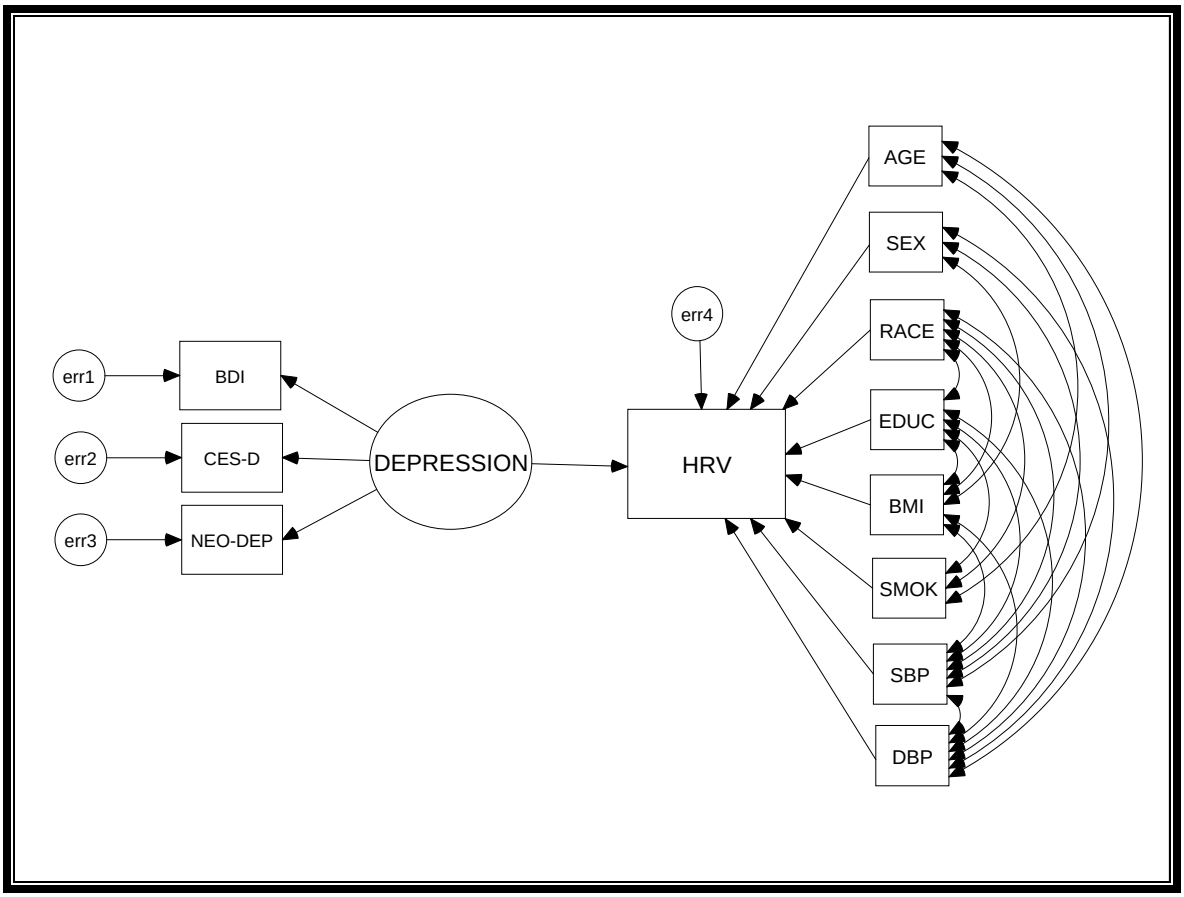

Figure 1, Hypothesis 1. Conceptual model depicting the relationship between depression and HRV (HF-HRV, LF-HRV, LF:HF-HRV).

Indicators (observed variables) of the latent construct of depression included the same three depression-related self-report questionnaires (BDI, CES-D, NEO-DEP) used in the factor analysis/regression approach described above. The latent construct of depression was scaled by constraining one of the factor loading parameters to a value of 1.0. CES-D was chosen as the reference item because it has the highest factor loading on depression and has high internal consistency reliability (Cronbach's coefficient $\alpha = .90$). In this model, there were 78 distinct sample moments (data points [12(12 + 1)/2]) and 42 unknown parameters to be estimated (i.e. 11 regression paths, 13 variances [4 error variances], and 18 covariances) resulting in 36 degrees of freedom. Three separate analyses were conducted examining HF, LF, and LF:HF HRV

individually as the dependent measures with covariate-adjustment (age, sex, race, education, BMI, smoking status, SBP, and DBP).

3.3.3.1 HF-HRV. With respect to HF-HRV, the chi-square test statistic $\chi^2(36, N=653) = 73.317$, $p<.001$ showed poor overall model fit. The chi-square test statistic, however, is dependent on sample size and subject to type II error in large samples. Thus, several other fit indices were also examined. The normed chi-square index (χ^2/df) = 2.037 fell below the cutoff value of 5, indicating good model fit (Bollen, 1989). Moreover, the root mean square error of approximation (RMSEA) = .040, 90% CI = .027-.053, p = .895 and the comparative fit index (CFI) = .978 both suggested close model fit. RMSEA values $\leq$ .05 (Brown & Cudeck, 1993) and CFI values > .95 (Hu & Bentler, 1999) reflect good model fit. Finally, the Akaike information criterion (AIC) = 157.317; this value may be used to compare non-hierarchical (non-nested) models, with smaller values indicating better fit. The standardized residual matrix was examined as a supplement to formal tests of model fit. Values deviating substantially from zero (i.e. perfect model fit) reflect discrepancies between the model-implied population and sample covariance matrices. In this model only 1.3% of data points were > 2.58 or considered "large" (Joreskog & Sorbom, 1988). A detailed description of the fit indices is found in the data analysis section and the fit indices for all models summarized in Table 12.

Table 12. Summary of fit indices comparing models testing Hypotheses 1-6.

	Cut-off values for adequate model fit	Hypothesis 1	Hypothesis 2	Hypothesis 3	Hypothesis 4 (Full Model)	Hypothesis 5 (Full Model)	Hypothesis 6 (Full Model) with depression and anger paths
HF-HRV							
(1) chi-square (χ^2)	P = n.s.	73.317	88.587	101.416	1323.629	412.779	400.421
df		36	36	36	111	111	109
$P_{chi\text{-}square}$		P <.001	P <.001	P <.001	P <.001	P <.001	P <.001
(2) normed (χ^2 / df)	5.0	2.037	2.461	2.817	11.925	3.719	3.674
(3) RMSEA	$\leq$ .08	.040	.047	.053	.129	.065	.064
90% CI		.027 - .053	.035 - .060	.041 - .065	.123 - .136	.058 - .071	.057 - .071
$P_{RMSEA \leq .05}$		P =.895	P = .618	P = .334	P = .000	P = .000	P = .000
(4) CFI	> .95	.978	.970	.961	.727	.932	.934
(5) AIC*	n.a.	157.317	172.587	185.416	1443.629	532.779	524.421
LF-HRV							
(1) chi-square (χ^2)	P = n.s.	72.225	82.990	100.512	1321.850	401.332	-
df		36	36	36	111	111	-
$P_{chi\text{-}square}$		P <.001	P <.001	P <.001	P <.001	P <.001	-
(2) normed (χ^2 / df)	5.0	2.006	2.305	2.792	11.925	3.616	-
(3) RMSEA	$\leq$ .08	.039	.045	.052	.129	.063	-
90% CI		.026 - .052	.032 - .057	.040 - .065	.123 - .136	.057 - .070	-
$P_{RMSEA \leq .05}$		P =.908	P = .738	P = .352	P = .000	P = .001	-
(4) CFI	> .95	.978	.973	.961	.727	.934	-
(5) AIC*	n.a.	156.225	166.990	184.512	1441.850	521.332	-
LF:HF-HRV							
(1) chi-square (χ^2)	P = n.s.	73.005	85.708	100.956	1323.773	403.760	-
df		36	36	36	111	111	-
$P_{chi\text{-}square}$		P <.001	P <.001	P <.001	P <.001	P <.001	-
(2) normed (χ^2 / df)	5.0	2.028	2.381	2.804	11.926	3.637	-
(3) RMSEA	$\leq$ .08	.040	.046	.053	.129	.064	-
90% CI		.026 - .053	.034 - .059	.041 - .065	.123 - .136	.057 - .070	-
$P_{RMSEA \leq .05}$		P = .899	P = .682	P = .343	P = .000	P = .000	-
(4) CFI	> .95	.978	.971	.960	.722	.933	-
(5) AIC*	n.a.	157.005	169.708	184.956	1443.773	523.760	-

Estimates of regression weights are summarized in Table 13 and represented in Figure 2.

Table 13. Estimates of regression weights derived from structural equation modeling of relationship between depression and HF-HRV (Hypothesis 1, Figure 2).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Depression → HF-HRV	-.199	-.330	.064	-5.135	<.001
Depression → BDI	.801	.971	.056	17.370	<.001
Depression → CES-D	.833	1.000	-	-	-
Depression → NEO-DEP	.671	5.233	.326	16.061	<.001
Age → HF-HRV	-.384	-.069	.006	-10.935	<.001
Sex → HF-HRV	.218	.550	.092	5.996	<.001
Race → HF-HRV	.077	.267	.124	2.150	.032
Education → HF-HRV	-.059	-.024	.015	-1.629	.103
BMI → HF-HRV	.009	.002	.008	.252	.801
Smoking → HF-HRV	.033	.084	.091	.924	.355
SBP → HF-HRV	-.026	-.002	.005	-.482	.629
DBP → HF-HRV	.006	.001	.008	.109	.914

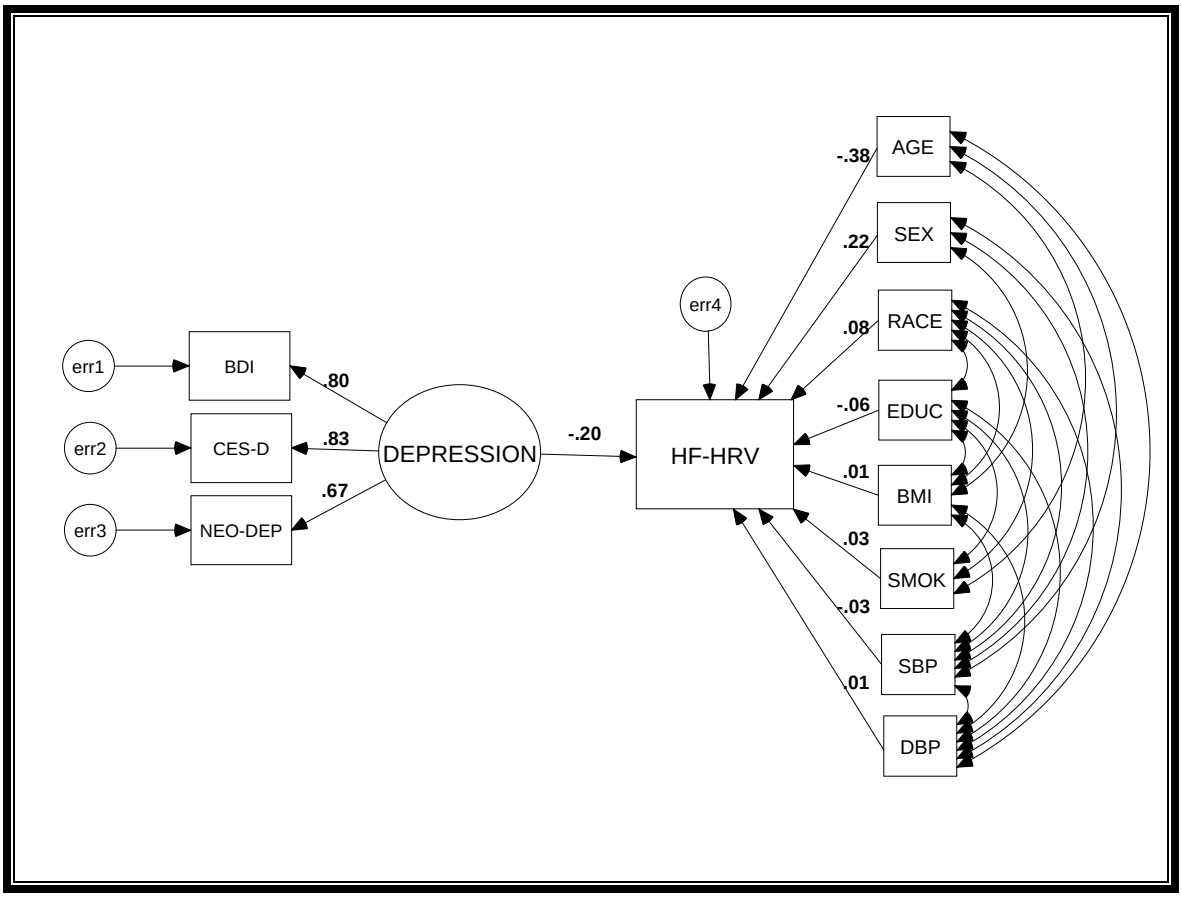

Figure 2, Hypothesis 1. Standardized estimates of relationship between depression and HF-HRV.

The unstandardized path coefficient between the latent construct of depression and HF-HRV was -.330, indicating that a 1-point increase in depression predicts a .330-point decrease in HF-HRV (with covariate adjustment); this path was significant at the .001 level. The standardized estimate of this relationship showed a 1 standard deviation increase in depression to correspond to a .199 decrease in HF-HRV (with covariate adjustment). Examination of the squared multiple correlations (SMCs) showed the latent construct of depression to explain 64.2% of the variance in BDI, 69.4% in CES-D, and 45.1% in NEO-DEP. Depression as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 25.2% of the variance in HF-HRV.

3.3.3.2 LF-HRV. With respect to LF-HRV, the chi-square test statistic $\chi^2(36, N=653) = 72.225$, $p<.001$ also showed poor overall model fit. Again, however, the normed chi-square index (χ^2/df) = 2.006, RMSEA = .039, 90% CI = .026-.052, p = .908, and the CFI = .978 all indicated close model fit. The AIC = 156.225 and 2.6% of values in the standardized residual matrix were > 2.58. See Table 12.

Estimates of regression weights are summarized in Table 14 and represented in Figure 3.

Table 14. Estimates of regression weights derived from structural equation modeling of relationship between depression and LF-HRV (Hypothesis 1, Figure 3).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Depression → LF-HRV	-.117	-.176	.060	-2.951	.003
Depression → BDI	.798	.963	.056	17.235	<.001
Depression → CES-D	.836	1.000	-	-	-
Depression → NEO-DEP	.672	5.223	.328	15.933	<.001
Age → LF-HRV	-.369	-.060	.006	-10.104	<.001
Sex → LF-HRV	-.067	-.153	.087	-1.771	.077
Race → LF-HRV	-.074	-.232	.117	-1.976	.048
Education → LF-HRV	.050	.019	.014	1.338	.181
BMI → LF-HRV	.014	.003	.008	.363	.717
Smoking → LF-HRV	.016	.038	.086	.444	.657
SBP → LF-HRV	-.193	-.016	.005	-3.453	<.001
DBP → LF-HRV	.179	.023	.007	3.203	<.001

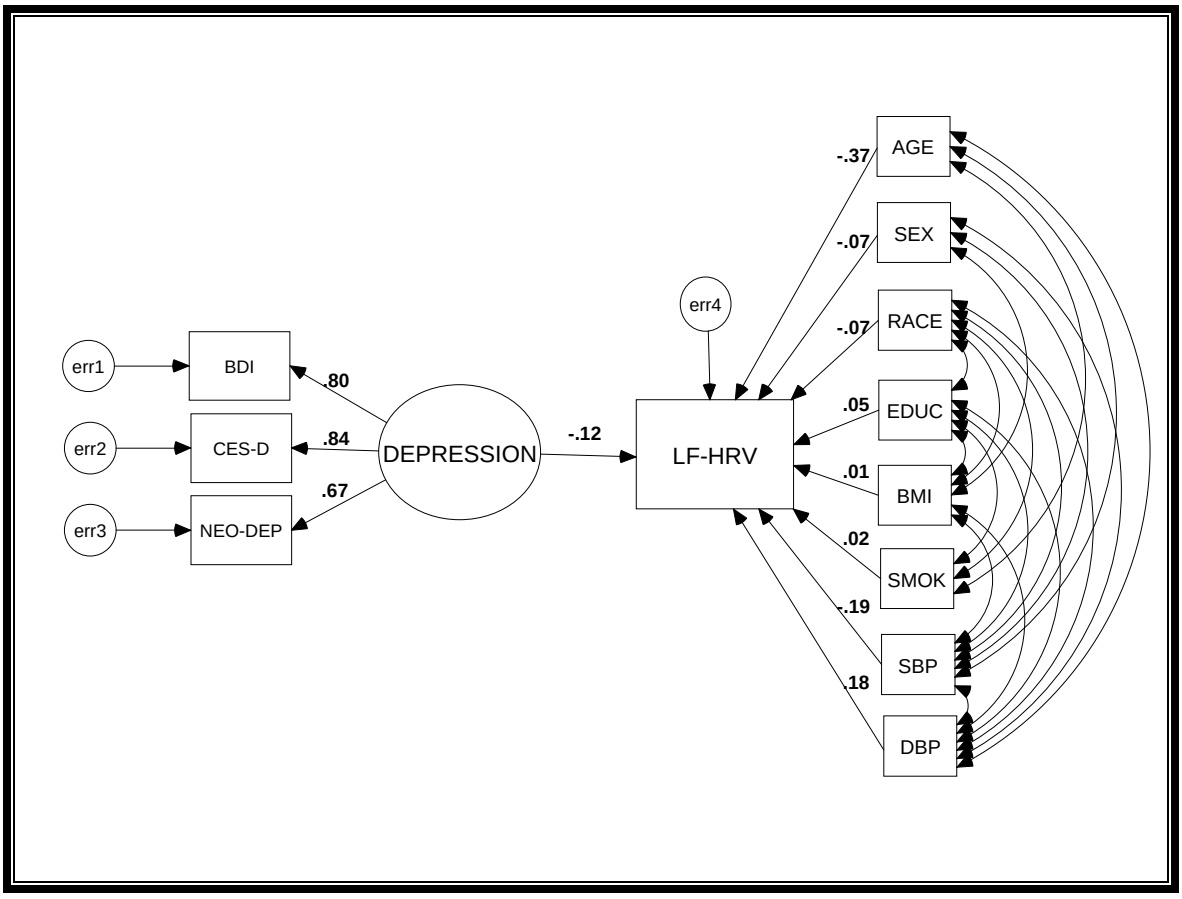

Figure 3, Hypothesis 1. Standardized estimates of relationship between depression and LF-HRV.

The unstandardized path coefficient between the latent construct of depression and LF-HRV was -.176, indicating that a 1-point increase in depression predicts a .176-point decrease in LF-HRV (with covariate-adjustment); this path was significant at the .01 level. The standardized estimate of this relationship showed a 1 standard deviation increase in depression to correspond to a .117 decrease in LF-HRV (with covariate adjustment). Examination of the SMCs showed the latent construct of depression to explain 63.6% of the variance in BDI, 69.8% in CES-D, and 45.2% in NEO-DEP. Depression as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 18.8% of the variance in LF-HRV.

3.3.3.3 LF:HF-HRV. With respect to LF:HV-HRV, fit indices showed a similar pattern of results. While the chi-square test statistic $\chi^2(36, N=653) = 73.005$, $p<.001$ showed poor overall model fit, the normed chi-square index (χ^2/df) = 2.028, RMSEA = .040, 90% CI = .026-.053, p = .899, and the CFI = .978 all showed close model fit. The AIC = 157.005 and 2.6% of values in the standardized residual matrix were > 2.58. See Table 12.

Estimates of regression weights are summarized in Table 15 and represented in Figure 4.

Table 15. Estimates of regression weights derived from structural equation modeling of relationship between depression and LF:HF-HRV (Hypothesis 1, Figure 4).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Depression → LF:HF-HRV	.091	.153	.069	2.228	.026
Depression → BDI	.799	.965	.056	17.168	<.001
Depression → CES-D	.835	1.000	-	-	-
Depression → NEO-DEP	.672	5.225	.328	15.930	<.001
Age → LF:HF-HRV	.048	.009	.007	1.289	.198
Sex → LF:HF-HRV	-.274	-.703	.100	-7.059	<.001
Race → LF:HF-HRV	-.142	-.500	.135	-3.699	<.001
Education → LF:HF-HRV	.103	.043	.016	2.663	.008
BMI → LF:HF-HRV	.003	.001	.009	.087	.931
Smoking → LF:HF-HRV	-.018	-.046	.099	-.462	.644
SBP → LF:HF-HRV	-.147	-.014	.055	-2.559	.010
DBP → LF:HF-HRV	.154	.022	.008	2.685	.007

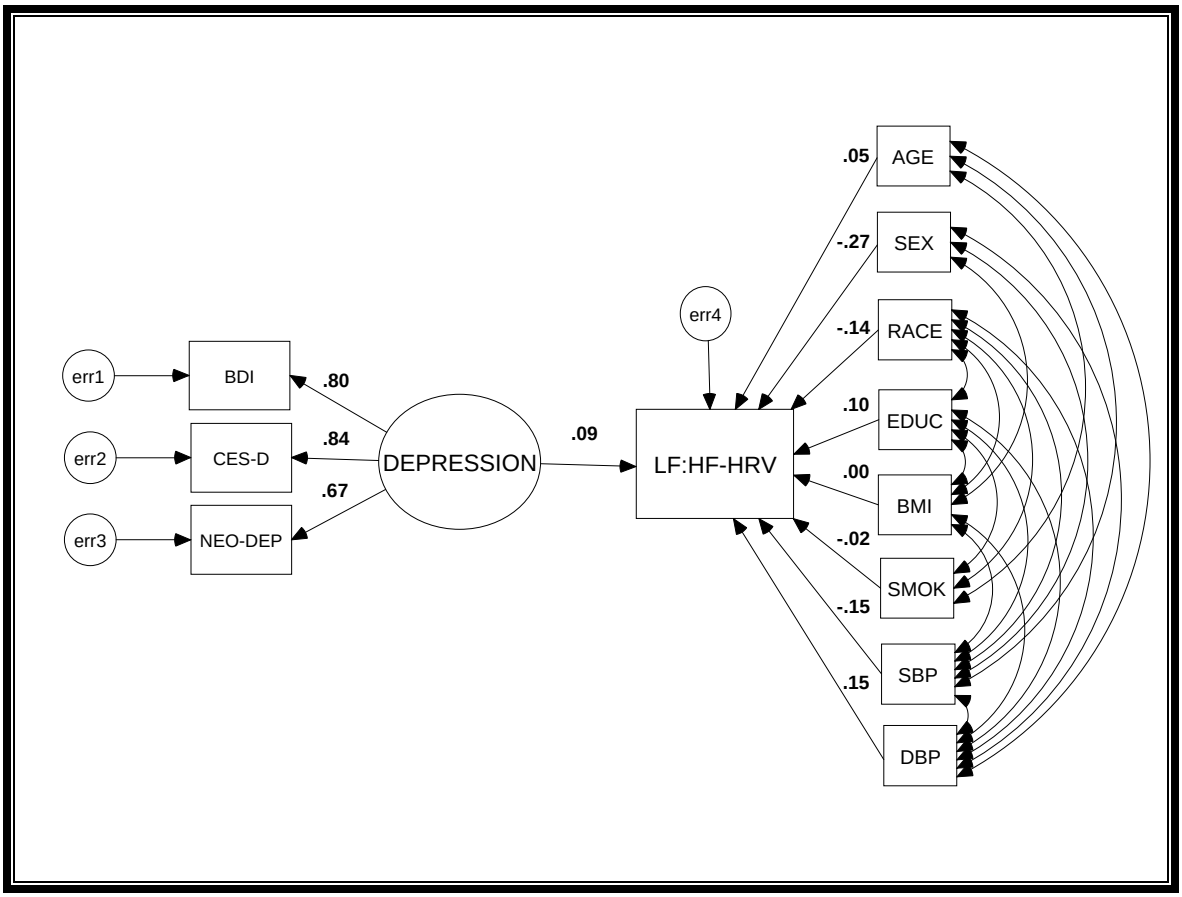

Figure 4, Hypothesis 1. Standardized estimates of relationship between depression and LF:HF-HRV.

The unstandardized path coefficient between the latent construct of depression and LF:HF-HRV was .153, indicating that a 1-point increase in depression predicts a .153-point *increase* in LF:HV-HRV (with covariate-adjustment); this path was significant at the .05 level. The standardized estimate of this relationship showed a 1 standard deviation increase in depression to correspond to a .091 *increase* in LF:HF-HRV (with covariate-adjustment). Examination of the SMCs showed the latent construct of depression to explain 63.8% of the variance in BDI, 69.7% in CES-D, and 45.2% in NEO-DEP. Depression as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 13.7% of the variance in LF:HF-HRV.

3.4 Hypothesis 2: Is anxiety related to variation in autonomic control of heart rate?

3.4.1 Factor analysis of anxiety scales.

As summarized in Table 16, factor analysis was performed on the full sample (n=653) to examine the factor structure underlying subjects' responses on three anxiety-related self-report questionnaires (STAI-T, NEO-ANX, TCI-HA). The total scores of each measure were entered

Table 16. Factor analysis of anxiety scales in full sample (N=653).

Items	Factor Loadings (h)	Communalities (h^2)	Variance Explained (%)
STAI-T*	.787	.620	
NEO-ANX	.808	.653	
TCI-HA	.760	.578	
Anxiety Factor			61.7%

*Measure logarithmically transformed.

simultaneously into the analysis. Factor extraction was based on principal axis factoring methods. Results showed a single factor, labeled "anxiety factor", to account for 61.7% of the variance in the anxiety-related measures; the eigenvalue for this factor (2.233) well exceeded the convention of 1 for factor extraction. Evidence that a single factor solution best fits the data was provided by visual inspection of the scree plot (eigenvalues plotted against factors), as well as examination of the residual correlation matrix showing differences between the observed and reproduced correlations to approximate 0. Internal consistency of the factor was good and the factor well defined by its items as indicated by high correlations between the anxiety factor and each measure: STAI-T (r=.79), NEO-ANX (r=.81), and TCI-HA (r=.76). Moreover, communality estimates were high, showing the anxiety factor to account for 62% of the variance

in STAI-T scores, 65% of the variance in NEO-ANX scores, and 58% of the variance in TCI-HA scores.

As summarized in Table 17 and Table 18, factor analysis of anxiety items examined in men and women separately and in White and Black subjects separately produced a single factor structure similar to findings reported in the full sample. Because this factor structure was invariant across sex and race sub-samples, the anxiety factor score from the full sample was retained for use in subsequent analyses.

Table 17. Factor analysis of anxiety scales in men (n=320) and women (n=333) separately.

Items	Factor Loadings (h)		Communalities (h^2)		Variance Explained (%)	
	Men	Women	Men	Women	Men	Women
STAI-T*	.829	.784	.687	.614		
NEO-ANX	.734	.864	.539	.746		
TCI-HA	.732	.779	.536	.607		
Anxiety Factor					58.8%	65.6%

*Measure logarithmically transformed.

Table 18. Factor analysis of anxiety scales in White (n=550) and Black (n=103) subjects separately.

Items	Factor Loadings (h)		Communalities (h^2)		Variance Explained (%)	
	White	Black	White	Black	White	Black
STAI-T*	.772	.898	.596	.806		
NEO-ANX	.826	.713	.682	.508		
TCI-HA	.768	.697	.589	.485		
Anxiety Factor					62.3%	60.0%

*Measure logarithmically transformed.

3.4.2 Multiple regression.

As summarized in Table 19, a series of multiple regression analyses were performed to assess the relationship between the anxiety factor score, derived from factor analysis (see results above),

and three frequency domain indices of heart rate variability (HF-HRV, LF-HRV, and LF:HF-HRV). These associations were first examined alone and then with covariate-adjustment by entering covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) simultaneously on the first step of each regression equation.

Table 19. Multiple regression analyses assessing the relationship between anxiety (anxiety factor score) and HRV (HF-HRV, LF-HRV, LF:HF-HRV) in the full sample.

	β	P	R^{2b}	ΔR^{2b}	b	95% CI (b)	
DV: HF-HRV							
1. Anxiety F-score	-.073	.061	.005	-	-.101	-.207	.005
After covariate-adjustment[a]:							
1. Covariates	-	-	.204	-	-	-	-
2. Anxiety F-score	-.134	.000	.222	.018	-.186	-.282	-.089
DV: LF-HRV							
1. Anxiety F-score	-.048	.220	.002	-	-.061	-.157	.036
After covariate-adjustment[a]:							
1. Covariates	-	-	.171	-	-	-	-
2. Anxiety F-score	-.081	.027	.177	.006	-.102	-.192	-.011
DV: LF:HF-HRV							
1. Anxiety F-score	.029	.464	.001	-	.040	-.068	.149
After covariate-adjustment[a]:							
1. Covariates	-	-	.124	-	-	-	-
2. Anxiety F-score	.060	.112	.127	.003	.084	-.020	.188

[a]Covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) were entered on the first step of each regression equation.
[b]R^2 and ΔR^2 values are reported for the final model of each regression equation.

Multiple regression analyses showed a statistical trend for higher anxiety factor scores to predict lower HF-HRV ($\beta = -.073$, $t_{(1, 651)} = -1.876$, $p = .061$). This relationship reached statistical significance after covariates were entered into the model ($\beta = -.134$, $t_{(9, 643)} = -3.784$, $p = .000$). Demographic and cardiovascular risk factors accounted for 20.4% and anxiety factor scores an additional 1.8% of the variance in HF-HRV; this addition to the model was statistically significant ($F_{change} = 14.321$, $p = .000$). Sex and age correlated significantly with HF-HRV in the final model; women ($\beta = .221$) exhibited higher HF-HRV while advancing age ($\beta = -.387$) was associated with lower HF-HRV (all p's <.05). Similarly, higher anxiety factor scores were associated with lower LF-HRV but only following covariate-adjustment ($\beta = -.081$, $t_{(9, 643)} = -2.214$, $p = .027$). Demographic and cardiovascular risk factors accounted for 17.1% and anxiety

factor scores an additional 0.6% of the variance in LF-HRV; this addition to the model was statistically significant (F_{change} = 4.902, p = .027). Age, SBP, and DBP correlated significantly with LF-HRV in the final model; older age (β = -.376) and higher SBP (β = -.173) were associated with lower LF-HRV and higher DBP (β = .170) was associated with higher LF-HRV (all p's <.01). In contrast, anxiety factor scores were not associated with LF:HF-HRV either before or after covariate-adjustment (β = .029, $t_{(1, 651)}$ = .733, p = .464 and β = .060, $t_{(9, 643)}$ = 1.593, p = .112, respectively). Demographic and cardiovascular risk factors accounted for 12.4% and anxiety factor scores only an additional 0.3% of the variance in LF:HF-HRV which was a non-significant contribution (p = .112). Women (β = -.279) and Black subjects (β = -.130) exhibited lower LF:HF-HRV; greater education (β = .106) and higher DBP (β = .149) were related to higher LF:HF-HRV while higher SBP (β = -.142) was related to lower LF:HF-HRV (all p's <.05).

3.4.3 Structural equation modeling.

The relationship between anxiety and HRV was reexamined using structural equation modeling. The conceptual model representing Hypothesis 2 is depicted in Figure 5. Indicators (observed variables) of the latent construct of anxiety included the same three anxiety-related self-report questionnaires (STAI-T, NEO-ANX, and TCI-HA) used in the factor analysis/regression approach described above. The latent construct of anxiety was scaled by constraining one of the

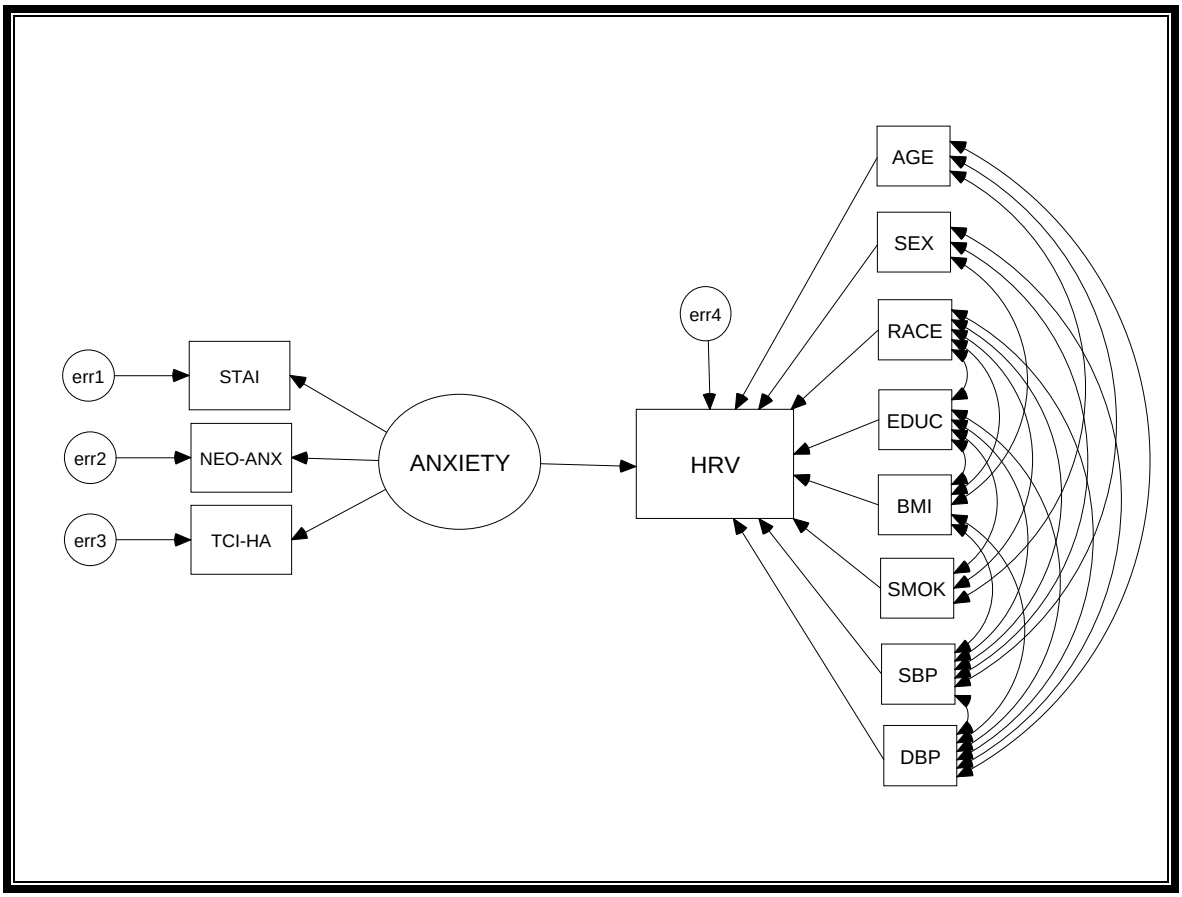

Figure 5, Hypothesis 2. Conceptual model depicting the relationship between anxiety and HRV (HF-HRV, LF-HRV, LF:HF-HRV).

factor loading parameters to a value of 1.0. NEO-ANX was chosen as the reference item because it has the highest factor loading on anxiety and has high internal consistency reliability (Cronbach's coefficient $\alpha = .80$). In this model, there were 78 distinct sample moments (data points [12(12 + 1)/2]) and 42 unknown parameters to be estimated (i.e. 11 regression paths, 13 variances [4 error variances], and 18 covariances) resulting in 36 degrees of freedom. Three separate analyses were conducted examining HF, LF, and LF:HF HRV individually as the dependent measures with covariate-adjustment (age, sex, race, education, BMI, smoking status, SBP, and DBP).

3.4.3.1 HF-HRV. With respect to HF-HRV, the chi-square test statistic $\chi^2(36, N=653) = 88.587$, $p<.001$ showed poor overall model fit. The normed chi-square index (χ^2/df) = 2.461, RMSEA = .047, 90% CI = .035-.060, p = .618, and the CFI = .970, however, all showed close model fit. The AIC = 172.587 and 3.8% of values in the standardized residual matrix were > 2.58. See Table 12.

Estimates of regression weights are summarized in Table 20 and represented in Figure 6. The unstandardized path coefficient between the latent construct of anxiety and HF-HRV was -.042, indicating that a 1-point increase in anxiety predicts a .042-point decrease in HF-HRV (with covariate-adjustment); this path was significant at the .001 level. The standardized estimate of this relationship showed a 1 standard deviation increase in anxiety to correspond to a .139 standard deviation decrease in HF-HRV (with covariate-adjustment). Examination of the SMCs showed the latent construct of anxiety to explain 62.7% of the variance in STAI-T, 65.2% in NEO-ANX, and 57.2% in TCI-HA. Anxiety as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 24.1% of the variance in HF-HRV.

Table 20. Estimates of regression weights derived from structural equation modeling of relationship between anxiety and HF-HRV (Hypothesis 2, Figure 6).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Anxiety → HF-HRV	-.139	-.042	.011	-3.624	<.001
Anxiety → STAI-T	.792	.050	.003	18.130	<.001
Anxiety → NEO-ANX	.807	1.000	-	-	-
Anxiety → TCI-HA	.756	1.229	.068	18.015	<.001
Age → HF-HRV	-.388	-.070	.006	-10.968	<.001
Sex → HF-HRV	.239	.608	.093	6.558	<.001
Race → HF-HRV	.067	.233	.126	1.854	.064
Education → HF-HRV	-.058	-.024	.015	-1.602	.109
BMI → HF-HRV	-.004	-.001	.008	-.117	.907
Smoking → HF-HRV	.023	.059	.092	.643	.520
SBP → HF-HRV	-.014	-.001	.005	-.264	.792
DBP → HF-HRV	.002	.000	.008	.036	.972

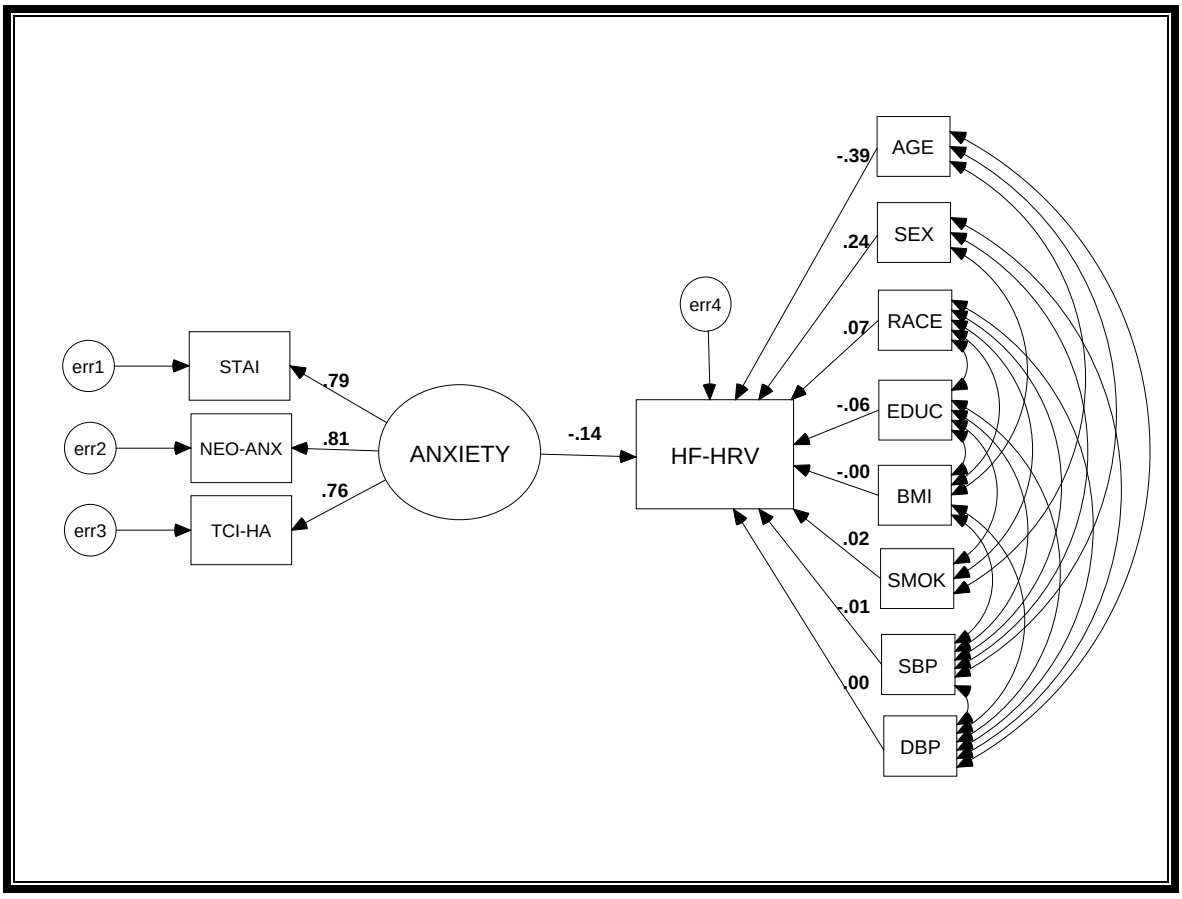

Figure 6, Hypothesis 2. Standardized estimates of relationship between anxiety and HF-HRV.

3.4.3.2 LF-HRV. With respect to LF-HRV, the chi-square test statistic $\chi^2(36, N=653) = 82.990$, $p<.001$ also showed poor overall model fit while the normed chi-square index (χ^2/df) = 2.305, RMSEA = .045, 90% CI = .032-.057, p = .738, and the CFI = .973 all showed close fit. The AIC = 166.990 and 3.8% of values in the standardized residual matrix were > 2.58. See Table 12

Estimates of regression weights are summarized in Table 21 and represented in Figure 7. The unstandardized path coefficient between the latent construct of anxiety and LF-HRV was -.022, indicating that a 1-point increase in anxiety predicts a .022-point decrease in LF-HRV (with covariate-adjustment); this path was significant at the .05 level. The standardized estimate of this relationship showed a 1 standard deviation increase in anxiety to correspond to a .080

standard deviation decrease in LF-HRV (with covariate-adjustment). Examination of the SMCs showed the latent construct of anxiety to explain 62.0% of the variance in STAI, 65.6% in NEO-ANX, and 57.5% in TCI-HA. Anxiety as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 18.2% of the variance in LF-HRV.

Table 21. Estimates of regression weights derived from structural equation modeling of relationship between anxiety and LF-HRV (Hypothesis 2, Figure 7).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Anxiety → LF-HRV	-.080	-.022	.011	-2.038	.042
Anxiety → STAI-T	.788	.049	.003	18.145	<.001
Anxiety → NEO-ANX	.810	1.000	-	-	-
Anxiety → TCI-HA	.758	1.228	.069	17.905	<.001
Age → LF-HRV	-.372	-.060	.006	-10.133	<.001
Sex → LF-HRV	-.053	-.122	.087	-1.406	.160
Race → LF-HRV	-.080	-.251	.118	-2.131	.033
Education → LF-HRV	.051	.019	.014	1.339	.181
BMI → LF-HRV	.006	.001	.008	.152	.879
Smoking → LF-HRV	.011	.025	.086	.288	.773
SBP → LF-HRV	-.186	-.016	.005	-3.323	<.001
DBP → LF-HRV	.176	.022	.007	3.149	.002

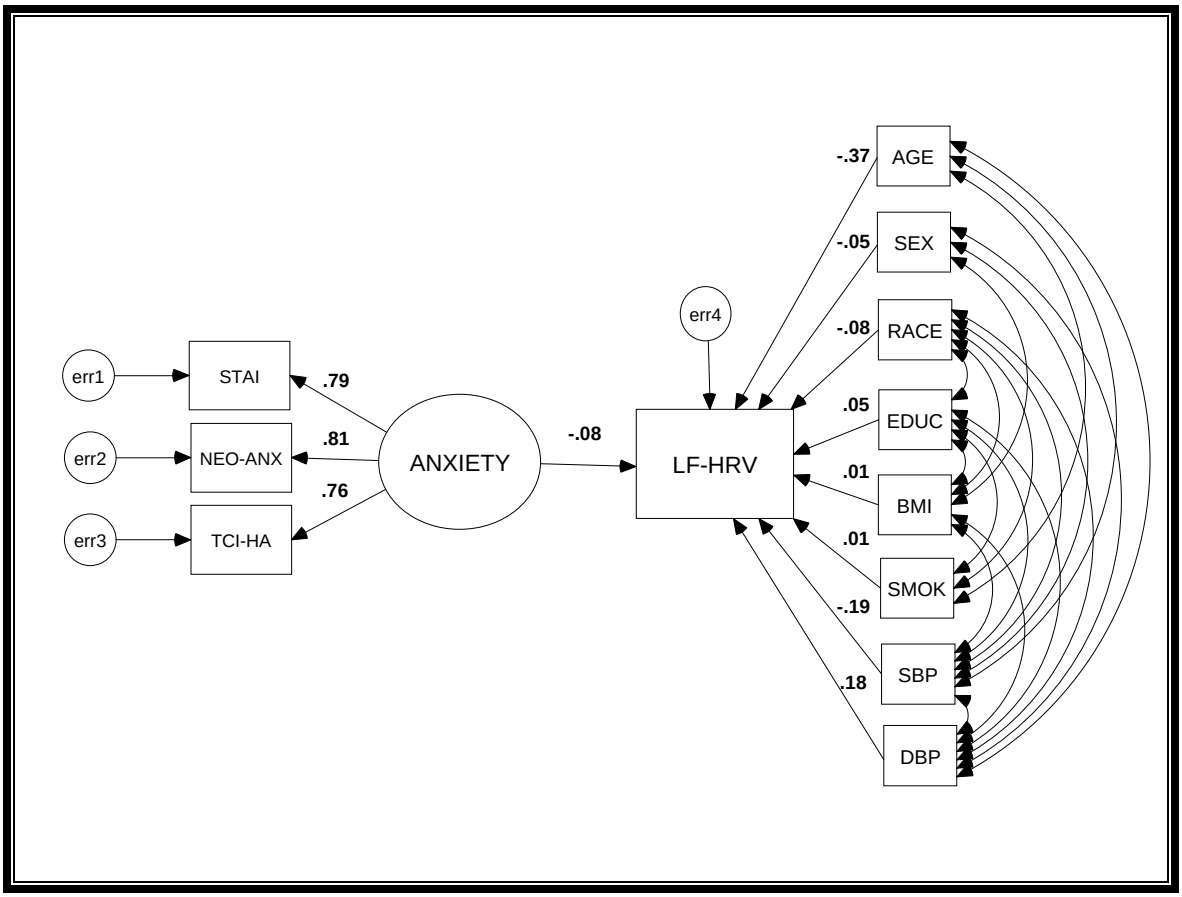

Figure 7, Hypothesis 2. Standardized estimates of relationship between anxiety and LF-HRV.

3.4.3.3 LF:HF-HRV. With respect to LF:HF-HRV, fit indices showed a similar pattern of results. While the chi-square test statistic $\chi^2(36, N=653) = 85.708$, $p<.001$ showed poor overall model fit, the normed chi-square index (χ^2/df) = 2.381, RMSEA = .046, 90% CI = .034-.059, p = .682, and the CFI = .971 all showed close model fit. The AIC = 169.708 and 3.8% of values in the standardized residual matrix were > 2.58. See Table 12

Estimates of regression weights are summarized in Table 22 and represented in Figure 8. The unstandardized path coefficient between the latent construct of anxiety and LF:HF-HRV was .020, indicating that a 1-point increase in anxiety predicts a .020-point *increase* in LF:HF-HRV (with covariate-adjustment); this path, however, was non-significant (p=107). The standardized

estimate of this relationship showed a 1 standard deviation increase in anxiety to correspond to a .066 standard deviation *increase* in LF:HF-HRV (with covariate-adjustment). Examination of the SMCs showed the latent construct of anxiety to explain 62.2% of the variance in STAI, 65.3% in NEO-ANX, and 57.6% in TCI-HA. Anxiety as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 13.7% of the variance in LF:HF-HRV.

Table 22. Estimates of regression weights derived from structural equation modeling of relationship between anxiety and LF:HF-HRV (Hypothesis 2, Figure 8).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Anxiety → LF:HF-HRV	.066	.020	.012	1.613	.107
Anxiety → STAI-T	.789	.049	.003	18.144	<.001
Anxiety → NEO-ANX	.808	1.000	-	-	-
Anxiety → TCI-HA	.759	1.232	.069	17.939	<.001
Age → LF:HF-HRV	.051	.009	.007	1.361	.173
Sex → LF:HF-HRV	-.284	-.730	.100	-7.320	<.001
Race → LF:HF-HRV	-.137	-.484	.135	-3.577	<.001
Education → LF:HF-HRV	.103	.043	.016	2.654	.008
BMI → LF:HF-HRV	.010	.002	.009	.244	.808
Smoking → LF:HF-HRV	-.013	-.034	.099	-.345	.644
SBP → LF:HF-HRV	-.152	-.015	.005	-2.649	.010
DBP → LF:HF-HRV	.155	.022	.008	2.709	.007

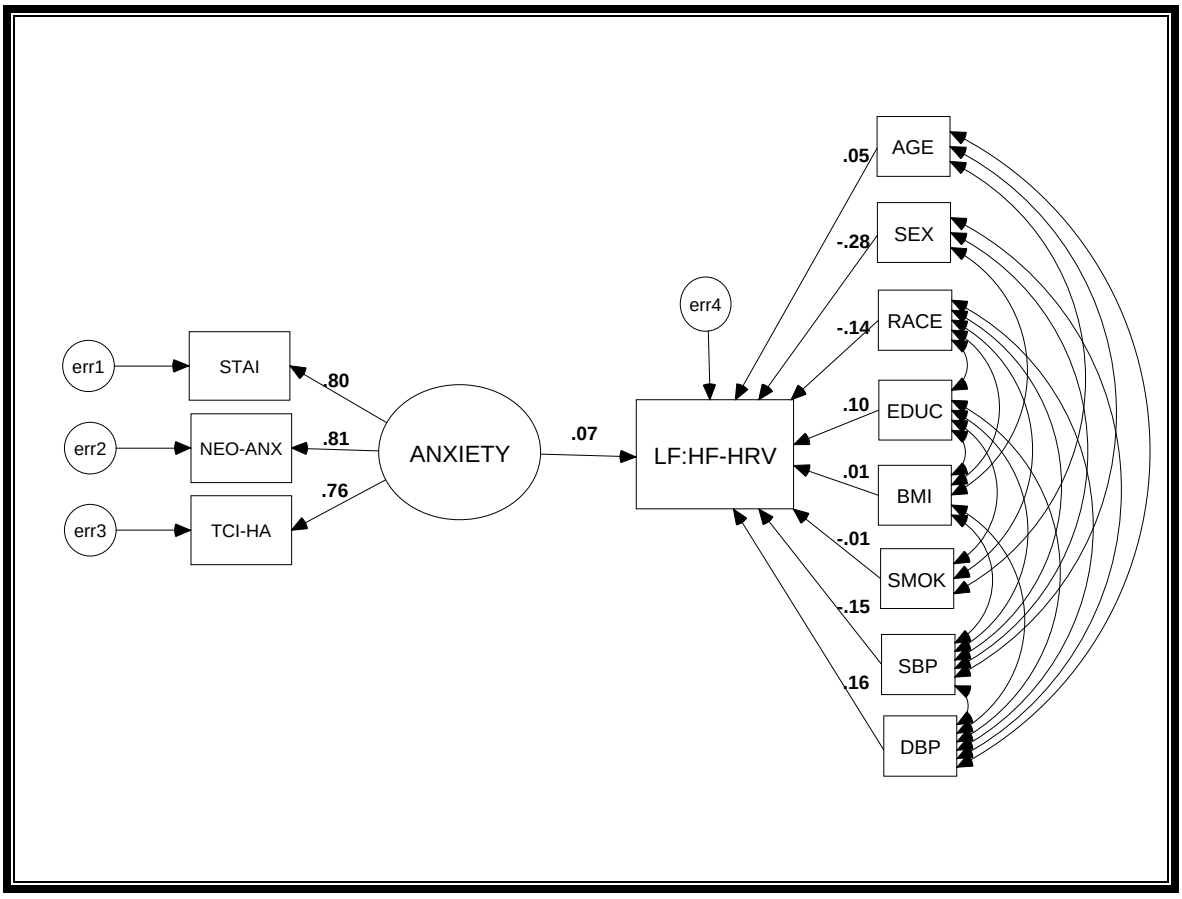

Figure 8, Hypothesis 2. Standardized estimates of relationship between anxiety and LF:HF-HRV.

3.5 Hypothesis 3: Is anger related to variation in autonomic control of heart rate?

3.5.1 Factor analysis of anger scales.

As summarized in Table 23, factor analysis was performed on the full sample (n=653) to examine the factor structure underlying subjects' responses on three anger-related self-report questionnaires (STAXI-T, STAXI-OUT, NEO-ANG). The total scores of each measure were

Table 23. Factor analysis of anger scales in the full sample (N=653).

Items	Factor Loadings (h)	Communalities (h^2)	Variance Explained (%)
STAXI-T*	.829	.688	
STAXI-OUT	.711	.506	
NEO-ANG	.751	.564	
Anger Factor			58.6.%

*Measure logarithmically transformed.

entered simultaneously into the analysis. Factor extraction was based on principal axis factoring methods. Results showed a single factor, labeled "anger factor", to account for 58.6% of the variance in the anger-related measures; the eigenvalue for this factor (2.166) well exceeded the convention of 1 for factor extraction. Evidence that a single factor solution best fits the data was provided by visual inspection of the scree plot (eigenvalues plotted against factors), as well as examination of the residual correlation matrix showing differences between the observed and reproduced correlations to approximate 0. Internal consistency of the factor was good and the factor well defined by its items as indicated by high correlations between the anger factor and each measure: STAXI-T (r=.83), STAXI-OUT (r=.71), and NEO-ANG (r=.75). Moreover, communality estimates were high, showing the anxiety factor to account for 69% of the variance in STAXI-T scores, 51% of the variance in STAXI-OUT scores, and 56% of the variance in NEO-ANG scores.

As summarized in Table 24 and Table 25, factor analysis of anger items examined in men and women separately and in White and Black subjects separately produced a single factor structure similar to findings reported in the full sample. Because this factor structure was invariant across sex and race sub-samples, the anger factor score from the full sample was retained for use in subsequent analyses.

Table 24. Factor analysis of anger scales in men (n=320) and women (n=333) separately.

Items	Factor Loadings (h)		Communalities (h^2)		Variance Explained (%)	
	Men	Women	Men	Women	Men	Women
STAXI-T*	.792	.874	.627	.764		
STAXI-OUT	.783	.642	.612	.412		
NEO-ANG	.786	.715	.618	.512		
Anger Factor					61.9%	56.3%

*Measure logarithmically transformed.

Table 25. Factor analysis of anger scales in White (n=550) and Black (n=103) subjects separately.

Items	Factor Loadings (h)		Communalities (h^2)		Variance Explained (%)	
	White	Black	White	Black	White	Black
STAXI-T*	.839	.750	.704	.563		
STAXI-OUT	.708	.758	.501	.574		
NEO-ANG	.773	.685	.597	.470		
Anger Factor					60.1%	53.6%

*Measure logarithmically transformed.

3.5.2 Multiple regression.

As summarized in Table 26, a series of multiple regression analyses were performed to assess the relationship between the anger factor score, derived from factor analysis (see results above), and three frequency domain indices of heart rate variability (HF-HRV, LF-HRV, and LF:HF-HRV). These associations were first examined alone and then with covariate-adjustment by entering covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) simultaneously on the first step of each regression equation.

Table 26. Multiple regression analyses assessing the relationship between anger (anger factor score) and HRV (HF-HRV, LF-HRV, LF:HF-HRV) in the full sample.

	β	p	R^{2b}	ΔR^{2b}	B	95% CI (b)	
DV: HF-HRV							
1. Anger F-score	.030	.451	.001	-	.041	-.066	.148
After covariate-adjustment[a]:							
1. Covariates	-	-	.204	-	-	-	-
2. Anger F-score	-.023	.519	.205	.001	-.033	-.131	.066
DV: LF-HRV							
1. Anger F-score	.008	.848	.000	-	.010	-.088	.107
After covariate-adjustment[a]:							
1. Covariates	-	-	.171	-	-	-	-
2. Anger F-score	-.055	.135	.174	.003	-.070	-.161	.022
DV: LF:HF-HRV							
1. Anger F-score	-.022	.572	.000	-	-.031	-.141	.078
After covariate-adjustment[a]:							
1. Covariates	-	-	.123	-	-	-	-
2. Anger F-score	-.026	.488	.124	.001	-.037	-.143	.068

[a]Covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) were entered on the first step of each regression equation.
[b]R^2 and ΔR^2 values are reported for the final model of each regression equation.

Multiple regression analyses showed no relationship between anger factor scores and HF-HRV before or after covariate-adjustment ($\beta = .030$, $t_{(1, 651)} = .753$, $p = .451$ and $\beta = -.023$, $t_{(9, 643)} = -.645$, $p = .519$. respectively). Demographic and cardiovascular risk factors accounted for 20.4% and anger factor scores only an additional 0.1% of the variance in HF-HRV ($F_{change} = .416$, $p = .519$). Sex and age correlated significantly with HF-HRV in the final model; women ($\beta = .235$) exhibited higher HF-HRV while advancing age ($\beta = -.388$) was associated with lower HF-HRV (all p's <.001). Similarly, anger factor scores were not related to LF-HRV (all p's >.05). Demographic and cardiovascular risk factors accounted for 17.1% and anger factor scores only an additional 0.3% of the variance in LF-HRV ($F_{change} = 2.238$, $p = .135$). Age, SBP, and

DBP correlated significantly with LF-HRV in the final model; older age (β = -.378) and higher SBP (β = -.170) were associated with lower LF-HRV and higher DBP (β = .165) was associated with higher LF-HRV (all p's <.01). Finally, anger factor scores were also unrelated to LF:HF-HRV (all p's >.05). Demographic and cardiovascular risk factors accounted for 12.3% and anger factor scores only an additional 0.1% of the variance in LF:HF-HRV (F_{change} = .482, p = .488). Women (β = -.275) and Black subjects (β = -.133) exhibited lower LF:HF-HRV; greater education (β = .097) and higher DBP (β = .152) were related to higher LF:HF-HRV while higher SBP (β = -.147) was related to lower LF:HF-HRV (all p's <.05).

3.5.3 Structural equation modeling.

The relationship between anger and HRV was reexamined using structural equation modeling. The conceptual model representing Hypothesis 3 is depicted in Figure 9. Indicators (observed

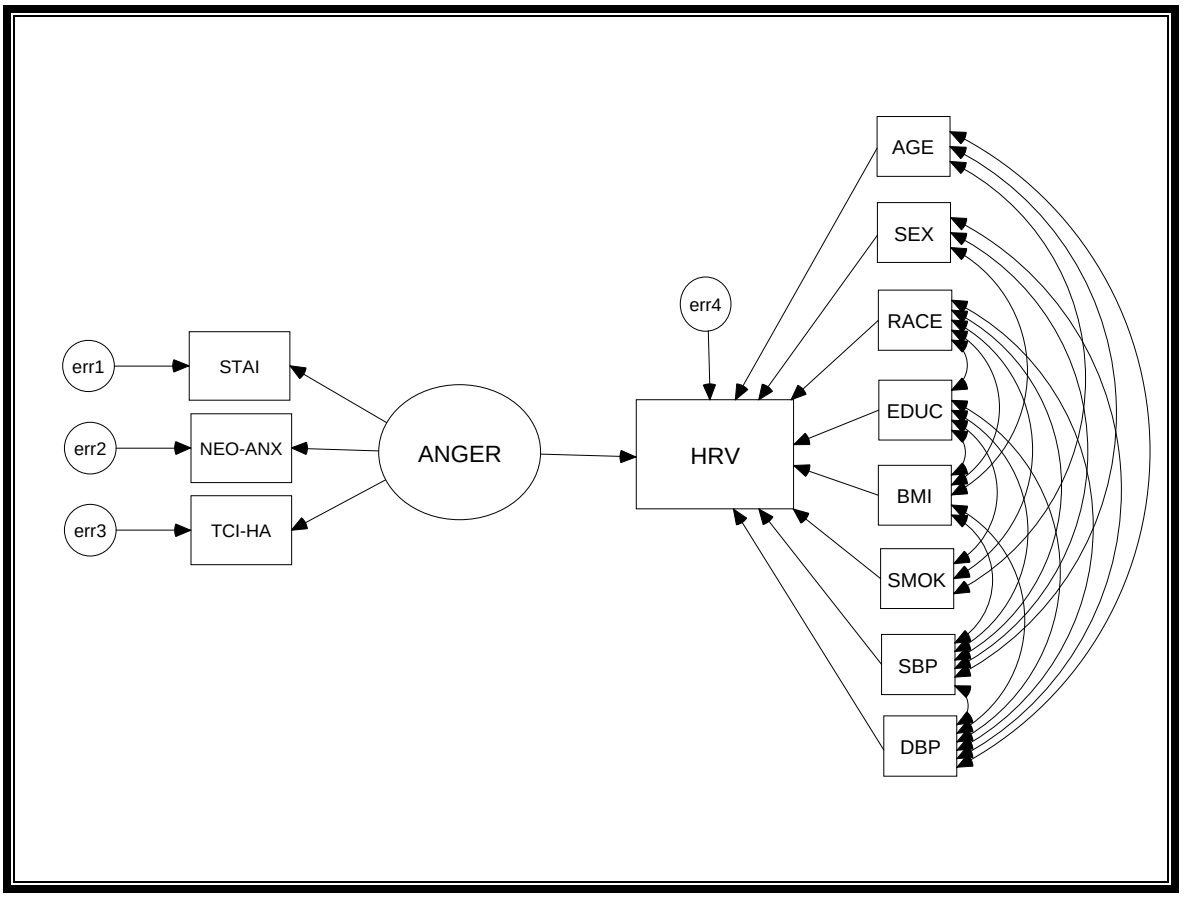

Figure 9, Hypothesis 3. Conceptual model depicting the relationship between anger and HRV (HF-HRV, LF-HRV, LF:HF-HRV).

variables) of the latent construct of anger included the same three anger-related self-report questionnaires (STAXI-T, STAXI-OUT, NEO-ANG) used in the factor analysis/regression approach described above. The latent construct of anger was scaled by constraining one of the factor loading parameters to a value of 1.0. STAXI-T was chosen as the reference item because it has the highest factor loading on anger and has high internal consistency reliability (Cronbach's coefficient $\alpha = .81$). In this model, there were 78 distinct sample moments (data points [12(12 + 1)/2]) and 42 unknown parameters to be estimated (i.e. 11 regression paths, 13 variances [4 error variances], and 18 covariances) resulting in 36 degrees of freedom. Three separate analyses were

conducted examining HF, LF, and LF:HF HRV individually as the dependent measures with covariate-adjustment (age, sex, race, education, BMI, smoking status, SBP, and DBP).

3.5.3.1 HF-HRV. With respect to HF-HRV, the chi-square test statistic $\chi^2(36, N=653) = 101.416$, $p<.001$ showed poor overall model fit. The normed chi-square index (χ^2/df) = 2.817, RMSEA = .053, 90% CI = .041-.065, p = .334, and the CFI = .961, however, all showed close model fit. The AIC = 185.416 and 6.4% of values in the standardized residual matrix were > 2.58. See Table 12.

Estimates of regression weights are summarized in Table 27 and represented in Figure 10. The unstandardized path coefficient between the latent construct of anger and HF-HRV was

Table 27. Estimates of regression weights derived from structural equation modeling of relationship between anger and HF-HRV (Hypothesis 3, Figure 10).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Anger → HF-HRV	-.023	-.148	.257	-.573	.566
Anger → STAXI-T	.830	1.000	-	-	-
Anger → STAXI-OUT	.711	13.163	.821	16.037	<.001
Anger → NEO-ANG	.750	20.446	1.246	16.414	<.001
Age → HF-HRV	-.383	-.068	.006	-10.558	<.001
Sex → HF-HRV	.231	.582	.093	6.235	<.001
Race → HF-HRV	.067	.231	.127	1.816	.069
Education → HF-HRV	-.048	-.020	.015	-1.296	.195
BMI → HF-HRV	-.008	-.002	.009	-.201	.841
Smoking → HF-HRV	.025	.064	.093	.684	.494
SBP → HF-HRV	-.007	-.001	.005	-.125	.901
DBP → HF-HRV	-.006	-.001	.008	-.114	.909

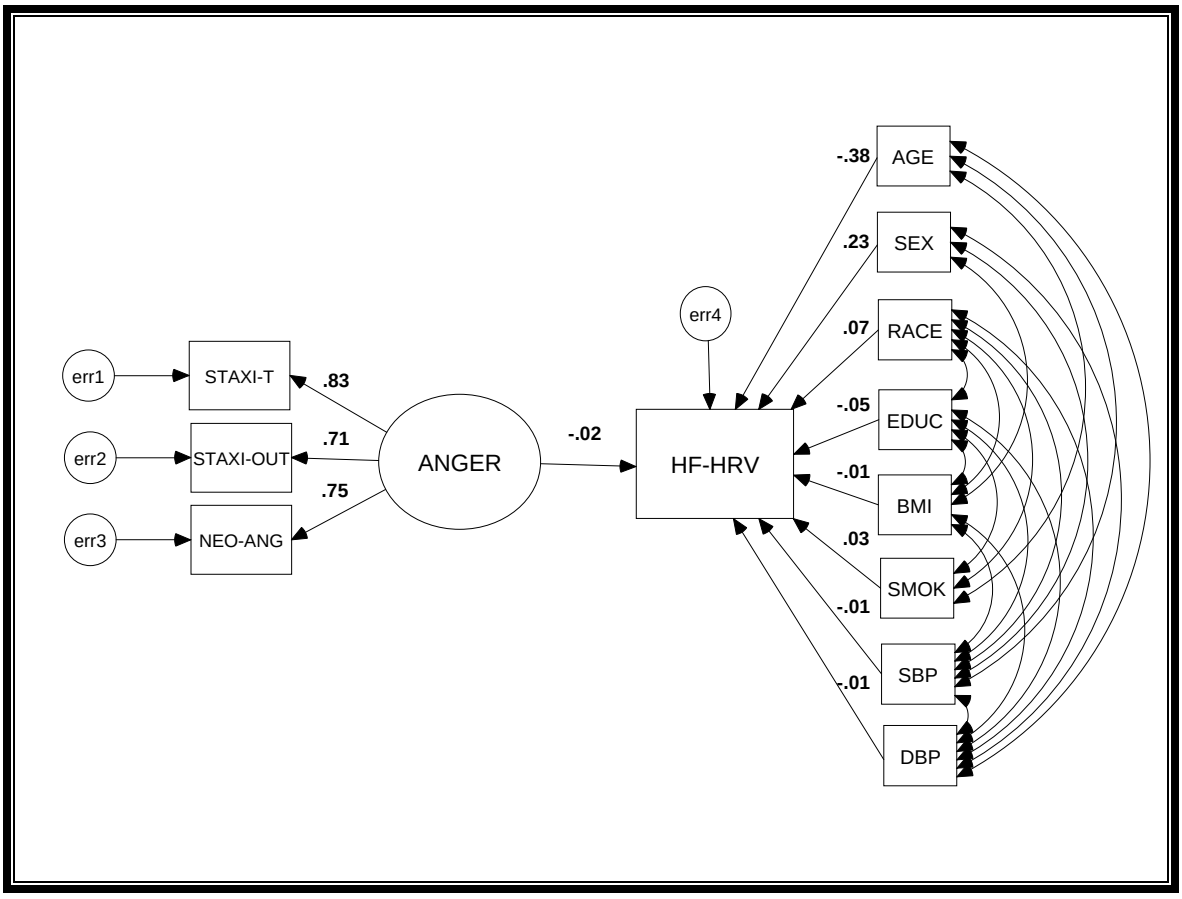

Figure 10, Hypothesis 3. Standardized estimates of relationship between anger and HF-HRV.

-.148, indicating that a 1-point increase in anger predicts a .148-point decrease in HF-HRV (with covariate-adjustment); this path, however, was non-significant (p=.566). The standardized estimate of this relationship showed a 1 standard deviation increase in anger to correspond to a .023 standard deviation decrease in HF-HRV (with covariate-adjustment). Examination of the SMCs showed the latent construct of anger to explain 69.0% of the variance in STAXI-T, 50.6% in STAXI-OUT, and 56.3% in NEO-ANG. Anger as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 21.2% of the variance in HF-HRV.

3.5.3.2 LF-HRV. With respect to LF-HRV, the chi-square test statistic $\chi^2(36, N=653) = 100.512$, $p<.001$ also showed poor overall model fit while the normed chi-square index (χ^2/df) = 2.792, RMSEA = .052, 90% CI = .040-.065, p = .352, and the CFI = .961 all showed close fit. The AIC = 184.512 and 6.4% of values in the standardized residual matrix were > 2.58. See Table 12.

Estimates of regression weights are summarized in Table 28 and represented in Figure 11. The unstandardized path coefficient between the latent construct of anger and LF-HRV was

Table 28. Estimates of regression weights derived from structural equation modeling of relationship between anger and LF-HRV (Hypothesis 3, Figure 11).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Anger → LF-HRV	-.054	-.324	.239	-1.355	.175
Anger → STAXI-T	.831	1.000	-	-	-
Anger → STAXI-OUT	.711	13.158	.820	16.046	<.001
Anger → NEO-ANG	.750	20.442	1.245	16.421	<.001
Age → LF-HRV	-.373	-.061	.006	-10.071	<.001
Sex → LF-HRV	-.060	-.138	.087	-1.591	.112
Race → LF-HRV	-.082	-.260	.118	-2.198	.028
Education → LF-HRV	.053	.020	.014	1.415	.157
BMI → LF-HRV	.008	.002	.008	.197	.843
Smoking → LF-HRV	.014	.033	.087	.379	.705
SBP → LF-HRV	-.182	-.016	.005	-3.257	.001
DBP → LF-HRV	.171	.022	.007	3.060	.002

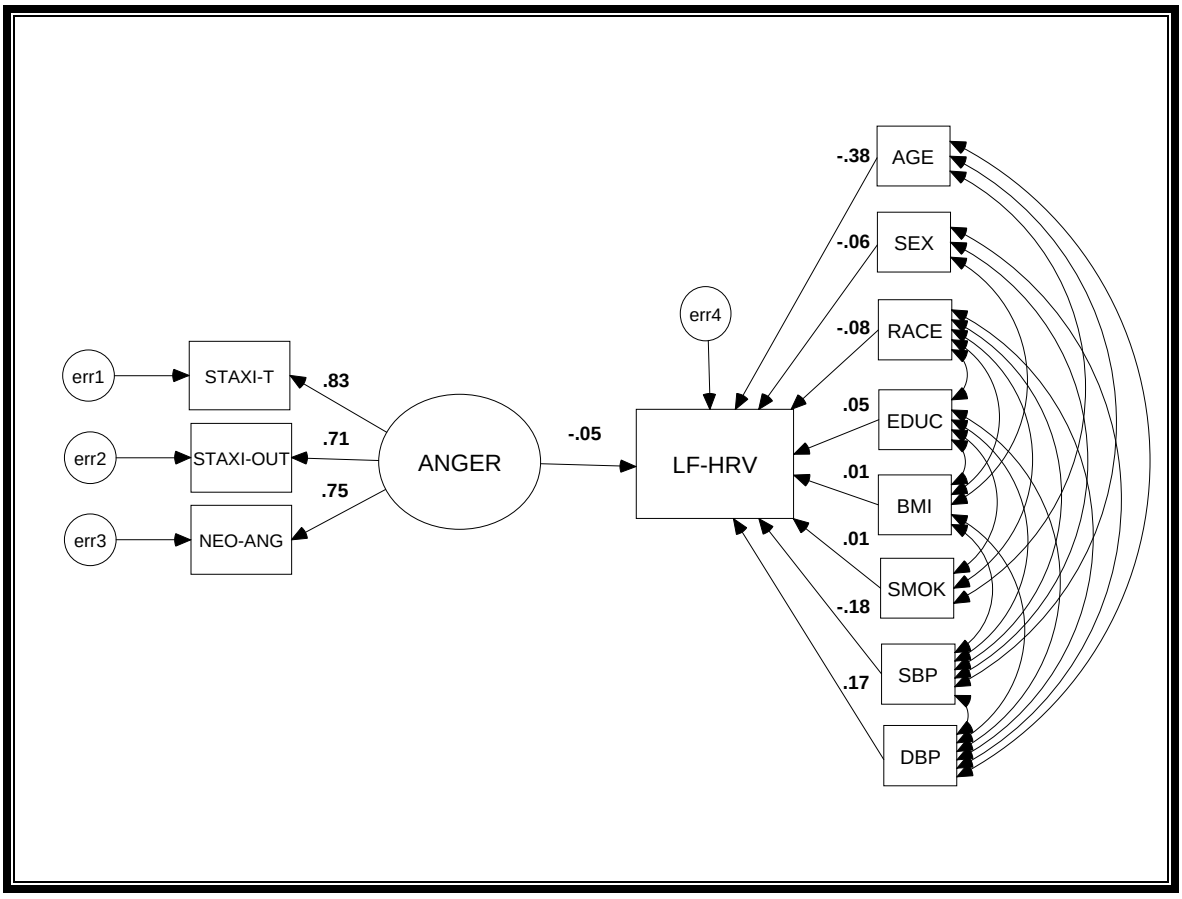

Figure 11, Hypothesis 3. Standardized estimates of relationship between anger and LF-HRV.

-.324, indicating that a 1-point increase in anger predicts a .324-point decrease in LF-HRV (with covariate-adjustment); this path, however, was non-significant (p=.175). The standardized estimate of this relationship showed a 1 standard deviation increase in anger to correspond to a .054 standard deviation decrease in LF-HRV (with covariate-adjustment). Examination of the squared multiple correlations showed the latent construct of anger to explain 69.0% of the variance in STAXI-T, 50.6% in STAXI-OUT, and 56.3% in NEO-ANG. Anger as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 17.9% of the variance in LF-HRV.

3.5.3.3 LF:HF-HRV. With respect to LF:HF-HRV, fit indices showed a similar pattern of results. While the chi-square test statistic $\chi^2(36, N=653) = 100.956$, $p<.001$ showed poor overall model fit, the normed chi-square index (χ^2/df) = 2.804, RMSEA = .053, 90% CI = .041-.065, p = .343, and the CFI = .971 all showed close model fit. The AIC = 184.956 and 6.4% of values in the standardized residual matrix were > 2.58. See Table 12.

Estimates of regression weights are summarized in Table 29 and represented in Figure 12. The unstandardized path coefficient between the latent construct of anger and LF:HF-HRV

Table 29. Estimates of regression weights derived from structural equation modeling of relationship between anger and LF:HF-HRV (Hypothesis 3, Figure 12).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Anger → LF:HF-HRV	-.027	-.177	.275	-.645	.519
Anger → STAXI-T	.831	1.000	-	-	-
Anger → STAXI-OUT	.711	13.147	.820	16.032	<.001
Anger → NEO-ANG	.750	20.438	1.247	16.393	<.001
Age → LF:HF-HRV	.043	.008	.007	1.118	.264
Sex → LF:HF-HRV	-.281	-.720	.100	-7.225	<.001
Race → LF:HF-HRV	-.139	-.490	.136	-3.614	<.001
Education → LF:HF-HRV	.095	.040	.016	2.446	.014
BMI → LF:HF-HRV	.014	.003	.009	.360	.719
Smoking → LF:HF-HRV	-.012	-.031	.099	-.311	.756
SBP → LF:HF-HRV	-.157	-.015	.005	-2.719	.007
DBP → LF:HF-HRV	.160	.023	.008	2.772	.006

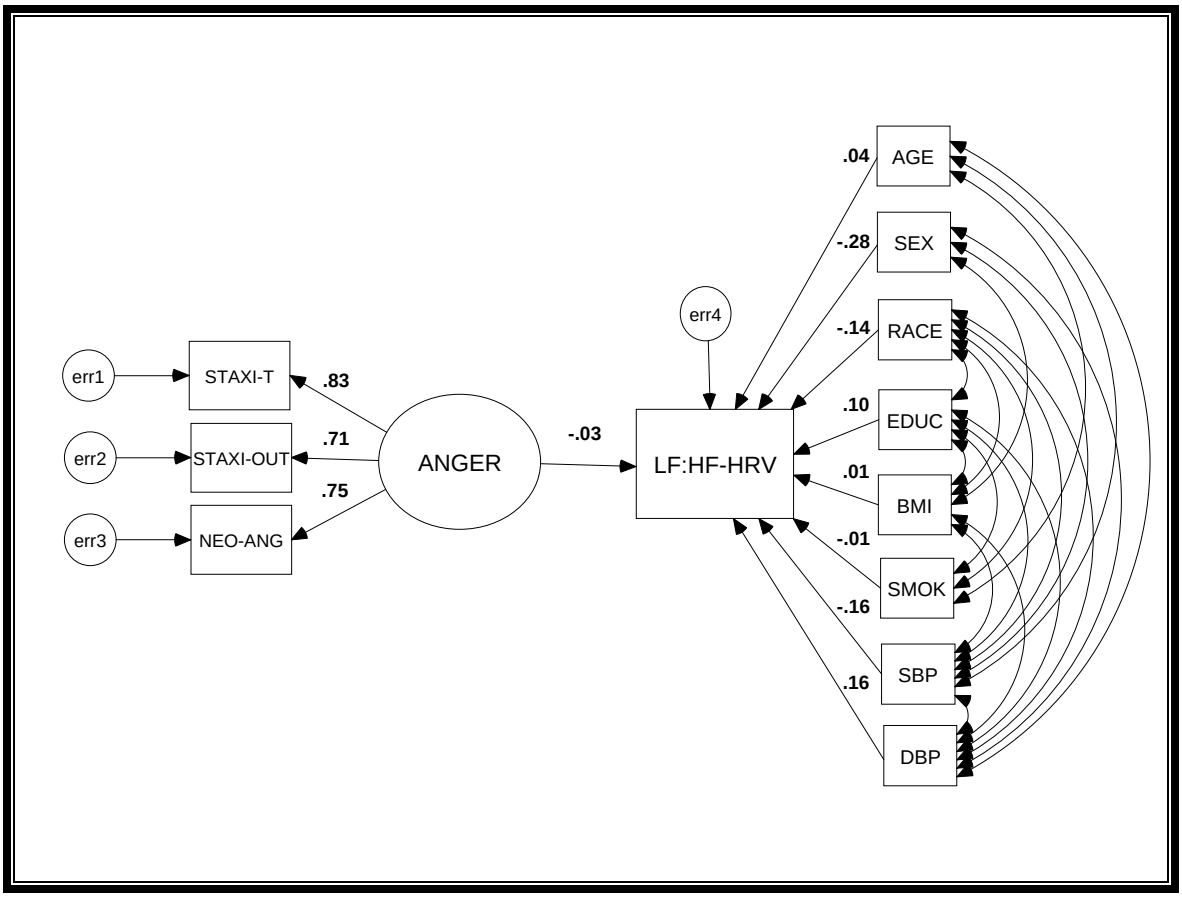

Figure 12, Hypothesis 3. Standardized estimates of relationship between anger and LF:HF-HRV.

was -.177, indicating that a 1-point increase in anger predicts a .177-point decrease in LF:HF-HRV (with covariate-adjustment); this path, however, was non-significant (p=.519). The standardized estimate of this relationship showed a 1 standard deviation increase in anger to correspond to a .027 standard deviation decrease in LF:HF-HRV (with covariate-adjustment). Examination of the SMCs showed the latent construct of anger to explain 69.0% of the variance in STAXI-T, 50.5% in STAXI-OUT, and 56.3% in NEO-ANG. Anger as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) accounted for 13.0% of the variance in LF:HF-HRV.

3.6 Hypothesis 4: When evaluated in the same model, is depression, anxiety, or anger related to variation in autonomic control of heart rate (model of unique variance)?

3.6.1 Multiple regression.

As summarized in Table 30, a series of multiple regression analyses were performed to assess the relationship between the depression, anxiety, and anger factor scores, and each of three frequency domain indices of heart rate variability (HF-HRV, LF-HRV, and LF:HF-HRV). The three factor scores derived from factor analysis (see results above), were entered simultaneously into each regression equation. Analyses were then repeated with covariate-adjustment by entering covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) simultaneously on the first step of each regression equation.

Table 30. Multiple regression analyses assessing the relationship between depression, anxiety, and anger factor scores (entered simultaneously) and HRV (HF-HRV, LF-HRV, LF:HF-HRV) among all subjects (N=653).

	β	p	R^{2b}	ΔR^{2b}	b	95% CI (b)	
DV: HF-HRV							
1. F-scores	-	-	.043	-	-	-	-
• Depression F-score	-.261	.000	-	-	-.359	-.511	-.207
• Anxiety F-score	.058	.323	-	-	.080	-.079	.239
• Anger F-score	.113	.012	-	-	.157	.035	.279
After covariate-adjustment[a]:							
1. Covariates	-	-	.205	-	-	-	-
2. F-Scores	-	-	.241	.036	-	-	-
• Depression F-score	-.192	.000	-	-	-.266	-.408	-.123
• Anxiety F-score	-.032	.559	-	-	-.044	-.192	.104
• Anger F-score	.076	.065	-	-	.106	-.007	.219
DV: LF-HRV							
1. F-scores	-	-	.011	-	-	-	-
• Depression F-score	-.124	.030	-	-	-.157	-.298	-.016
• Anxiety F-score	.014	.808	-	-	.018	-.129	.166
• Anger F-score	.054	.235	-	-	.069	-.045	.182
After covariate-adjustment[a]:							
1. Covariates	-	-	.171	-	-	-	-
2. F-Scores	-	-	.182	.011	-	-	-
• Depression F-score	-.099	.068	-	-	-.125	-.259	.009
• Anxiety F-score	-.003	.965	-	-	-.003	-.143	.137
• Anger F-score	-.011	.802	-	-	-.014	-.120	.093
DV: LF:HF-HRV							
1. F-scores	-	-	.012	-	-	-	-
• Depression F-score	.144	.012	-	-	.203	.045	.360
• Anxiety F-score	-.044	.463	-	-	-.062	-.226	.103
• Anger F-score	-.062	.171	-	-	-.088	-.215	.038
After covariate-adjustment[a]:							
1. Covariates	-	-	.123	-	-	-	-
2. F-Scores	-	-	.135	.012	-	-	-
• Depression F-score	.100	.075	-	-	.140	-.014	.295
• Anxiety F-score	.029	.617	-	-	.041	-.120	.202
• Anger F-score	-.085	.055	-	-	-.120	-.242	.003

[a]Covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) were entered on the first step of each regression equation.
[b]R^2 and ΔR^2 values are reported for the final model of each regression equation.

3.6.1.1 HF-HRV. When depression, anxiety, and anger factor scores were enter simultaneously as independent variables in multiple regression analyses, results showed higher depression factor scores to predict *lower* HF-HRV (β = -.261, $t_{(3, 649)}$ = -4.648, p = .000) and higher anger factor scores to predict *higher* HF-HRV (β = .113, $t_{(3, 649)}$ = 2.526, p = .012); anxiety factor scores were not related to HF-HRV (β = .058, $t_{(3, 649)}$ = .990, p = .323). After covariate-adjustment, the relationship between depression factor scores and HF-HRV remained significant (β = -.192, $t_{(11, 641)}$ = -3.662, p = .000) while the relationship between anger factor scores and HF-HRV was attenuated to a statistical trend (β = .076, $t_{(11, 641)}$ = 1.845, p = .065); again, anxiety factor scores were not related to HF-HRV (β = -.032, $t_{(11, 641)}$ = -.584, p = .559). In the full model, 20.5% of the variance in HF-HRV was accounted for by demographic and cardiovascular risk factors with an additional 3.6% of the variance explained collectively by the depression, anxiety, and anger factor scores; this addition to the model was statistically significant (F_{change} = 10.073, p = .000). Gender, age, and race correlated significantly with HF-HRV in the final model; women (β = .224) and Black subjects (β = .081) exhibited higher HF-HRV and greater age (β = -.378) was associated with lower HF-HRV (all p's <.05).

3.6.1.2 LF-HRV. Similarly, higher depression factor scores were associated with *lower* LF-HRV (β = -.124, $t_{(3, 649)}$ = -2.180, p = .030). However, both anxiety and anger factor scores showed no relationship to LF-HRV (β = .014, $t_{(3, 649)}$ = .243, p = .808) and (β = .054, $t_{(3, 649)}$ = 1.188, p = .235), respectively. After covariate-adjustment, the pattern of results was similar though the relationship of the depression factor score with LF-HRV was attenuated (β = -.099, $t_{(11, 641)}$ = -1.829, p = .068). In the full model, 17.1% of the variance in LF-HRV was accounted for by demographic and cardiovascular risk factors with an additional 1.1% of the variance

explained by the collective contribution of depression, anxiety, and anger factor scores; this addition to the model was statistically significant ($F_{change} = 2.818$, $p = .038$). Greater age and SBP was related to lower LF-HRV ($\beta = -.372$, $p = .000$ and $\beta = -.180$, $p = .002$, respectively) and greater DBP was related to higher LF-HRV ($\beta = .171$, $p = .002$).

3.6.1.3 LF:HF-HRV. In contrast, higher depression factor scores were associated with *higher* LF:HF-HRV ($\beta = .144$, $t_{(3, 649)} = 2.523$, $p = .012$); this relationship was attenuated to a statistical trend after covariate-adjustment ($\beta = .100$, $t_{(11, 641)} = 1.786$, $p = .075$). Higher anger factor scores were associated with *lower* LF:HF-HRV but only after covariate-adjustment ($\beta = -.062$, $t_{(3, 649)} = -1.369$, $p = .171$ and $\beta = -.085$, $t_{(11, 641)} = -1.919$, $p = .055$, respectively). Anxiety factor scores were unrelated to LF:HF-HRV ($\beta = -.044$, $t_{(3, 649)} = -.735$, $p = .463$; $\beta = .029$, $t_{(11, 641)} = .500$, $p = .617$). Demographic and cardiovascular risk factors accounted for 12.3% and depression, anxiety, anger factor scores collectively accounted for an additional 1.2% of the variance in LF:HF-HRV; this addition to the model was statistically significant ($F_{change} = 2.929$, $p = .033$). Women and Black subjects exhibited lower LF:HF-HRV ($\beta = -.271$, $p=.000$ and $\beta = -.140$, $p=.000$, respectively); higher education and DBP were related to LF:HF-HRV positively ($\beta = .103$, $p=.009$ and $\beta = .144$, $p=.013$, respectively) while SBP was related to LF:HF-HRV negatively ($\beta = -.135$, $p=.021$).

3.6.2 Structural equation modeling.

The simultaneous analysis of depression, anxiety, and anger in relationship to HRV was reexamined using a two-step approach in structural equation modeling. First, the "measurement" portion of the model was evaluated. This model included the three latent constructs of interest

and their measured indicator variables. The conceptual model representing the measurement model (i.e. first order confirmatory factor analysis) is depicted in Figure 13. After the adequacy

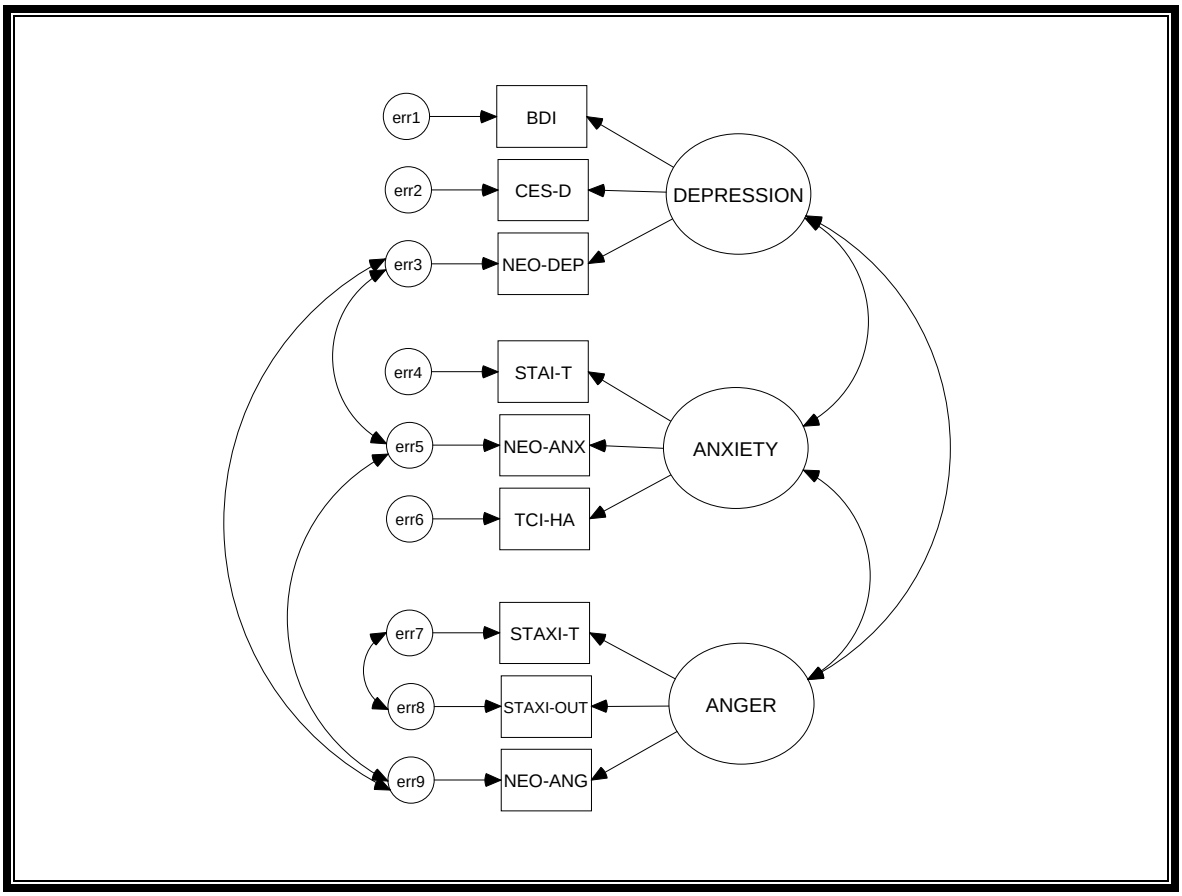

Figure 13, Hypothesis 4. Conceptual model of first order confirmatory factor analysis (measurement model).

of this model was established, the "full" model was then evaluated. The full model included the measurement model as well as the paths between each latent construct and the outcome variables of interest. The conceptual model representing the full model is depicted in Figure 15.

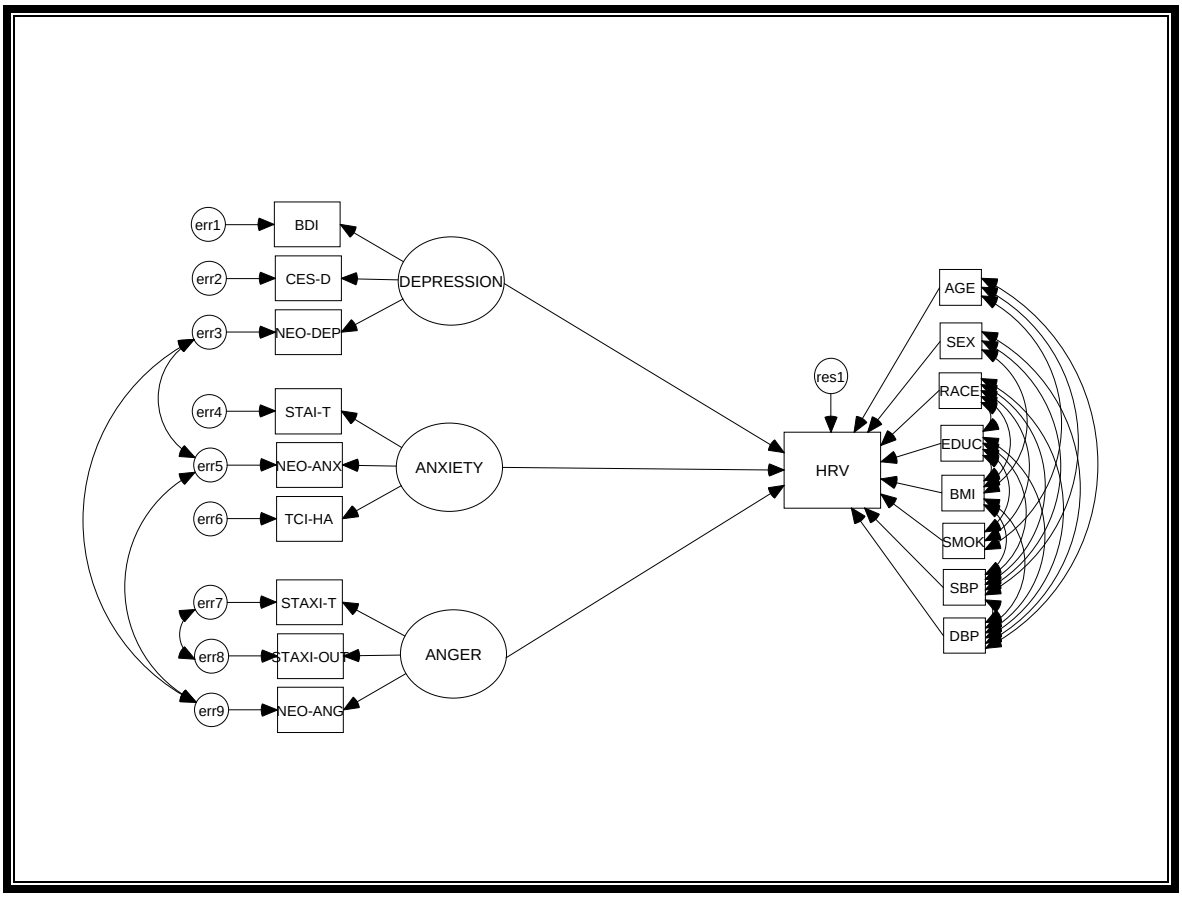

Figure 14, Hypothesis 4. Conceptual model of the full model depicting relationship between latent constructs of depression, anxiety, and anger and HRV (HF-HRV, LF-HRV, LF:HF-HRV).

3.6.2.1 Measurement model. The measurement model or first order confirmatory factor analysis included 3 latent constructs, depression, anxiety, and anger, and their respective indicators (observed variables). Depression was measured by BDI, CES-D, and NEO-DEP, anxiety by STAI-T, NEO-ANX, and TCI-HA, and anger by STAXI-T, STAXI-OUT, and NEO-ANG. Each latent construct was scaled by constraining a factor loading parameter to 1, using CES-D, NEO-ANX, and STAXI-T as reference items. In this model, there were 45 distinct sample moments (data points [9(9 + 1)/2]) and 25 unknown parameters to be estimated (i.e. 6 regression paths, 12 variances [9 error variances], and 7 covariances) resulting in 20 degrees of

freedom. Of note, because initial model testing efforts indicated substantial model improvement when error terms were allowed to correlate, covariances among those measurement error terms from the same questionnaires were incorporated directly into the model. Thus, error terms of the depression, anxiety, and anger facet scales (NEO-DEP, NEO-ANX, NEO-ANG) from the NEO PI-R were allowed to correlate and error terms of the trait anger and anger-out scales (STAXI-T, STAXI-OUT) from the STAXI were allowed to correlate.

Model fit indices of the measurement model showed poor overall model fit according to the chi-square test statistic $\chi^2(20, N=653) = 163.919$, $p<.001$ and the normed chi-square index (χ^2/df) = 8.196. The RMSEA = .105, 90% CI = .090-.120, p = .000, however, indicated marginal to poor fit and the CFI = .956 indicated good fit. The AIC = 213.919 and 2.2% of values in the standardized residual matrix were > 2.58.

Estimates of regression weights are summarized in Table 31 and represented in Figure 14. Unstandardized regression weights showed all paths were significant at the .001 level.

Table 31. Estimates of regression weights derived from structural equation modeling of measurement model (first order confirmatory factor analysis) (Hypothesis 4, Figure 14).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Depression → BDI	.742	.971	.049	19.929	<.001
Depression → CES-D	.771	1.000	-	-	-
Depression → NEO-DEP	.787	6.635	.326	20.359	<.001
Anxiety → STAI-T	.952	.072	.004	19.756	<.001
Anxiety → NEO-ANX	.672	1.000	-	-	-
Anxiety → TCI-HA	.638	1.251	.082	15.212	<.001
Anger → STAXI-T	.676	1.000	-	-	-
Anger → STAXI-OUT	.574	13.062	.810	16.128	<.001
Anger → NEO-ANG	.915	30.430	2.198	13.846	<.001

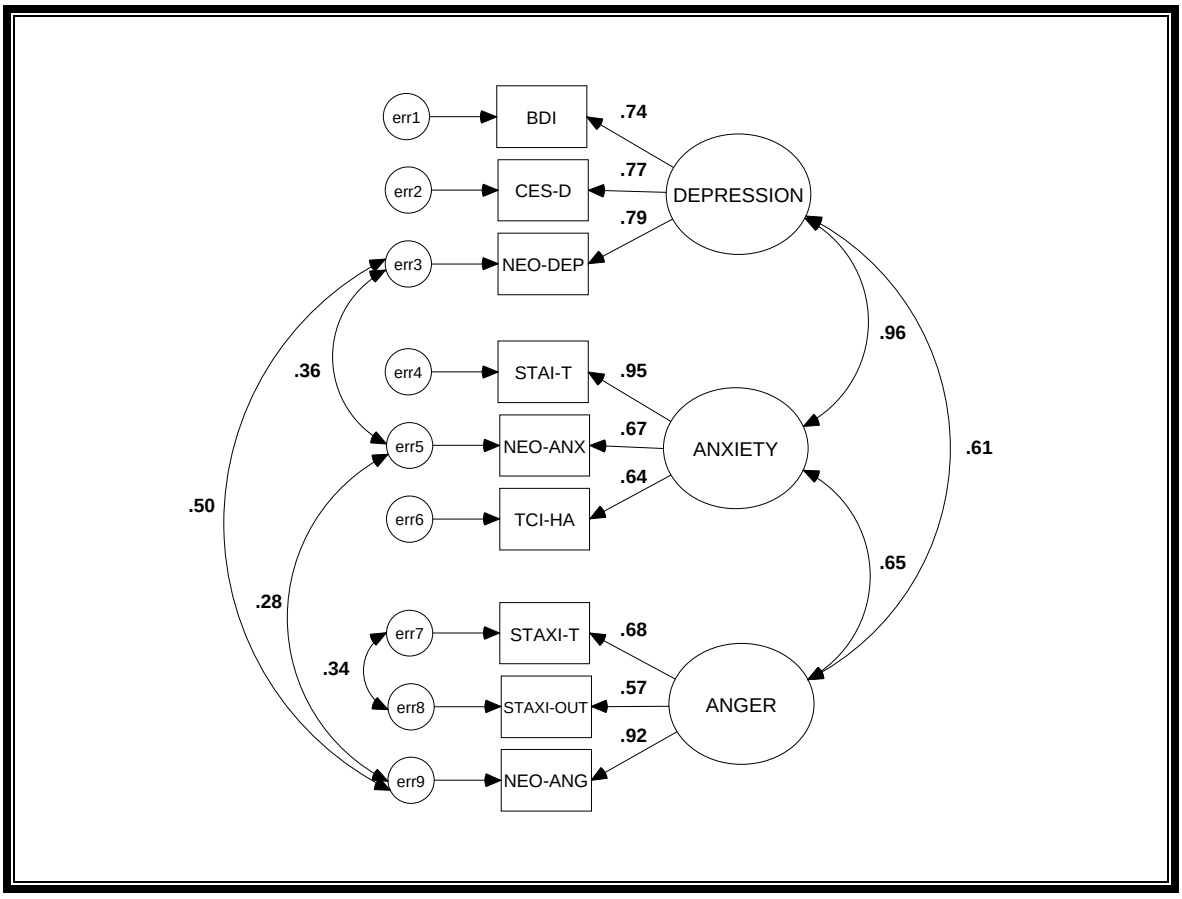

Figure 15, Hypothesis 4. Standardized estimates of first order confirmatory factor analysis (measurement model).

Standardized estimates of these paths showed a 1 standard deviation increase in depression related to increases in indicators between .74 - .79 standard deviations. Additionally, 1 standard deviation increases in anxiety and anger were related to increases in indicators between .64 - .95 and .57 - .92 standard deviations, respectively. Examination of the SMCs showed the latent construct of depression to explain 55.1% of the variance in BDI, 59.5% of the variance in CES-D, and 62.0% of the variance in NEO-DEP. The latent construct of anxiety explained 90.7% of the variance in STAI-T, 45.1% of the variance in NEO-ANX, and 40.7% of the variance in TCI-HA. Finally, the latent construct of anger explained 45.7% of the variance in STAXI-T, 33.0% of the variance in STAXI-OUT, and 83.8% of the variance in NEO-ANG.

3.6.2.2 Full model. Although the model fit indices for the measurement model showed mixed support for its adequacy, evaluation of the full model was pursued. The full model included the measurement model as well as the paths between the 3 latent constructs and HRV. Three separate analyses were conducted to examine HF, LF, and LF:HF HRV individually as the dependent measures while adjusting for covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP). In this model, there were 171 distinct sample moments (data points [18(18 + 1)/2]) and 60 unknown parameters to be estimated (i.e. 17 regression paths, 21 variances [10 error variances], and 22 covariances) resulting in 111 degrees of freedom.

Model fit indices for each of the three full models showed very poor correspondence between the model-implied population and sample covariance matrices. With respect to HF-HRV, the chi-square test statistic $\chi^2(111, N=653) = 1323.629$, $p<.001$; $\chi^2/df = 11.925$; RMSEA = .129, 90% CI = .123-.136, p = .000; CFI = .727; and the AIC = 1443.629. With respect to LF-HRV, the chi-square test statistic $\chi^2(111, N=653) = 1321.850$, $p<.001$; $\chi^2/df = 11.925$; RMSEA = .129, 90% CI = .123-.136, p = .000; CFI = .727; and the AIC = 1441.850. Finally, with respect to LF:HF-HRV, the chi-square test statistic $\chi^2(111, N=653) = 1323.773$, $p<.001$; $\chi^2/df = 11.926$; RMSEA = .129, 90% CI = .123-.136, p = .000; CFI = .722; and the AIC = 1443.773. Additionally, examination of the standardized residual matrices (across HF-HRV, LF-HRV, and HF:LF-HRV outcomes) showed 17.0% of the values were above >2.58, indicating a large portion of residual covariances were statistically different from zero (i.e. perfect fit). See Table 12. Poor model fit precluded the examination of individual parameter estimates. Thus, the path coefficients, variances, and covariances for these models are not reported.

3.7 Hypothesis 5: Is negative affectivity related to variation in autonomic control of heart rate (model of common variance)?

3.7.1 Factor analysis of depression, anxiety, and anger scales.

As summarized in Table 32, factor analysis was performed on the full sample (n=653) to examine the factor structure underlying subjects' responses on all nine self-report questionnaires, three measures for each of three psychological domains: depression (BDI, CES-D, and NEO-DEP), anxiety (STAI-T, NEO-ANX, and TCI-HA), and anger (STAXI-T, STAXI-OUT, and NEO-ANG). The total scores of each measure were entered simultaneously into the analysis.

Table 32. Factor analysis of depression, anxiety, and anger scales in the full sample (N=653).

Items	Factor Loadings (h)	Communalities (h^2)	Variance Explained (%)
BDI*	.667	.445	
CES-D*	.689	.474	
NEO-DEP	.818	.670	
STAI-T*	.898	.806	
NEO-ANX	.717	.514	
TCI-HA	.657	.431	
STAXI-T*	.553	.306	
STAXI-OUT	.441	.194	
NEO-ANG	.710	.503	
Negative Affect Factor			48.3%

*Measure logarithmically transformed.

Factor extraction was based on principal axis factoring methods. Results show a single factor, labeled "negative affect", to account for 48.3% of the variance in the nine psychosocial measures; the eigenvalue for this factor (4.807) well exceeded the convention of 1 for factor extraction. Evidence that a single factor solution best fits the data was provided by visual

inspection of the scree plot (eigenvalues plotted against factors). Internal consistency of the factor was good and the factor well defined by its items as indicated by high correlations between the negative affect factor and each measure: BDI (r=.67), CES-D (r=.69), NEO-DEP (r=.82), STAI-T (r=.90), NEO-ANX (r=.72), TCI-HA (r=.66), STAXI-T (r=.55), STAXI-OUT (r=.44), and NEO-ANG (r=.71). Moreover, communality estimates were moderate to high, showing the negative affect factor to account for 19-81% of the variance in the psychosocial measures.

As summarized in Table 33 and Table 34, factor analysis of all 9 psychosocial measures examined in men and women separately and in White and Black subjects separately produced a single factor structure similar to findings reported in the full sample. Because this factor structure was invariant across sex and race sub-samples, the negative affect factor score from the full sample was retained for use in subsequent analyses.

Table 33. Factor analysis of depression, anxiety, and anger scales in men (n=320) and women (n=333) separately.

Items	Factor Loadings (h)		Communalities (h^2)		Variance Explained (%)	
	Men	Women	Men	Women	Men	Women
BDI*	.685	.648	.470	.420		
CES-D*	.694	.686	.482	.471		
NEO-DEP	.805	.838	.647	.702		
STAI-T*	.906	.887	.822	.786		
NEO-ANX	.688	.763	.473	.582		
TCI-HA	.644	.691	.415	.477		
STAXI-T*	.559	.545	.313	.297		
STAXI-OUT	.524	.362	.275	.131		
NEO-ANG	.706	.714	.498	.509		
Negative Affect Factor					48.8%	48.6%

*Measure logarithmically transformed.

Table 34. Factor analysis of depression, anxiety, and anger scales in White (n=550) and Black (n=103) subjects separately.

Items	Factor Loadings (h)		Communalities (h^2)		Variance Explained (%)	
	White	Black	White	Black	White	Black
BDI*	.684	.575	.468	.331		
CES-D*	.684	.729	.467	.531		
NEO-DEP	.823	.789	.678	.622		
STAI-T*	.900	.881	.810	.777		
NEO-ANX	.712	.751	.506	.564		
TCI-HA	.655	.656	.429	.430		
STAXI-T*	.553	.578	.306	.334		
STAXI-OUT	.444	.469	.197	.220		
NEO-ANG	.720	.654	.518	.427		
Negative Affect Factor					48.7%	47.1%

*Measure logarithmically transformed.

3.7.2 Multiple regression.

As summarized in Table 35, a series of multiple regression analyses were performed to assess the relationship between the negative affect factor score, derived from factor analysis (see results above), and three frequency domain indices of heart rate variability (HF-HRV, LF-HRV, and LF-HF-HRV). These associations were first examined alone and then with covariate-adjustment by entering covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) simultaneously on the first step of each regression equation.

Table 35. Multiple regression analyses assessing the relationship between negative affect (factor score) and HRV (HF-HRV, LF-HRV, LF:HF-HRV) in the full sample.

	β	P	R^{2b}	ΔR^{2b}	b	95% CI (b)	
DV: HF-HRV							
1. Negative Affect F-score	-.092	.018	.009	-	-.121	-.221	-.020
After covariate-adjustment[a]:							
1. Covariates	-	-	.204	-	-	-	-
2. Negative Affect F-score	-.141	.000	.223	.019	-.185	-.277	-.093
DV: LF-HRV							
1. Negative Affect F-score	-.041	.295	.002	-	-.049	-.141	.043
After covariate-adjustment[a]:							
1. Covariates	-	-	.171	-	-	-	-
2. Negative Affect F-score	-.089	.015	.179	.008	-.107	-.192	-.021
DV: LF:HF-HRV							
1. Negative Affect F-score	.049	.213	.002	-	.200	-.115	.515
After covariate-adjustment[a]:							
1. Covariates	-	-	.124	-	-	-	-
2. Negative Affect F-score	.059	.121	.127	.003	.078	-.021	.177

[a]Covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) were entered on the first step of each regression equation.
[b]R^2 and ΔR^2 values are reported for the final model of each regression equation.

Multiple regression analyses showed higher negative affect factor scores to predict lower HF-HRV ($\beta = -.092$, $t_{(1, 651)} = -2.365$, $p = .018$). This relationship persisted after covariates were entered into the model ($\beta = -.141$, $t_{(9, 643)} = -3.962$, $p = .000$). Demographic and cardiovascular risk factors accounted for 20.4% and negative affect factor scores an additional 1.9% of the variance in HF-HRV; this addition to the model was statistically significant ($F_{change} = 15.695$, $p = .000$). Gender, and age correlated significantly with HF-HRV in the final model; women ($\beta = .231$) exhibited higher HF-HRV and older age ($\beta = -.399$) was related to lower HF-HRV (all p's <.001). Similarly, higher negative affect factor scores were associated with lower LF-HRV ($\beta = -.041$, $t_{(1, 651)} = -1.047$, $p = .295$), but only significantly so following covariate-adjustment ($\beta = -$

.089, $t_{(9, 643)}$ = -2.447, p = .015). Demographic and cardiovascular risk factors accounted for 17.1% and negative affect factor scores an additional 0.8% of the variance in LF-HRV; this addition to the model was statistically significant (F_{change} = 5.989, p = .015). Age (β = -.378, p = .000) and SBP (β = -.175, p = .002) were correlated with LF-HRV negatively and DBP (β = .169, p = .003) positively. In contrast, negative affect factor scores were not related significantly to LF:HF-HRV (p's >.05). Demographic and cardiovascular risk factors accounted for 12.3% and negative affect factor scores an additional 0.3% of the variance in LF:HF-HRV (F_{change} = 2.413, p = .121). Women and Black subjects exhibited lower LF:HF-HRV (β = -.273, p = .000 and β = -.130, p = .001, respectively); higher education and DBP were related to LF:HF-HRV positively (β = .105, p = .008 and β = .150, p = .010, respectively) while SBP was related to LF:HF-HRV negatively (β = -.141, p = .016).

3.7.3 Structural equation modeling.

The relationship between negative affect and HRV was reexamined using the same two-step approach in structural equation modeling as was described in testing Hypothesis 4. First the "measurement" portion of the model was evaluated. This model included the first order confirmatory factor analysis proposed previously but was extended to include a second order latent factor of negative affect. The conceptual model representing the measurement model (i.e. second order confirmatory factor analysis) is depicted in Figure 16. After the adequacy of this

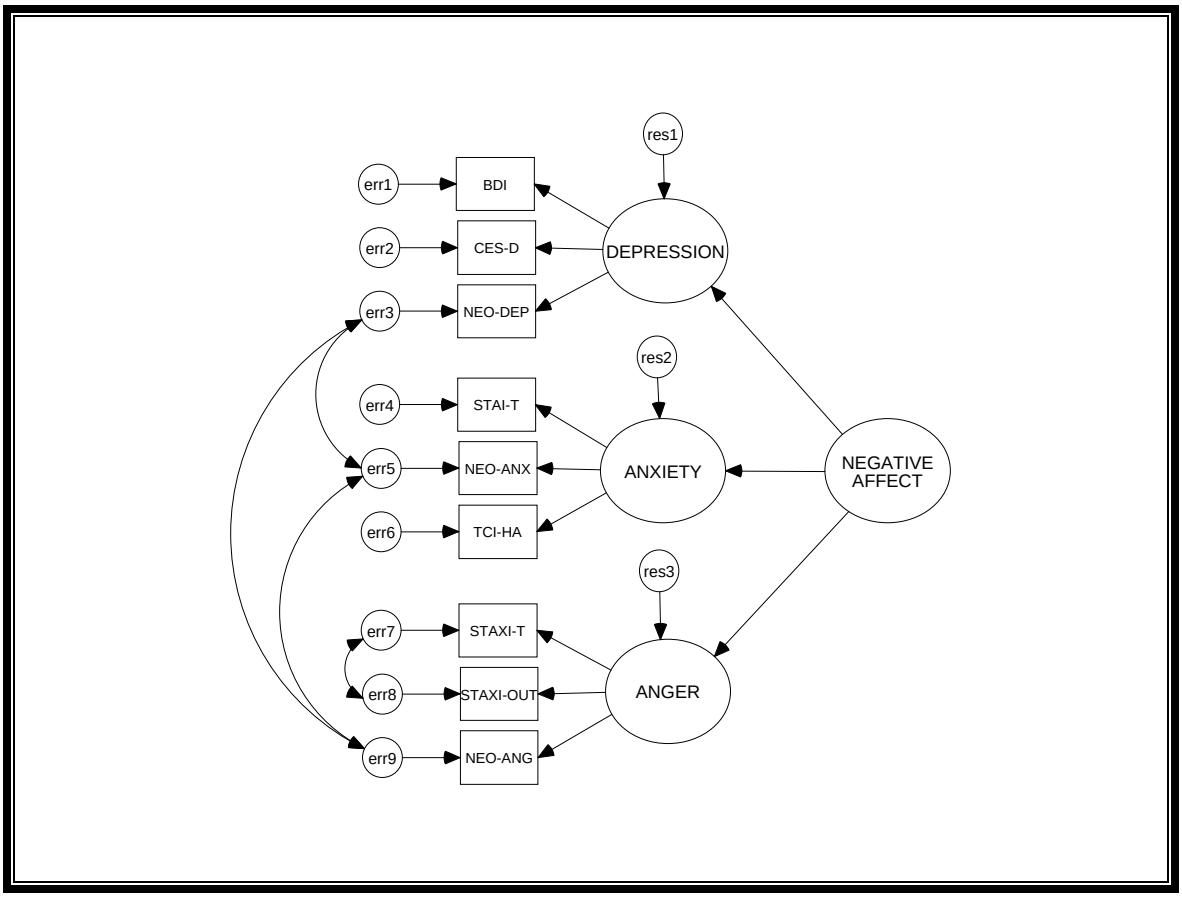

Figure 16, Hypothesis 5. Conceptual model of second order confirmatory factor analysis (measurement model).

model was established, the "full" model was then evaluated. The full model included the measurement model as well as the path between negative affect and the outcome variables of interest. The conceptual model representing the full model is depicted in Figure 18.

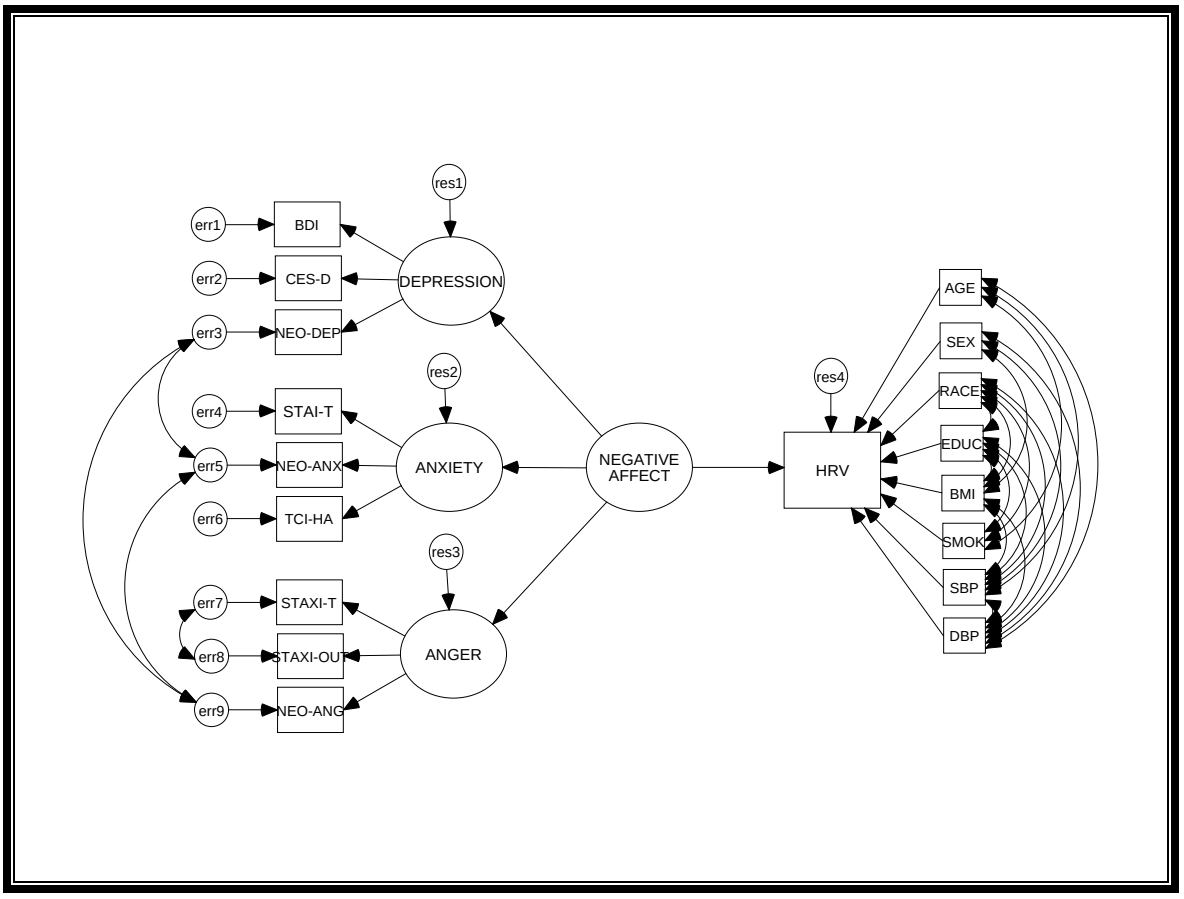

Figure 17, Hypothesis 5. Conceptual model of the full model depicting relationship between negative affect and HRV (HF-HRV, LF-HRV, LF:HF-HRV).

3.7.3.1 Measurement model. The measurement model or second order confirmatory factor analysis included 3 latent constructs (depression, anxiety, and anger), their respective indicators (observed variables), and the second order factor of negative affect. The latent construct of negative affect was scaled by constraining a factor loading parameter to 1, using anxiety as the reference item. In this model, there were 45 distinct sample moments (data points [9(9 + 1)/2]) and 25 unknown parameters to be estimated (i.e. 8 regression paths, 13 variances [12 error variances], and 4 covariances) resulting in 20 degrees of freedom. Examination of parameter estimates showed the presence of one negative variance value. Such nonsensical values (i.e.

Heywood cases) may result from model problems such as model misspecification or small sample size. In this case, evidence suggested problems with multicollinearity as indicated by model-implied correlation coefficients >.90 and tolerance values ($1\text{-}R^2_{smc}$) <.01. Although not encouraged, constraints may be placed on parameters to prevent Heywood cases (Chen, Bollen, Paxton, Curran, & Kirby, 2001). Here, the residual variance for anxiety was scaled to the residual variance for depression by using an equality constraint. In this modified model there were 24 unknown parameters to be estimated (i.e. 8 regression paths, 12 variances [12 error variances], and 4 covariances) resulting in 21 degrees of freedom.

Fit indices for this model showed mixed results. The chi-square test statistic $\chi^2(21, N=653) = 164.618$, $p<.001$ and the normed chi-square index (χ^2/df) = 7.839 showed poor fit, while the RMSEA = .102, 90% CI = .088-.117, p = .000 showed marginal to poor fit and the CFI = .956 good fit. The AIC = 212.618 and 2.2% of values from the standardized residual matrix were >2.58. See Table 12.

Estimates of regression weights are summarized in Table 36 and represented in Figure 17. Unstandardized regression weights showed all paths significant at the .001 level.

Table 36. Estimates of regression weights derived from structural equation modeling of measurement model (second order confirmatory factor analysis) (Hypothesis 5, Figure 17).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Negative Affect → Depression	.962	.193	.011	16.995	<.001
Negative Affect → Anxiety	.998	1.000	-	-	-
Negative Affect → Anger	.644	.029	.003	10.632	<.001
Depression → BDI	.743	.971	.049	19.952	<.001
Depression → CES-D	.772	1.000	-	-	-
Depression → NEO-DEP	.787	6.635	.325	20.387	<.001
Anxiety → STAI-T	.955	.072	.004	19.773	<.001
Anxiety → NEO-ANX	.671	1.000	-	-	-
Anxiety → TCI-HA	.637	1.250	.082	15.182	<.001
Anger → STAXI-T	.675	1.000	-	-	-
Anger → STAXI-OUT	.575	13.084	.810	16.150	<.001
Anger → NEO-ANG	.917	30.547	2.207	13.841	<.001

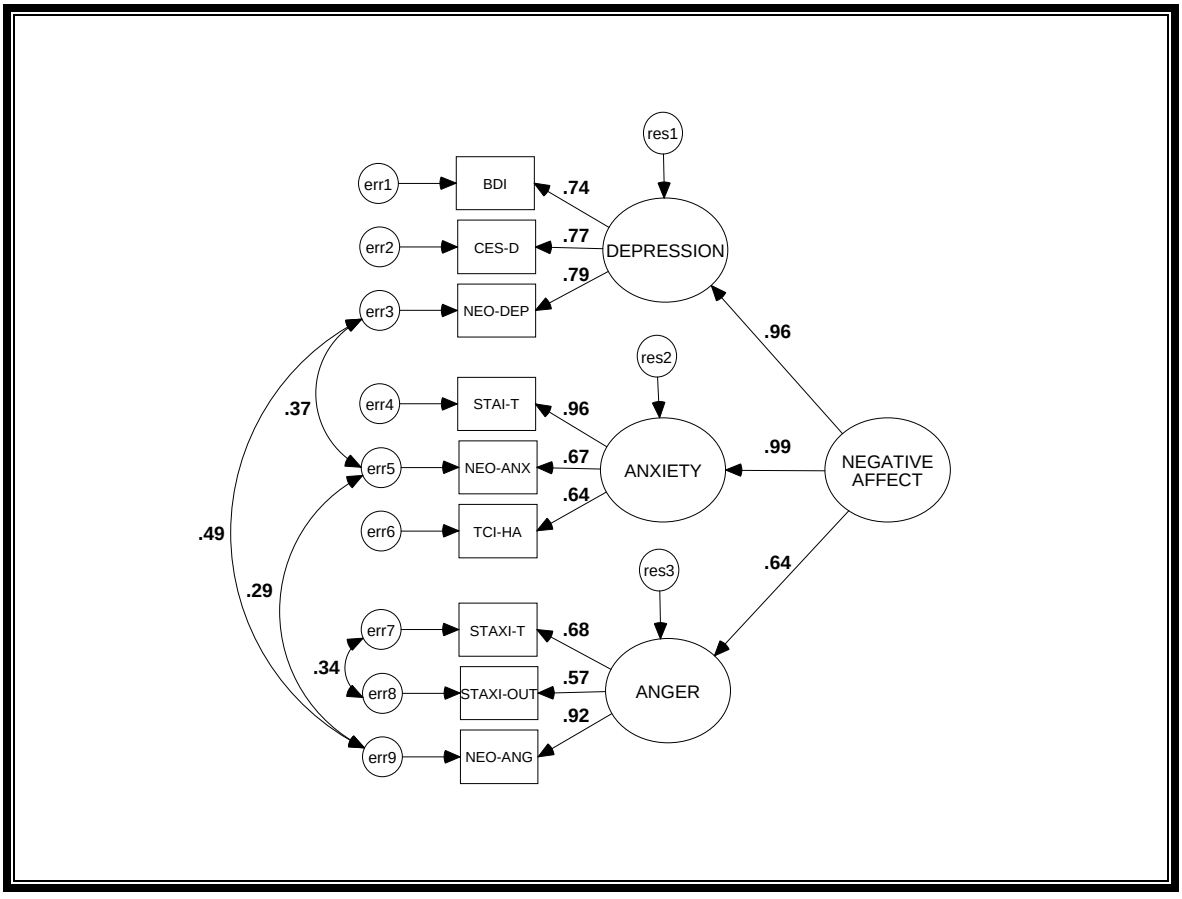

Figure 18, Hypothesis 5. Standardized estimates of second order confirmatory factor analysis (measurement model).

Standardized estimates of these paths showed a 1 standard deviation increase in negative affect related to a .96 standard deviation increase in depression, .99 standard deviation increase in anxiety, and a .64 standard deviation increase in anger. Examination of the SMCs showed the second order latent construct of negative affect to explain 92.5% of the variance in the first order latent construct of depression, 99.7% of anxiety, and 41.4% of anger. Tolerance values ($1\text{-}R^2_{smc}$) for the depression (.075) and anxiety (.003) constructs indicated multicollinearity.

3.7.3.2 Full model. Although the model fit indices for the measurement model showed mixed support for its adequacy, evaluation of the full model was pursued. The full model included the measurement model (i.e. second order confirmatory factor analysis) as well as the path between the second order latent construct of negative affect and HRV. Three separate analyses were conducted to examine HF, LF, and LF:HF-HRV individually as the dependent measures while adjusting for covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP). In this model, there were 171 distinct sample moments (data points [18(18 + 1)/2]) and 60 unknown parameters to be estimated (i.e. 17 regression paths, 21 variances [12 error variances], and 22 covariances) resulting in 111 degrees of freedom.

3.7.3.2.1 HF-HRV. With respect to HF-HRV, the chi-square test statistic $\chi^2(111, N=653) = 412.779$, $p<.001$ showed poor overall model fit. The normed chi-square index (χ^2/df) = 3.719 and RMSEA = .065, 90% CI = .058-.071, p = .000 showed adequate fit and the CFI = .932 showed good fit. AIC = 532.779 and 7.0% of values in the standardized residual matrix were >2.58. See Table 12

Estimates of regression weights are summarized in Table 37 and represented in Figure 19. The unstandardized regression weight between the latent construct of negative affect and HF-

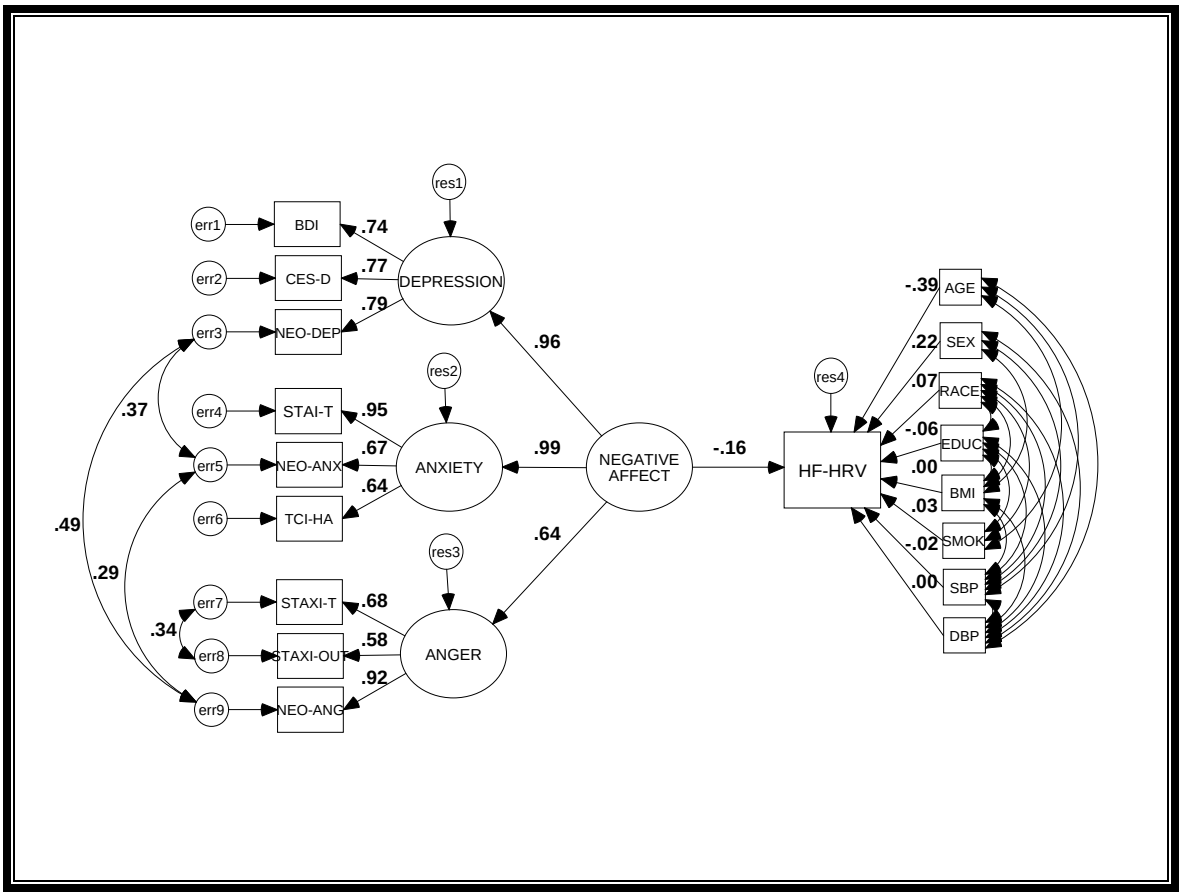

Figure 19, Hypothesis 5. Standardized estimates of the full model depicting relationship between negative affect and HF-HRV.

HRV was -.059, indicating that a 1-point increase in negative affect predicts a .059-point decrease in HF-HRV (with covariate-adjustment); this path was significant at the .001 level. The standardized estimate of this relationship showed a 1 standard deviation increase in negative affect to correspond to a .163 standard deviation decrease in HF-HRV (with covariate-adjustment). Examination of the SMCs showed negative affect as well as covariates (age, sex,

race, education, BMI, smoking status, SBP, and DBP) to explain 24.7% of the variance in HF-HRV.

Table 37. Estimates of regression weights derived from structural equation modeling of full model depicting relationship between negative affect and HF-HRV (Hypothesis 5, Figure 19).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Negative Affect → HF-HRV	-.163	-.059	.013	-4.466	<.001
Negative Affect → Depression	.963	.194	.011	17.015	<.001
Negative Affect → Anxiety	.999	1.000	-	-	-
Negative Affect → Anger	.643	.029	.003	10.615	<.001
Depression → BDI	.743	.972	.049	19.980	<.001
Depression → CES-D	.772	1.000	-	-	-
Depression → NEO-DEP	.787	6.631	.325	20.401	<.001
Anxiety → STAI-T	.955	.072	.004	19.819	<.001
Anxiety → NEO-ANX	.671	1.000	-	-	-
Anxiety → TCI-HA	.637	1.249	.082	15.174	<.001
Anger → STAXI-T	.675	1.000	-	-	-
Anger → STAXI-OUT	.575	13.089	.810	16.153	<.001
Anger → NEO-ANG	.917	30.535	2.210	13.817	<.001
Age → HF-HRV	-.393	-.071	.006	-11.139	<.001
Sex → HF-HRV	.224	.569	.092	6.192	<.001
Race → HF-HRV	.069	.242	.125	1.936	.053
Education → HF-HRV	-.059	-.024	.015	-1.625	.104
BMI → HF-HRV	.004	.001	.008	.106	.916
Smoking → HF-HRV	.029	.076	.091	.832	.406
SBP → HF-HRV	-.020	-.002	.005	-.379	.705
DBP → HF-HRV	.002	.000	.008	.037	.971

3.7.3.2.2 LF-HRV. With respect to LF-HRV, the chi-square test statistic $\chi^2(111, N=653) = 401.332$, $p<.001$ also showed poor model fit while the normed chi-square index (χ^2/df) = 3.616 and RMSEA = .063, 90% CI = .057-.070, p = .001 showed adequate and the CFI = .934 good fit. AIC = 521.332 and 5.8% of values in the standardized residual matrix were >2.58. See Table 12

Estimates of regression weights are summarized in Table 38 and represented in Figure 20. The unstandardized regression weight between the latent construct of negative affect and LF-HRV was -.028, indicating that a 1-point increase in negative affect predicts a .028-point decrease in LF-HRV (with covariate-adjustment); this path was significant at the .05 level. The standardized estimate of this relationship showed a 1 standard deviation increase in negative affect to correspond to a .085 standard deviation decrease in LF-HRV (with covariate-adjustment). Examination of the SMCs showed negative affect as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) to explain 18.4% of the variance in LF-HRV.

Table 38. Estimates of regression weights derived from structural equation modeling of full model depicting relationship between negative affect and LF-HRV (Hypothesis 5, Figure 20).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Negative Affect → LF-HRV	-.085	-.028	.012	-2.266	.023
Negative Affect → Depression	.962	.193	.011	17.015	<.001
Negative Affect → Anxiety	.999	1.000	-	-	-
Negative Affect → Anger	.644	.029	.003	10.637	<.001
Depression → BDI	.743	.972	.049	19.958	<.001
Depression → CES-D	.772	1.000	-	-	-
Depression → NEO-DEP	.788	6.637	.325	20.393	<.001
Anxiety → STAI-T	.954	.072	.004	19.809	<.001
Anxiety → NEO-ANX	.671	1.000	-	-	-
Anxiety → TCI-HA	.637	1.250	.082	15.199	<.001
Anger → STAXI-T	.675	1.000	-	-	-
Anger → STAXI-OUT	.575	13.084	.810	16.151	<.001
Anger → NEO-ANG	.917	30.543	2.206	13.843	<.001
Age → LF-HRV	-.373	-.061	.006	-10.176	<.001
Sex → LF-HRV	-.062	-.142	.087	-1.636	.102
Race → LF-HRV	-.078	-.246	.118	-2.094	.036
Education → LF-HRV	.051	.019	.014	1.354	.176
BMI → LF-HRV	.010	.002	.008	.257	.797
Smoking → LF-HRV	.014	.033	.086	.383	.702
SBP → LF-HRV	-.189	-.016	.005	-3.372	<.001
DBP → LF-HRV	.175	.022	.007	3.145	.002

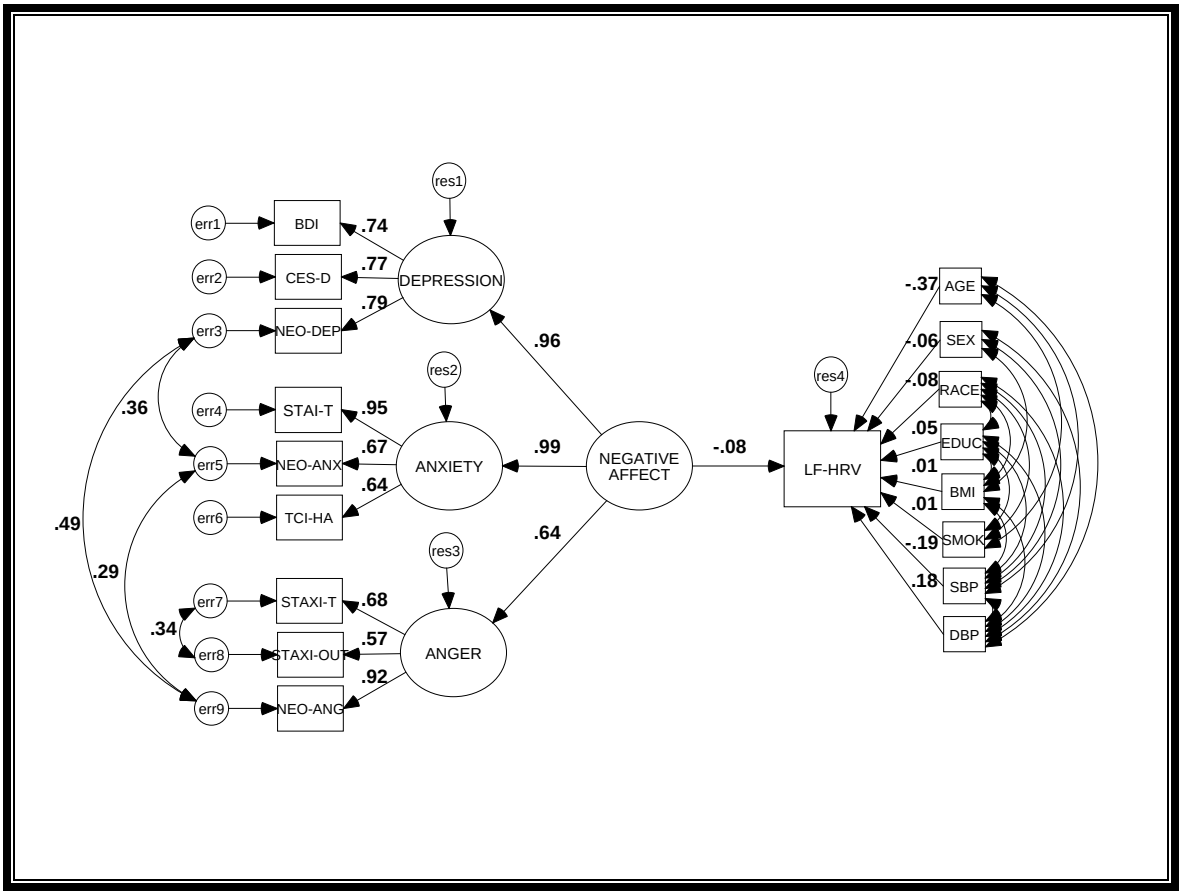

Figure 20, Hypothesis 5. Standardized estimates of the full model depicting relationship between negative affect and LF-HRV.

3.7.3.2.3 LF:HF-HRV. With respect to LF:HF-HRV, fit indices showed a similar pattern of results. While the chi-square test statistic $\chi^2(111, N=653) = 403.760$, $p<.001$ showed poor model fit, the normed chi-square index (χ^2/df) = 3.637 and RMSEA = .064, 90% CI = .057-.070, p = .000 showed adequate and the CFI = .933 good fit. AIC = 523.760 and 5.8% of values in the standardized residual matrix were >2.58. See Table 12.

Estimates of regression weights are summarized in Table 39 and represented in Figure 21. The unstandardized regression weight between the latent construct of negative affect and

Table 39. Estimates of regression weights derived from structural equation modeling of full model depicting relationship between negative affect and LF:HF-HRV (Hypothesis 5, Figure 21).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Negative Affect → LF:HF-HRV	.085	.031	.014	2.223	.026
Negative Affect → Depression	.961	.193	.011	16.987	<.001
Negative Affect → Anxiety	.998	1.000	-	-	-
Negative Affect → Anger	.643	.029	.003	10.620	<.001
Depression → BDI	.743	.972	.049	19.960	<.001
Depression → CES-D	.772	1.000	-	-	-
Depression → NEO-DEP	.787	6.632	.325	20.388	<.001
Anxiety → STAI-T	.956	.072	.004	19.759	<.001
Anxiety → NEO-ANX	.670	1.000	-	-	-
Anxiety → TCI-HA	.636	1.250	.082	15.164	<.001
Anger → STAXI-T	.675	1.000	-	-	-
Anger → STAXI-OUT	.575	13.087	.810	16.150	<.001
Anger → NEO-ANG	.917	30.544	2.209	13.828	<.001
Age → LF:HF-HRV	.054	.010	.007	1.439	.150
Sex → LF:HF-HRV	-.277	-.711	.099	-7.155	<.001
Race → LF:HF-HRV	-.139	-.488	.135	-3.617	<.001
Education → LF:HF-HRV	.104	.044	.016	2.684	.007
BMI → LF:HF-HRV	.005	.001	.009	.126	.899
Smoking → LF:HF-HRV	-.017	-.043	.099	-.436	.663
SBP → LF:HF-HRV	-.149	-.014	.005	-2.589	.010
DBP → LF:HF-HRV	.155	.022	.008	2.708	.007

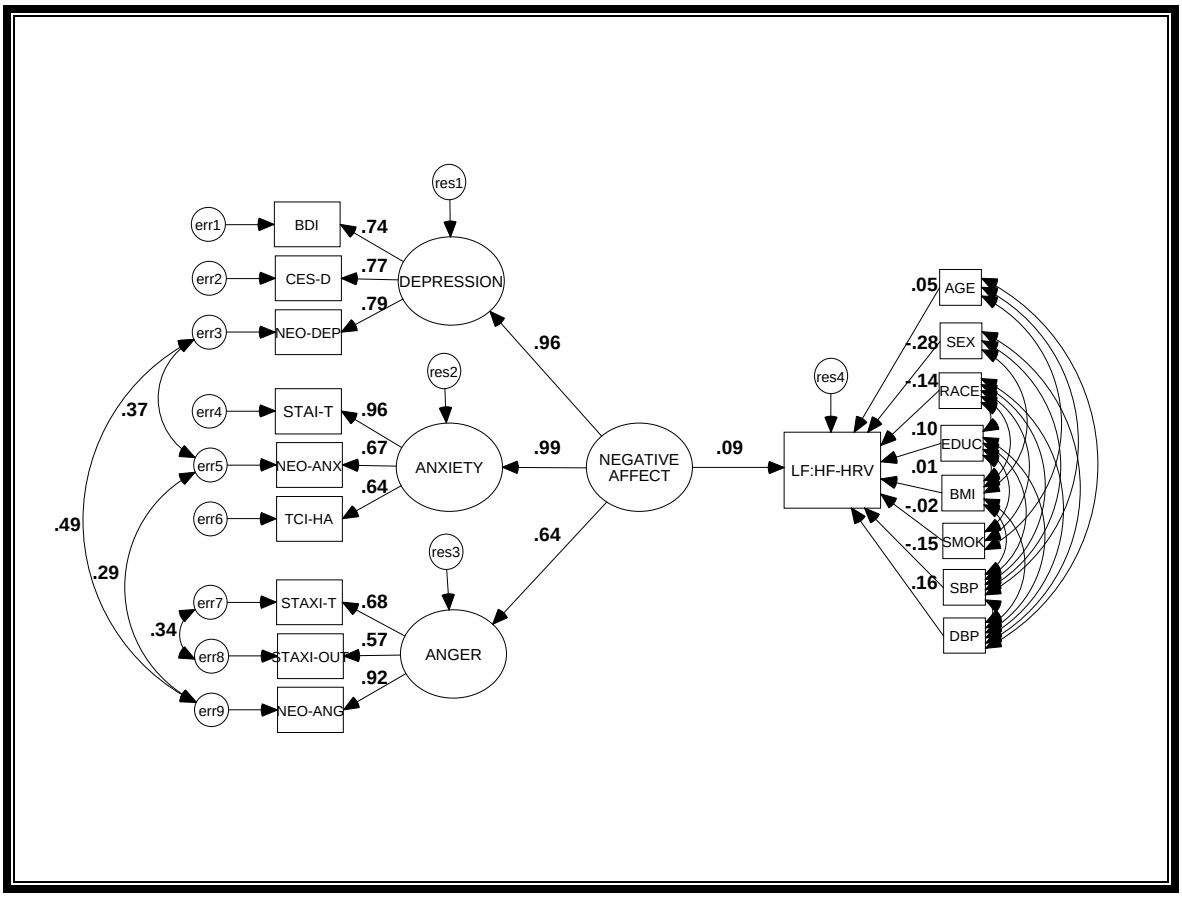

Figure 21, Hypothesis 5. Standardized estimates of the full model depicting relationship between negative affect and LF:HF-HRV.

LF:HF-HRV was .031, indicating a 1-point increase in negative affect predicts a .031-point *increase* in LF:HF-HRV (with covariate-adjustment); this path was significant at the .05 level. The standardized estimate of this relationship showed a 1 standard deviation increase in negative affect to correspond to a .085 standard deviation *increase* in LF:HF-HRV (with covariate-adjustment). Examination of SMCs showed the latent construct of negative affect as well as covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) to explain 13.8% of the variance in LF:HF-HRV.

3.8 Hypothesis 6: Are depression, anxiety, anger related to variation in autonomic control of heart rate independently of negative affect (model of unique and common variance)?

3.8.1 Multiple regression.

As summarized in Table 40, a series of multiple regression analyses were performed to assess the relationship of depression, anxiety, and anger to HRV independently of negative affect. Negative affect factor scores, derived from factor analysis (see results above), were entered on the first step, and depression, anxiety, and anger factor scores, also derived from factors analysis, were entered simultaneously on the second step of each of three regression equations examining HF-HRV, LF-HRV, and LF:HF-HRV individually. These associations were first examined alone and then with covariate-adjustment by entering covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP) into the model. In the covariate-adjusted models, covariates were entered on step 1, negative affect on step 2, and depression, anxiety, and anger simultaneously on step 3.

Table 40. Multiple regression analyses assessing the relationship between depression, anxiety, and anger factor scores (entered simultaneously) and HRV (HF-HRV, LF-HRV, LF:HF-HRV) after controlling for negative affect factor in the full sample.

	β	p	R^{2b}	ΔR^{2b}	b	95% CI (b)	
DV: HF-HRV							
1. Negative Affect F-Score	-.082	.706	.009	-	-.107	-.666	.451
2. F-scores	-	-	.043	.035	-	-	-
• Depression F-Score	-.232	.015	-	-	-.319	-.576	-.062
• Anxiety F-Score	.101	.430	-	-	.139	-.206	.484
• Anger F-Score	.136	.070	-	-	.189	-.016	.393
1. Covariates[a]	-	-	.204	-	-	-	-
2. Negative Affect F-Score	-.010	.961	.223	.019	-.013	-.530	.504
3. F-scores	-	-	.241	.017	-	-	-
• Depression F-Score	-.188	.030	-	-	-.261	-.496	-.026
• Anxiety F-Score	-.027	.824	-	-	-.037	-.362	.288
• Anger F-Score	.079	.250	-	-	.110	-.077	.297
DV: LF-HRV							
1. Negative Affect F-Score	.441	.046	.002	-	.528	.010	1.05
2. F-scores	-	-	.017	.015	-	-	-
• Depression F-Score	-.280	.004	-	-	-.353	-.591	-.114
• Anxiety F-Score	-.215	.096	-	-	-.271	-.591	.049
• Anger F-Score	-.068	.373	-	-	-.086	-.276	.103
1. Covariates[a]	-	-	.171	-	-	-	-
2. Negative Affect F-Score	.155	.456	.179	.008	.185	-.302	.672
3. F-scores	-	-	.182	.004	-	-	-
• Depression F-Score	-.153	.090	-	-	-.192	-.414	.030
• Anxiety F-Score	-.085	.495	-	-	-.107	-.413	.200
• Anger F-Score	-.053	.456	-	-	-.067	-.243	.109
DV: LF:HF-HRV							
1. Negative Affect F-Score	.475	.031	.003	-	.635	.057	1.21
2. F-scores	-	-	.019	.016	-	-	-
• Depression F-Score	-.024	.806	-	-	-.033	-.300	.233
• Anxiety F-Score	-.291	.025	-	-	-.410	-.767	-.053
• Anger F-Score	-.194	.011	-	-	-.275	-.486	-.063
1. Covariates[a]	-	-	.123	-	-	-	-
2. Negative Affect F-Score	.148	.489	.127	.003	.198	-.363	.759
3. F-scores	-	-	.136	.009	-	-	-
• Depression F-Score	.049	.597	-	-	.069	-.186	.324
• Anxiety F-Score	-.049	.698	-	-	-.070	-.422	.283
• Anger F-Score	-.125	.088	-	-	-.177	-.380	.026

[a]β, p, b, and CI values not reported for step 1 (covariates) of each regression equation.
[b]R^2 and ΔR^2 values are reported for the final model of each regression equation.

After the negative affect factor score was entered into the model, the depression factor score predicted lower HF-HRV (β = -.232, $t_{(4, 648)}$ = -2.438, p = .015) and the anger factor score predicted *higher* HF-HRV albeit a statistical trend (β = .136, $t_{(4, 648)}$ = 1.812, p = .070). After covariate adjustment, only the depression factor score continued to predict lower HF-HRV (β = -.188, $t_{(12, 640)}$ = -2.177, p = .030). Demographic and cardiovascular risk factors accounted for 20.4%, negative affect factor scores an additional 1.9% (F_{change} = 15.695, p = .000), and depression, anxiety, and anger factor score collectively an additional 1.7% (F_{change} = 4.724, p = .003) of the variance in HF-HRV. Sex, age, and race correlated significantly with HF-HRV in the final model; women (β = .224) and Black subjects (β = .081) exhibited higher HF-HRV and older age (β = -.378) was related to lower HF-HRV (all p's <.05). Similarly, after the negative affect factor score was entered into the model, the depression factor score predicted lower LF-HRV (β = -.280, $t_{(4, 648)}$ = -2.905, p = .004). This relationship was attenuated after covariate adjustment (β = -.153, $t_{(12, 640)}$ = -1.701, p = .090). Demographic and cardiovascular risk factors accounted for 17.1%, negative affect factor scores an additional 0.8% (F_{change} = 5.989, p=.015), and depression, anxiety, and anger factor score collectively an additional 0.4% (F_{change} = 1.005, p=.390) of the variance in LF-HRV. Age (β = -.370, p = .000) and SBP (β = -.180, p = .002) were correlated with LF-HRV negatively and DBP (β = .172, p = .002) positively. In contrast, after negative affect factor score was entered into the model, anxiety and anger factor scores predicted lower LF:HF-HRV (β = -.291, $t_{(4, 648)}$ = -2.254, p = .025 and β = -.194, $t_{(4, 648)}$ = -2.549, p = .011, respectively). These relationships were no longer present after covariate-adjustment. Demographic and cardiovascular risk factors accounted for 17.1%, negative affect factor scores an additional 0.3% (F_{change} = 2.413, p = .121), and depression, anxiety, and anger factor score collectively an additional 0.9% (F_{change} = 2.278, p = .079) of the variance in LF:HF-HRV.

Women and Black subjects exhibited lower LF:HF-HRV (β = -.265, p = .000 and β = -.140, p = .001, respectively); higher education and DBP were related to LF:HF-HRV positively (β = .102, p = .010 and β = .145, p = .013, respectively) while SBP was related to LF:HF-HRV negatively (β = -.135, p = .021).

3.8.2 Structural equation modeling.

In addition to the mediated path by which the effects of depression, anxiety, and anger on HRV were transmitted through negative affect (Hypothesis 5), the *direct* effects of depression, anxiety, and anger on HRV were also examined. In order to determine whether these direct paths contribute to the prediction of HRV beyond negative affect, each path was examined individually and the chi-square difference test and the AIC used to compare statistical fit between the models. The conceptual model representing the direct paths between these latent constructs and HRV is depicted in Figure 22.

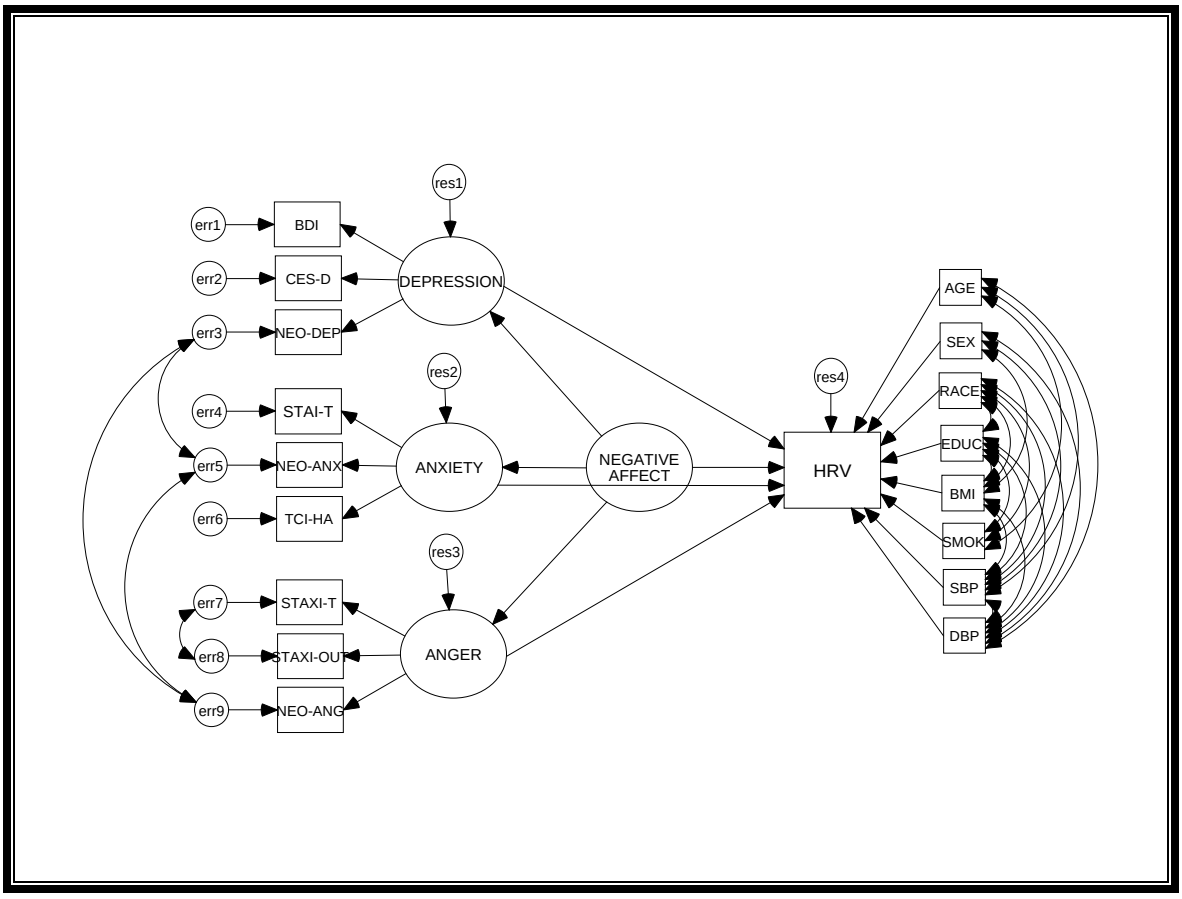

Figure 22, Hypothesis 6. Conceptual model depicting relationship between negative affect and HRV as well as the direct paths between the latent constructs of depression, anxiety, and anger and HRV (HF-HRV, LF-HRV, LF:HF-HRV).

3.8.2.1 HF-HRV. First, a direct path between depression and HF-HRV was estimated; the chi-square test statistic for this model was $\chi^2(110, N=653) = 406.812$, $p<.001$; AIC = 528.812. When compared to the chi-square test statistic for the original model *without* any direct paths $\chi^2(111, N=653) = 412.779$, $p<.001$; AIC = 532.779, the chi-square difference test showed the modified model to be superior statistically to the original model $\chi^2_{difference}(1, N=653) = 5.967$, $p <.025$. Second, a direct path between anxiety and HF-HRV was estimated; the chi-square test statistic for this model was $\chi^2(110, N=653) = 411.643$, $p<.001$. The chi-square difference test showed no improvement in the model with the addition of this path, $\chi^2_{difference}(1, N=653) = 1.136$, n.s.; AIC

= 533.643. Third, a direct path between anger and HF-HRV was estimated; the chi-square test statistic for this model was $\chi^2(110, N=653) = 403.897$, $p<.001$. The chi-square difference showed the modified model to be superior statistically to the original model $\chi^2_{difference}(1, N=653) = 8.882$, $p <.005$; AIC = 525.897.

Because the addition of a direct depression-HF-HRV path and a direct anger-HF-HRV path improved the fit of the original model, both paths were added and the model re-estimated. The chi-square test statistic for this model was $\chi^2(109, N=653) = 400.421$, $p<.001$ with the chi-square difference test $\chi^2_{difference}(2, N=653) = 12.358$, $p <.005$ (AIC = 524.421) showing superior fit statistically. Moreover, comparison of the AIC values across all models suggested this model (with both the depression and anger paths estimated) to have the best relative fit. The normed chi-square index (χ^2/df) = 3.674 and the RMSEA = .064, 90% CI = .057-.071, p = .000 showed adequate and the CFI = .934 good fit. Additionally, 6.4% of covariances in the standardized residual matrix were >2.58. See Table 12.

Estimates of regression weights are summarized in Table 41 and represented in Figure 23. The unstandardized regression weights showed a 1-point increase in negative affect related to a .092-point increase in HF-HRV; this path, however, was nonsignificant (p=.390). A 1-point increase in depression was related to a .921-point decrease in HF-HRV; this path was a statistical trend (p=.080). Finally, a 1-point increase in anger was related to a 1.044-point increase in HF-HRV; this path was significant at the .05 level (with covariate-adjustment). Standardized estimates of these paths showed a 1 standard deviation increase in negative affect related to a .256 standard deviation increase in HF-HRV, a 1 standard deviation increase in depression related to a .517 decrease in HF-HRV, and a 1 standard deviation increase in anger related to a .130-point increase in HF-HRV (with covariate-adjustment).

Table 41. Estimates of regression weights derived from structural equation modeling of full model depicting the relationship between negative affect and HF-HRV as well as the direct paths between anger and depression and HF-HRV (Hypothesis 6, Figure 23).

Parameters	Standardized Estimate	Unstandardized Estimate	S.E.	C.R.	P
Depression → HF-HRV	-.517	-.921	.526	-.1.749	.080
Anger → HF-HRV	.130	1.044	.415	2.516	.012
Negative Affect → HF-HRV	.256	.092	.107	.859	.390
Negative Affect → Depression	.961	.194	.011	17.013	<.001
Negative Affect → Anxiety	.998	1.000	-	-	-
Negative Affect → Anger	.643	.029	.003	10.619	<.001
Depression → BDI	.745	.973	.049	20.049	<.001
Depression → CES-D	.772	1.000	-	-	-
Depression → NEO-DEP	.786	6.613	.324	20.396	<.001
Anxiety → STAI-T	.955	.072	.004	19.763	<.001
Anxiety → NEO-ANX	.670	1.000	-	-	-
Anxiety → TCI-HA	.637	1.251	.082	15.165	<.001
Anger → STAXI-T	.674	1.000	-	-	-
Anger → STAXI-OUT	.574	13.082	.811	16.138	<.001
Anger → NEO-ANG	.919	30.639	2.206	13.891	<.001
Age → HF-HRV	-.381	-.068	.006	-10.754	<.001
Sex → HF-HRV	.219	.552	.092	5.994	<.001
Race → HF-HRV	.074	.257	.124	2.075	.038
Education → HF-HRV	-.048	-.020	.015	-1.331	.189
BMI → HF-HRV	.007	.002	.008	.196	.845
Smoking → HF-HRV	.028	.071	.091	.778	.437
SBP → HF-HRV	-.028	-.003	.005	-.522	.602
DBP → HF-HRV	.002	.000	.007	.045	.964

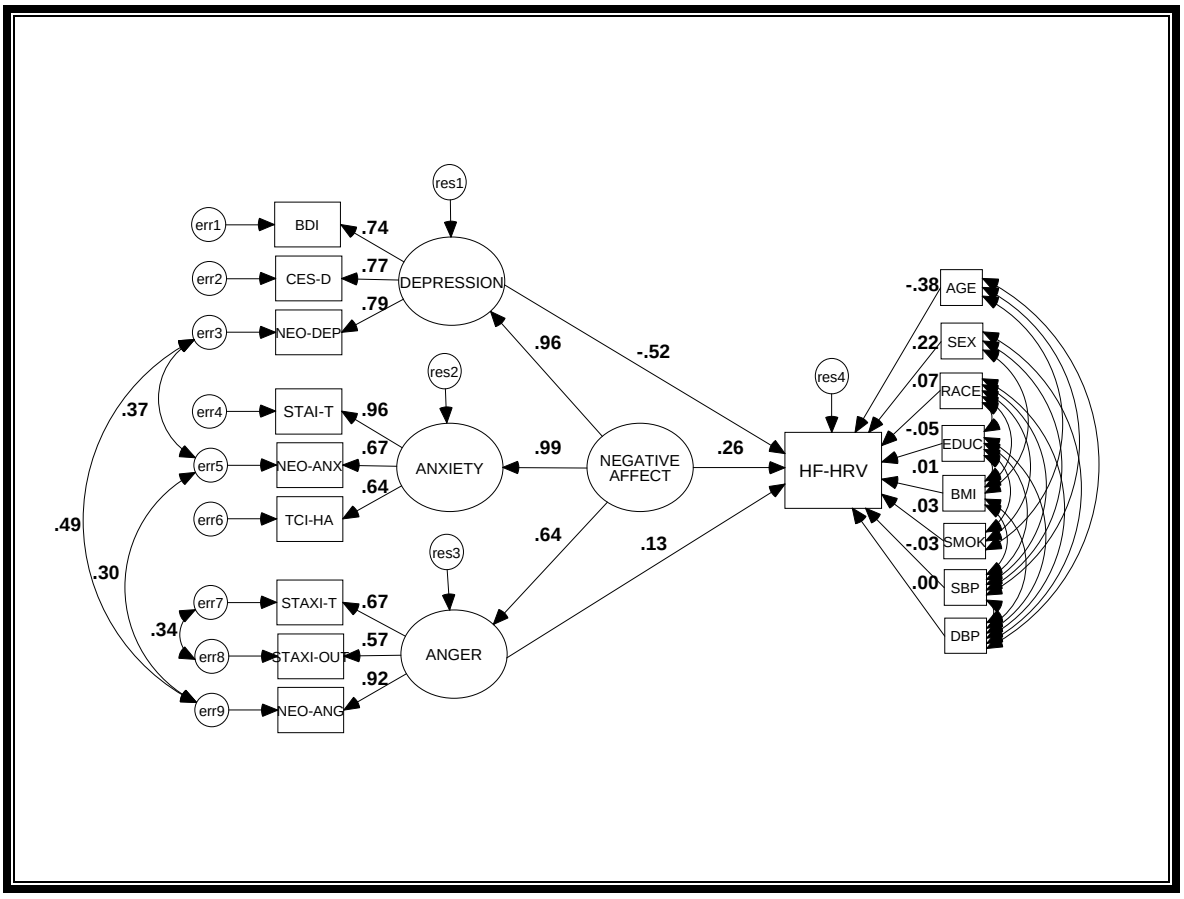

Figure 23, Hypothesis 6. Standardized estimates of full model depicting relationship between negative affect and HF-HRV as well as direct paths between the latent constructs of depression and HF-HRV and anger and HF-HRV.

Examination of SMCs showed the predictors of HF-HRV to explain 26.5% of its variance, including the mediated effect of negative affect and the direct effects of depression, anger, and covariates (age, sex, race, education, BMI, smoking status, SBP, and DBP). This is a 1.8% increase in variance explained compared to the original model in which the direct paths between depression and HF-HRV and anger and HF-HRV were not included.

3.8.2.2 LF-HRV and LF:HF-HRV. Inclusion of direct paths between depression, anxiety, and anger and LF-HRV (as well as LF:HF-HRV) did not show model improvement (all chi-square difference tests with p's >.05).

4.0 DISCUSSION

4.1 Summary of findings

The co-occurrence of mood and anxiety disorders as well as self-reported symptoms of depression, anxiety, and anger in both psychiatric and non-clinical samples may be explained by a common underlying dimension of negative emotionality, characterizing an individual's tendency to experience negative emotion in general. While individual negative affective dispositions have been studied in relation to risk for coronary heart disease (CHD), the degree to which a general tendency to experience negative emotion (trait negative affect) may better account for these relationships is not known. Relations between individual negative affective dispositions (e.g. depression) and CHD as well as trait negative affect and CHD must be evaluated simultaneously to determine whether risk for CHD is conferred by variance unique to individual negative affective dispositions, by variance that is common to negative affective dispositions, or by both. Thus, in a community-based sample of men and women, the goal of the present study was to identify the unique and common pathways by which individual differences in depression, anxiety, and anger are related to variation in autonomic control of heart rate as indexed by heart rate variability (HRV), a risk factor for cardiovascular atherosclerotic disease, coronary clinical events, and mortality (e.g. Dekker et al., 2000; Hayano et al., 1991). To this end, six primary hypotheses were proposed.

To summarize, in relation to Hypothesis 1, depression was related to HF-HRV and LF-HRV negatively and LF:HF-HRV positively. Regarding Hypothesis 2, anxiety was also related to HF-HRV and LF-HRV negatively, but was unrelated to LF:HF-HRV. In contrast, in

Hypothesis 3, anger was unrelated to any index of HRV. Findings from Hypotheses 1-3 were supported both by multiple regression and SEM data analytical approaches. With respect to Hypothesis 4 in which depression, anxiety, and anger were evaluated simultaneously in multiple regression analyses, depression was related negatively and anger related positively (albeit marginally statistically significant) to HF-HRV. In SEM, however, models depicting the simultaneous analysis of depression, anxiety, and anger in relation to HRV were poor fitting. Thus, individual parameter estimates examining the relative significance of these paths could not be interpreted. In Hypothesis 5, negative affect was related to HF-HRV and LF-HRV negatively in multiple regression; findings were similar in SEM analyses with the exception that in SEM negative affect was also related to LF:HF-HRV positively. Finally, in Hypothesis 6, when both negative affect and direct paths between depression, anxiety, and anger and HRV were examined, evidence from both data analytical strategies suggested that, in addition to negative affect, depression was independently related to HF-HRV negatively and anger was independently related to HF-HRV positively.

4.2 Dual data analytical approach

Before considering the current results in more detail, it is necessary to revisit the data analytical context within which the study findings will be discussed. As stated earlier, our goal in using both a conventional significance-testing approach by multiple regression analysis and a model-fitting approach by SEM was two-fold. First, we were interested in generating study results comparable to existing literatures, which almost exclusively use conventional statistical methods. Secondly, we were also interested in advancing the current literature by conducting more sophisticated modeling analyses that are, as of yet, less common but growing in popularity

because of their advantages, including increased flexibility in estimating associations among both observed and latent variables (Herschberger, 2003). Moreover, this dual statistical approach provided a unique opportunity to compare findings across analytical methods, but within the same sample. By in large, this effort showed results from both sets of analyses to point to similar conclusions across hypotheses. Differences in results, however, are noted throughout this discussion and attempts made to reconcile these discrepancies by integrating information provided by each approach uniquely.

Findings from Hypotheses 1-3 were supported uniformly by both data analytic strategies. That is, SEM models were close fitting and the same path coefficients across multiple regression and SEM were statistically significant. In Hypothesis 4, however, the simultaneous analysis of depression, anxiety, and anger (in relation to HRV) by multiple regression suggested one pattern of associations, whereas results from SEM indicated that these models were so poor fitting they were not interpretable. Model-fitting information from SEM suggested that the hypothesized models were not a good fit to the data, rendering individual parameter estimates meaningless. That multiple regression and SEM analyses led to different outcomes was not unexpected. While SEM estimates associations among all the variables in a given model simultaneously in an attempt to maximize similarity between the model-implied and sample covariance matrices, multiple regression instead examines individual relations between variables in a sequential fashion. Thus, in the case of Hypothesis 4, SEM information was used to conclude that the pathways by which depression, anxiety, and anger are related to HRV (when tested simultaneously) are not best depicted as being direct. This finding was later corroborated by results from Hypotheses 5 and 6 showing these effects on HRV to be mediated by negative affect (see section “Negative Affect” for extended discussion). In Hypothesis 5, the relation of negative

affect to HRV was supported by both types of analyses. Finally, slight differences in conclusions emerged in Hypothesis 6, with the full SEM model showing that, in addition to the mediated path, the best fitting model included a direct and independent path between anger and HF-HRV, as well as a direct and independent path between depression and HF-HRV. Although the depression-HF-HRV path was also observed in multiple regression, the anger-HF-HRV path was only present before, and not after, covariate-adjustment.

This summary may suggest that SEM results were favored when differences between multiple regression and SEM were found, implying that SEM data analytical strategies may have been sufficient in addressing the proposed hypotheses. This is not entirely true, however, as several concerns arose with the SEM models. First, the measurement models presented in Hypotheses 4 and 5, depicting a first and second order confirmatory factor analysis, respectively, showed marginal support for their fit. Despite this, in both cases, the full models (including the measurement model and the path model) showed adequate support. Thus, modification of the measurement models on the first step of these analyses might be considered. Additionally, models depicting Hypotheses 4-6 all exhibited problems with multicollinearity according to high squared multiple correlations and low tolerance values among the latent factors. Although SEM is an application that better manages high correlations, when associations exceed .85 muticollinearity becomes a problem in SEM as well. One recommended method by which multicollinearity may be corrected is to delete or collapse across the redundant items or factors. In the present analysis, one obvious source of multicollinearity resided between the depression and anxiety factors. Thus, in an exploratory model (results not shown) these factors were collapsed and the model re-estimated. This modification proved unhelpful, however, as the model fit actually deteriorated. Future analyses are needed in which other modifications may be

explored in an effort to reduce multicollinearity and improve the models' fit. In conclusion, though results showed some differences across regression and SEM approaches, as well as marginal model fit of the proposed measurement models, in total, both sets of analyses provided valuable information that when taken together showed substantial convergence.

4.3 Measurement of latent constructs

In the current study, each psychological construct of interest was measured by three well established and commonly administered self-report questionnaires. Depression was measured by the BDI, CES-D, and the Depression facet scale of the NEO PI-R, anxiety by the Trait Anxiety scale of the STAI, the Anxiety facet scale of the NEO PI-R, and the Harm Avoidance scale of the TCI, and anger by the Trait Anger and Anger Out scales of the STAXI and the Angry Hostility facet scale of the NEO PI-R. The availability of multiple measures of each construct provided a unique opportunity to evaluate the structure underlying these measures by modeling latent constructs (both by factor analysis and SEM) hypothesized to reflect their common variance. Identifying latent constructs better captured the goals of the present study and likely those of most research investigators who are interested in studying constructs such as depression rather than their respective measures (e.g. BDI). This promotes our understanding of psychological phenomena independent of their measurement, while increasing the generalizability of research findings. Moreover, this measurement approach increases both the reliability and the validity of constructs in a way that is not possible when an individual measure is used. This is true because the use of multiple measures reduces measurement error, thereby improving the construct's reliability. Additionally, the extent to which each measure loads highly on the predicted construct provides evidence for the construct's validity. In sum, the use of latent variable

modeling techniques in the present study reflects an important step forward with respect to the study of constructs, rather than individual measures, while also improving construct reliability and validity.

4.4 Depression and HRV

Although simple associations between depression and HRV have been reported in numerous studies (e.g. Agelink et al., 2002; O'Connor et al., 2002), few studies have considered the potential complexities of this relationship. Here, we first replicated the approach taken in the majority of studies in which depression was examined as an individual predictor of HRV. We then extended this approach by also evaluating (1) whether depression contributes to the prediction of HRV when examined concurrently with anxiety and anger, (2) whether any effect of depression on HRV may be mediated by the variance it shares with anxiety and anger (i.e. negative affect), and finally, (3) whether depression predicts HRV independently of negative affect. Moreover, we also included covariates in all analyses to rule out possible confounding by risk factor status. Findings showed that depression individually predicts HRV, with greater depression associated with reduced parasympathetically-mediated HRV as well as greater relative sympathetic dominance of cardiac autonomic control. Greater depression, when examined with anxiety and anger concurrently, was also associated with reduced parasympathetically-mediated HRV, though poor model fit necessitated cautious interpretation of this finding. Alternatively, the incorporation of negative affect into this model improved its fit, suggesting that the effect of depression on HRV was mediated, at least partially, by negative affect. Finally, in addition to the mediated pathway through which depression predicted HRV (i.e. negative affect), greater depression also independently predicted reduced

parasympathetically-mediated HRV. In sum, the effects of depression on HRV appear to be both indirect (i.e. mediated by negative affect) and direct. In other words, aspects of depression that are common to anxiety and anger are related to HRV, as are aspects of depression that are unique. This underscores the potency of depression as a risk factor for impaired HRV and implicates the full spectrum of depressive symptoms as being detrimental. In conclusion, depressive symptoms may, by both common and unique pathways, place otherwise healthy individuals at risk for impairments in autonomic modulation of HR with lower HF and LF HRV reflecting decrements in vagal function and higher LF:HF ratio HRV reflecting greater sympathetic relative to parasympathetic influences on HR. Importantly, evidence suggests such impairments confer subsequent risk for premature cardiovascular morbidity and mortality (e.g. Dekker et al., 2000; Tsuji et al., 1996).

How do results relating depression to cardiac autonomic function from the present study correspond to findings in relevant literatures? In healthy or otherwise unselected samples, substantial evidence shows depression, when examined individually, to predict coronary endpoints. Both depression diagnoses (i.e. major and minor depression) and depressive symptomatology are related prospectively to incident myocardial infarction (e.g. Barefoot et al., 1996; Ford et al., 1998; Pratt et al., 1996) and cardiac-specific mortality (e.g. Anda et al., 1993; Aromaa et al., 1994; Penninx et al, 2001). The relation of depression, also when examined individually, to autonomic function (as a potential mechanism by which depression confers risk for CHD) is less clear. Findings suggest depression diagnoses and depressive symptomatology among psychiatric and cardiac patients are related to indices of reduced vagal function, compared to controls (e.g. Agelink et al., 2002; Carney et al., 2001; Guinjoan et al., 1995; Imaoka et al., 1985; Stein et al., 2000). However, evidence supporting this association in samples

without known psychiatric or cardiac disease is equivocal. Review of these studies shows two investigations relating greater depressive symptoms to lower vagal activity (Light et al., 1998) and lower overall HRV (Kim et al., 2005). Other studies of healthy individuals reported lower LF:HF ratio HRV among individuals endorsing depressive symptoms (Horsten et al., 1999) or no relationship to HRV at all (Hughes & Stoney, 2000; Virtanen et al., 2003). Thus, results from the current analysis are among the first to demonstrate that the relationship between depression and HRV documented among psychiatric and cardiac patients also extends to healthy individuals. Additionally, current results may also be among the first to suggest that depression affects autonomic function both indirectly and directly. Notably, because no other study to date has similarly partitioned the variance in depression to determine whether its association with HRV may be attributable to trait negative affect, to unique aspects of depression, or both, findings from the current study lack a supporting literature, making necessary the replication of this finding in future investigation.

That depression is related to indices of autonomic function among psychiatric and cardiac patients, but is less consistently related to similar outcomes among healthy samples, raises speculation that only diagnostic classifications of depressive symptom clusters confer significant risk for impairment in autonomic function or that depressive symptoms confer risk for such impairment only in the context of pre-existing coronary artery disease. By extension, it may be postulated that any associations between depression and HRV observed in healthy samples may be driven by a subset of individuals who are not evaluated formally, but nonetheless meet criteria for a mood disorder diagnosis. In order to rule out this possibility in the present study, all subjects meeting criteria for depression diagnoses (N=109) according to assessment by the structured clinical interview (SCID) were excluded and the analyses re-run. Excluded subjects

were individuals meeting criteria for major depressive disorder (N=88), dysthymia (N=2), and/or depression not otherwise specified (N=20) presently or in the past. These analyses showed the same pattern of results. This suggests that normative variation in depressive symptomatology confers risk for reduced autonomic function among individuals who are both physically healthy and free of a current or past depression-related diagnosis.

4.5 Anxiety and HRV

In a parallel series of analyses, anxiety was evaluated both as an individual predictor of HRV and in multivariate analysis to determine (1) whether anxiety predicts HRV when examined concurrently with depression and anger, (2) whether any effect of anxiety on HRV may be mediated by the variance it shares with depression and anger (i.e. negative affect), and finally, (3) whether anxiety predicts HRV independently of negative affect. Again, all analyses included covariate-adjustment to eliminate potential confounding by risk factors. Findings show that anxiety individually predicts HRV, with greater anxiety associated with reduced parasympathetically-mediated HRV. Anxiety did not remain related to HRV in subsequent analyses, however, suggesting that its effects on HRV are not independent. The relationship between anxiety and HRV observed when anxiety is examined in isolation appears to result from its common association with depression ($r = .73$) and anger ($r = .51$). In other words, effects of anxiety on HRV are mediated by negative affect.

To illustrate, a simple mediational analysis in multiple regression was performed, including only anxiety, negative affect, and HF-HRV (with covariate-adjustment). Here, the relationship between anxiety and HF-HRV ($\beta = -.148$, $p = .000$) was fully attenuated after entering negative affect into the model ($\beta = -.032$, $p = .724$). Notably, negative affect accounts

for a sizable portion of the variance in anxiety. The negative affect factor score accounted for 43-81% of the variance in the anxiety measures (STAI-T, NEO-ANX, TCI-HA) while the second order latent construct of negative affect explained 99.7% of the variance in the first order latent construct of anxiety. Because the variance in anxiety is essentially subsumed by negative affect, there is little variance remaining by which anxiety might continue to predict HRV. In conclusion, anxiety symptoms may indirectly place otherwise healthy individuals at risk for impairments in autonomic modulation of HR, reflecting decrements in vagal function known to predict subsequent cardiovascular morbidity and mortality (e.g. Dekker et al., 2000; Tsuji et al., 1996). Specifically, risk is conferred by the variance in anxiety reflecting trait negative affect rather than elements that are unique to anxiety.

How do results relating anxiety to cardiac autonomic function from the present study correspond to findings in relevant literatures? Among population-based samples, evidence shows anxiety, when examined individually, to predict both nonfatal clinical events and sudden coronary death (e.g. Eaker et al., 1992; Haines et al., 1987; Kawachi et al., 1992; Kawachi et al., 1994). This relationship is further supported by studies of anxiety disordered patients in whom risk is heightened for various coronary outcomes (e.g. MI) (e.g. Kubzansky et al., 1997; Weissman et al., 1990). However, findings vary between psychiatric and healthy samples when anxiety is examined in relation to cardiac autonomic control as a potential pathway linking anxiety to CHD. Individuals with current anxiety disorders exhibit reduced parasympathetic activity (e.g. Kollai et al., Thayer et al., 1996; Yeragani et al., 1991) and occasional concomitant increases in relative sympathetic to parasympathetic activity (e.g. Friedman et al., 1998; Tucker et al., 1997), compared to non-clinical controls. In contrast, findings among healthy samples are mixed. Several studies have reported no association between anxiety symptoms and HRV indices

(Dishman et al., 2000; Hughes et al., 2000; Ramaekers et al., 1998; Virtanen et al., 2003), whereas others suggest attenuated cardiac vagal control among individuals with greater trait anxiety (Fuller et al., 1992; Watkins et al., 1998) and anxiety of a phobic nature (Kawachi et al., 1995). Thus, the current results may be offered as evidence that anxiety is an important predictor of HRV among healthy individuals, but only to the extent that anxiety symptoms correlate with the dispositional tendency to experience negative emotions in general. In fact, inconsistencies in the literature may be due to the fact that only a portion of the variance in anxiety (that which reflects trait negative affect) is so-called toxic. Again, because no other study to date has similarly partitioned the variance in anxiety to assess whether its association with HRV may be attributable to trait negative affect, the unique aspects of anxiety, or both, these findings warrant replication in future investigation.

Although anxiety may not predict HRV independently, it remains possible that aspects of anxiety are uniquely relevant to alternate physiological processes. Key among these are four pathophysiological mechanisms highlighted in a recent review by Everson-Rose & Lewis (2005), including activation of the hypothalamic-pituitary-adrenal (HPA) axis, serotonergic dysfunction, secretion of proinflammatory cytokines, and platelet activation. These authors offer an elaborated account of several interrelated biological systems proposed originally in a model by Markovitz & Matthews (1991) explaining associations between psychosocial factors and atherosclerotic cardiovascular and cerebrovascular disease development. Although the role of anxiety has not been specifically elucidated in this context, much research has documented relations between anxiety and markers of impairment in these systems, such as elevated cortisol levels (e.g. Tafet et al., 2001; Takahashi et al., 2005), alterations in serotonergic receptor function (e.g. den Boer, 2000; Leonard, 1996), and increases in circulating cytokine

concentrations (e.g. Brambilla et al., 1994; Zorrilla, Redei, & De Rueis, 1994). Thus, anxiety symptoms may in fact be directly integral to one or more of these pathways, though much work is needed to better characterize the differential role anxiety may play when examined in the context of other negative affective dispositions.

4.6 Anger and HRV

As in analyses relating depression and anxiety to HRV, anger was also examined as an individual predictor of HRV and in multivariate analysis to determine (1) whether anger predicts HRV when examined concurrently with depression and anxiety, (2) whether any effect of anger on HRV may be mediated by the variance it shares with depression and anxiety (i.e. negative affect), and finally, (3) whether anger predicts HRV independently of negative affect. Similarly, all analyses included covariate-adjustment to eliminate potential confounding by risk factors. Findings showed that anger does not individually predict any index of HRV. When anger was examined with depression and anxiety concurrently, however, a positive, though marginally significant ($p = .065$), association between anger and HF-HRV emerged. As described earlier, due to poor model fit, this finding must be interpreted cautiously. Alternatively, the incorporation of negative affect into this model improved the model's fit, suggesting that a mediational model by which the common effects of depression, anxiety, and anger on HRV are transmitted through negative affect is superior to a model of direct effects. Finally, in addition to this mediated pathway, greater anger also predicted *increased* parasympathetically-mediated HRV independently. Interestingly, the variance that anger shares with depression and anxiety appears to be related to HF-HRV in the negative direction, while the variance that is unique to anger is related to HF-HRV in the positive direction. In sum, anger does not individually predict HRV,

though the part of its variance represented by negative affect is related to reduced vagal activity and its remaining variance is related independently to increased vagal activity.

How do results relating anger to cardiac autonomic function from the present study correspond to findings in relevant literatures? Although few studies have examined anger explicitly (as opposed to its representation in components of the Type A behavior pattern or hostility), there is some evidence supporting a link between anger and both fatal and nonfatal coronary clinical events (Williams et al., 2000). With respect to the role of anger in cardiac autonomic function specifically, findings across studies are highly variable. For example, in Horsten et al. (1999) women who suppressed their anger had lower overall HRV and LF HRV than women who were willing to discuss angry feelings with others. In this same study, anger symptoms, anger-in, and anger-out were all unrelated to indices of HRV. In Virtanen et al. (2003), the anger-out scale from the STAXI correlated positively with LF-HRV but did not remain related to this outcome in multivariate analysis when multiple predictors were examined together. Finally, in Ramaekers et al. (1998), an anger dimension of coping was related to higher parasympathetically-mediated HRV in men, but not women. Taken together, these findings illustrate that anger, in fact, may play a role in cardiac autonomic function, but that the nature of the relationship between anger and indices of HRV varies widely. This pattern of results presents a particularly confusing picture with respect to understanding how anger may be related to vagally-mediated HRV both negatively and positively. Inconsistencies in findings may be due to differences in the type of anger under investigation (e.g. anger inhibition versus expression), as well as variation in sample characteristics (e.g. differences between men and women). Additionally, results from the current study offer one other explanation. That is, anger may relate differently to different HRV outcomes because it is itself a multifaceted construct. For example,

it is possible that the affective and non-affective components of anger may be differentially related to HRV indices such that the negative affective elements of anger relate to reduced parasympathetic activity and the non-affective elements of anger relate to increased parasympathetic activity.

The current finding that greater anger is related to both decreased and increased parasympathetically-mediated HRV suggests that anger acts concurrently as a risk-promoting and risk-protective factor in CHD development. Fleshing out the potentially dual role of anger in this context is informed by closer inspection of the emotion of anger itself. Two motivational systems have been proposed (Gray, 1994), each describing the neurobiological underpinnings of individual differences in behavior and emotion. The behavioral activation system (BAS), triggered by perceived incentives, encompasses behaviors and emotions that move an individual toward a specified goal. Alternatively, the behavioral inhibition system (BIS), triggered by perceived threats, encompasses behaviors and emotions that facilitate withdrawal from danger. Individuals are thought to vary in their sensitivity to incentive and threat cues and thus vary in their characteristic ways of behaving and experiencing emotion. Following from this, the BAS has been linked to positive emotion (e.g. excitement) and the BIS to negative emotion (e.g. anxiety) (Carver & White, 1994). These differences have been further corroborated by studies showing the BAS and associated positive emotions related to higher relative activation of the left prefrontal cerebral cortex and the BIS and associated negative emotions related to higher relative activation of the right prefrontal cerebral cortex (Davidson, 1992, 1998).

Recent evidence suggests correlations of positive emotionality and relative left-sided activation with the BAS and negative emotionality and relative right-sided activation with the BIS may be an overly simplified account of these relationships. Carver (2004) presents empirical

support for the idea that emotions of both valences are connected to these systems. Across three studies, individual differences in self-reported BAS sensitivity, a putative marker of this motivational system, predicted anger-related outcomes conceptualized as the failure to reach a specified goal within the approach system. The decomposition of anger in the current study revealed differences in anger that may be specific to the approach and the inhibition systems. Specifically, the variance in anger that is common to depression and anxiety (i.e. negative affect) may be more BIS-like and the variance that is unique to anger (that which remains after removing negative affect) more BAS-like. Taken one step further, the approach elements of anger when examined independently of negative affect may reflect adaptive behavioral and affective responding. In other words, the positive relation of the BAS-like variance in anger to basal level HF-HRV is consistent with the hypothesis that greater vagal tone allows an individual to launch an appropriate stress response whereby parasympathetic activity is efficiently withdrawn and subsequently reinstated in response to environmental challenge (Heponiemi, Keltikangas-Jarvinen, Kettunen, Puttonen, & Ravaja, 2004; Porges, 1992).

4.7 Negative affect and HRV

One of the primary objectives of the present study was to evaluate the possibility that individual negative affective dispositions (i.e. depression, anxiety, and anger) may share a common underlying dimension of negative emotionality through which effects of these individual dispositions on HRV may be transmitted. We postulated that tests of this common pathway would provide clues to better understanding which elements across these dispositions are specifically cardiotoxic. For example, relations between individual negative affective dispositions and HRV may be due to the general tendency to experience negative emotion, to

elements unique to these dispositions, or to both. In sum, results support that both common and unique pathways link psychosocial risk factors to HRV. With respect to the common negative affect pathway, results are particularly compelling. In multiple regression, the negative affect factor, which accounted for almost 50% of the variance in depression, anxiety, and anger measurements, was related to reduced vagal modulation of HR. Findings in SEM both supported and extended this conclusion by demonstrating that negative affect at least partially mediates effects of depression, anxiety, and anger on HRV. Evidence for this conclusion stemmed from the comparison of models estimated before and after inclusion of the second order latent construct of negative affect. Improvements in model fit with the addition of negative affect suggested that the mediational model was superior to the model of direct effects. Examination of path coefficients within the mediational model showed negative affect to predict both reduced vagally-mediated HRV and greater relative sympathetic to parasympathetic modulation of HR.

Support for the hypothesis that negative affect may largely drive relations observed between individual psychosocial risk factors and CHD is derived from several literatures describing high correlations among these factors, as well as structural data analyses showing negative affect to underlie multiple negative emotions (e.g. Krueger, 1999; Watson, 1988). Despite a rather large body of supporting evidence, few studies of CHD outcomes or CHD-relevant processes have actually included multiple psychosocial risk factors in the same analysis and even fewer have considered the role of negative affect specifically. However, there are some notable exceptions. Among several depression-, anxiety-, and anger-related constructs, Eaker et al. (1992) reported anxiety, loneliness, and tension to predict CHD events in women. In contrast, Haynes et al. (1980) reported Type A behavior and suppressed hostility, but not anxiety, to predict CHD events in a population-based sample of both men and women. Findings from these

and similar studies of cardiac patients are mixed and difficult to synthesize due differences in the constructs included for analysis. Moreover, to our knowledge no study has taken this approach with respect to examination of HRV specifically. In a recent review, Suls & Bunde (2005) urge investigators to discontinue decades of research practice in which effects of individual psychosocial risk factors on CHD outcomes are assumed to be independent. Rather, these authors encourage careful consideration of the ways in which multiple psychosocial risk factors may be interrelated, both by redundancy of measurement and conceptual overlap. In this regard, the current study is timely in its contribution to the existing literature, showing that the examination of multiple psychological constructs in the same analysis can yield important information about the relative importance of each. Here, the significance of negative affect as a common pathway linking depression, anxiety, and anger to variation in autonomic modulation of HR was well established. Additionally, independent effects of depression and anger on HRV were also noted.

4.8 Study limitations

Several strengths of the current investigation have been highlighted throughout this report, including a large sample size, incorporation of latent variable modeling, use of multiple, well-validated questionnaire measures, and careful sample characterization by disease risk factor status. However, there are several notable limitations. First, depression, anxiety, and anger were measured by self-report questionnaires, which are subject to response biases (e.g. social desirability) inherent in all such instruments. To counter this shortcoming, measures from other reporters (e.g. significant others) or interview strategies might be utilized to enhance construct validity. Additionally, all hypotheses were examined cross-sectionally, precluding the

opportunity to gain information about the direction of association between the variables. Thus, it remains unclear whether negative affective dispositions lead to alterations in HRV, occur subsequent to these changes, or covary due to a common third variable that influences both. Because the sample was free from significant clinical cardiovascular disease, however, it is at least plausible to assume that psychiatric symptom reporting was unconfounded by disease status, particularly with respect to somatic symptoms (e.g. shortness of breath) that are common to both psychiatric and CHD presentations. Finally, although SEM is the preferred data analytical approach when working with potentially highly correlated constructs, both regression as well as SEM analyses were ultimately limited by multicollinearity. The research questions of interest in the current study present unique challenges analytically, as by their very nature multicollinearity cannot be eliminated. Rather, the examination of interrelated psychological constructs both by measurement and conceptual overlap is itself an exploration of their multicollinearity and will by definition be limited by the ability of available statistical methods to accommodate this. Efforts to reduce multicollinearity in future analyses are possible, however, and might include item-level analyses with elimination of items that do not discriminate between psychological constructs.

4.9 Future directions

As mentioned previously, results from the present study must be considered preliminary as few studies have similarly examined multiple psychosocial factors in the same analysis or considered the role of negative affect specifically in predicting CHD. Moreover, to our knowledge, no study has taken this approach in relation to cardiac autonomic function. Thus, findings must be replicated in future investigations before firm conclusions can be drawn regarding the relative

significance of each of these psychosocial factors in explaining individual differences in vagal modulation of heart rate.

Additionally, the current findings suggest that variance common to depression, anxiety, and anger (i.e. negative affect) and variance unique to depression and anger specifically predict variation in cardiac autonomic function. Yet these findings are not informative in identifying which elements of these traits are represented by this common and unique variance. For example, here the "unique" aspects of depression were conceptualized as the variance in depression remaining after the common variance (negative affect) was removed. Thus, the aspects of depression that are not shared by anxiety or anger (e.g. anhedonia) remain, as of yet, unidentified. Future analyses are necessary to determine which aspects of depression, anxiety, and anger are specifically captured in the common and unique pathways tested in the present study. Specifically, an item-level exploratory factor analysis may be employed in which the questionnaire items that load on the negative affect factor are identified and differentiated from those items that are uniquely related to depression and anger.

4.10 Conclusions

Comorbidities among discrete classifications of psychiatric disorders and correlated variation in psychiatric symptoms may be explained by individual differences in the tendency to experience negative emotions, termed "trait negative affect" (e.g. Krueger et al., 1996; Trull & Sher, 1994). This assertion is supported by the personality and psychopathology literatures in which structural data analytic methods show a single latent factor to account for a substantial portion of variance in multiple negative emotions (e.g. Watson, 1988; Watson et al., 1984). Although these same affective traits have been studied in relation to CHD risk (e.g. Anda et al., 1993; Barefoot et al.,

1996), few studies have examined multiple affective dispositions in the same analysis or considered the role of generalized negative affect specifically. Thus, it is not known whether the cardiotoxic elements of these dispositions observed at the single-trait level of analysis are related to (1) variance that is unique to an individual factor (e.g. depression), (2) variance that is common across psychosocial factors (trait negative affect), or (3) a combination of both unique and common variance (e.g. negative affect and depression). Here, in a community-based sample of men and women, we tested these unique and common pathways in an effort to differentiate the relative contribution of depression, anxiety, and anger in predicting variation in autonomic control of heart rate, as indexed by heart rate variability (HRV).

Findings suggest that both common and unique pathways between psychosocial factors and HRV are operative. First, depression examined individually was related to reduced vagal activity and increased relative sympathetic to parasympathetic activity. When depression was examined in the full model (including all psychosocial predictors) its effects on HRV were shown to be both indirect (i.e. mediated by negative affect) and direct. Thus, the relation of depression to HRV is partially mediated by its common associations with anxiety and anger (negative effect), yet it also remains a significant independent predictor of HRV. Secondly, anxiety examined individually was also related to reduced vagal activity. Examination of anxiety in the full model, however, indicated that effects of anxiety on HRV were fully mediated by negative affect. That is, anxiety is only indirectly associated with HRV because of its common relations to depression and anger. Thirdly, anger, examined individually, was unrelated to any index of HRV. Its relation to HRV emerged in the full model, however, showing it to be a positive and independent predictor of increased vagal activity. Interestingly, the variance that anger shares, with depression and anxiety is related to reduced vagal activity while the variance

that is unique to anger is related to increased vagal activity. In sum, negative affect mediates the common effects of psychosocial risk factors for CHD on cardiac autonomic function with unique aspects of depression and anger independently related to reduced and increased vagal modulation of heart rate, respectively. These findings underscore the importance of examining multiple negative affective dispositions in the same analysis to identify the elements of these traits that are specifically cardiotoxic.

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