Myocardial Ischemia and Reduced Heart Rate Variability In Coronary Artery Disease Patients with Mood and Anxiety Disorders: The Impact of Anxiety Sensitivity

Kim Louise Lavoie

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By: **Kim Louise Lavoie**

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	Chair
for Dr. Linden	External Examiner
	Examiner
	Examiner
	Examiner
	Supervisor

Approved _____
Chair of Department or Graduate Programme Director

June 4 2003

_____
Dean of Faculty

ABSTRACT

Myocardial Ischemia and Reduced Heart Rate Variability in
Coronary Artery Disease Patients with Mood and Anxiety Disorders:
The Impact of Anxiety Sensitivity

Kim L. Lavoie, Ph.D.
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There is evidence linking mood disorders (MDs) and anxiety disorders (ADs) to coronary artery disease (CAD) risk, morbidity and mortality. However, research on the mechanisms mediating this association is immature. Mental stress-induced myocardial ischemia and reduced heart rate variability (HRV) (a marker of autonomic nervous system (ANS) dysregulation) are two mechanisms proposed to link MDs and ADs to CAD risk. The aim of this study was to evaluate (1) the frequency, duration and triggers of myocardial ischemia during daily life in CAD patients with comorbid MDs and ADs; (2) HRV in panic disorder (PD) patients with established CAD; and (3) the relationship between Hi versus Lo anxiety sensitivity (AS) and HRV in patients with CAD. Seventy-one patients (n=28 with primary AD (n=20 with PD); n=20 with primary MD; n=23 controls) with exercise ischemia underwent 48-hour Holter monitoring to evaluate ST-segment depressions (ischemia) and HRV (time and frequency domain indices). Patients completed a diary and the Anxiety Sensitivity Index (ASI), Beck Depression Inventory (BDI), State-Trait Anxiety and Anger Inventories (STAI-STAXI), and the Cook-Medley Hostility Inventory (CMHO). All patients were maintained on cardiac medication. Chi-squares and ANCOVAs were conducted for nominal and continuous variables respectively; frequency domain indices of HRV were assessed via spectral analysis. A total of 21 ischemic episodes

were recorded for 6 patients. Because so few patients had ischemia results were not significant. While 2/21 ischemic episodes occurred in controls (mean=1; mean duration=20 min) 19 episodes occurred in AD patients (mean= 4.75; mean duration=127 min). Diaries indicated that 42% of episodes in AD patients (versus none in controls) were preceded by mental stress (negative emotions). Interestingly, more MD patients (70%) reported having at least 1 episode of chest pain during the 48-hour period compared to AD patients (50%) and controls (30%) ($p<0.05$). MD patients also reported having more episodes of chest pain (4.45) compared to AD patients (1.75) and controls (0.87) ($p<0.05$). HRV analyses showed that after controlling for important confounders, PD patients with CAD exhibited significantly lower LF:HF ratios compared to controls ($p<0.05$), and HiAS patients exhibited significantly lower LF, VLF and ULF power relative to LoAS patients (p's<0.05). Interestingly, HRV was not related to BDI, STAI, STAXI or CMHO scores. Findings suggest that CAD patients with a MD reported more chest pain (without evidence of ischemia) but those with an AD demonstrated more (though not significantly) mental stress-induced ischemia relative to patients with a MD or no psychiatric diagnosis. Findings also suggest that PD patients with CAD show dominant parasympathetic tone under baseline (ordinary daily life) conditions that may reflect a dysregulation of ANS functioning. Finally, results show that high AS is associated with reduced HRV suggesting an association between high AS and dysregulated cardiac autonomic tone.

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INTRODUCTION

Epidemiology of Coronary Artery Disease

Epidemiological studies have identified coronary artery disease (CAD) as the leading cause of death in the United States and Canada among both men and women (American Heart Association, 1992; Statistics Canada, 1995; Thom, Epsten, Feldman & Leaverton, 1985). CAD has been defined as a group of related pathophysiological processes, including atherosclerosis, myocardial ischemia, and angina pectoris, which result from an insufficient supply of blood to the heart (Rozanski, Blumenthal, & Kaplan, 1999). According to Health Canada, one in every five dollars spent on hospital operating costs, and one tenth of all medical expenditures are for the care of patients with CAD (Statistics Canada, 1995). Expenditures for the care and treatment of CHD account for an estimated total cost of more than $60 billion annually in the United States (American Heart Association, 1992) and approximately $4 billion annually in Canada (Statistics Canada, 1995). Identifying potential risk factors for the disease therefore represents an area of considerable research interest. Because traditional risk factors, such as high blood pressure, elevated serum cholesterol, and cigarette smoking only account for approximately 50% of CAD cases (Brand, Rosenman, Sholtz, & Friedman, 1976), there has been growing interest in examining the potential influence of psychological factors in the pathogenesis of CAD. One risk factor which has recently gained attention is psychological or mental stress.

Psychiatric Disorders and Coronary Artery Disease

Two classes of Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, American Psychiatric Association, 1994) AXIS I psychiatric disorders are commonly diagnosed among patients with CAD. These include mood disorders and anxiety disorders (Brand, Rosenman, Sholtz, & Friedman, 1976; Lavoie & Fleet, 2000; Fleet, Lavoie, & Beitman, 2000; Frasure-Smith, Lesperance, & Talajic, 1995c). There are also reports indicating greater cardiac morbidity and mortality among CAD patients with specific mood and anxiety disorders (e.g., major depressive disorder, MDD and panic disorder, PD respectively) (Frasure-Smith, Lesperance, & Talajic, 1995b); Fleet, Arsenault, Lesperance et al., 2000).

Major Depressive Disorder (MDD) and CAD

Over the last decade, research has documented a disproportionately high rate of depression and depressive symptomatology among patients with established CAD. MDD is characterized by persistent ($\geq$ 2 weeks) depressed mood and/or significant loss of pleasure or interest in almost all activities and four or more of the symptoms presented in Table I. Major depression is a relatively common mood disorder, representing one of the five most common disorders seen in primary care (US Department of Health and Human Services, 1993). The point prevalence of depressive symptomatology is estimated to be between 40% and 65% in patients who have recently suffered an acute myocardial infarction (MI) (Carney, Freedland, Rich & Jaffe, 1995). MDD alone, as defined by DSM-III-R criteria (American Psychiatric Association, 1987) affects 16% to 22% of MI patients (Schleifer et al., 1989; Frasure-

Smith, Lesperance, & Talajic, 1993; Frasure-Smith, Lesperance, & Talajic, 1995) and 18% of patients with no history of MI but with documented CAD (Carney et al., 1987; Rich, TeVelde, Saini, Clark, & Jaffe, 1987). The disproportionately high rate of depression among cardiac patients is further emphasized when you consider that the point prevalence of MDD in the general population is estimated to be between 5-9% for women and 2-3% for men (American Psychiatric Association (APA), 1994; Blazer, Keller, McGonagle & Schwartz, 1994).

Table 1: Summary* of DSM-IV diagnostic criteria of Major Depressive Disorder (MDD):

A) Patients must have at least (1) depressed mood and/or (2) loss of interest or pleasure and four or more of the following symptoms during the same 2-week period and represent a change from previous functioning:

- **→ Significant appetite or weight changes**
- **→ Insomnia or hypersomnia almost daily**
- **→ Psychomotor agitation or retardation almost daily**
- **→ Loss of energy or fatigue**
- **→ Feelings of worthlessness or guilt**
- **→ Reduced ability to concentrate, think, or make decisions**
- **→ Recurrent thoughts of death or suicidal ideation**

B) These symptoms must cause significant distress or functional impairment (e.g., at work or in social relationships) and cannot be attributed to drug abuse or medication use

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***For complete diagnostic criteria, refer to the DSM-IV (APA, 1994).**

Clinical Significance of Major Depression in CAD Patients

Perhaps it comes as no surprise that patients with CAD may become depressed, given the chronic, debilitating nature of the disease. However, recent investigations have found that a significant number of depressed cardiac patients actually have a prior history of depression and/or depressive symptomatology which

predates the development of CAD by several years (Anda et al., 1993; Freedland, Carney, Lustman, Rich, & Jaffe, 1992; Lesperance, Frasure-Smith, & Talajic, 1996). These findings have lead researchers to speculate that clinical depression may represent an important risk factor for both the development and progression of CAD, and several lines of research have accumulated support for this hypothesis. A large-scale prospective study of 409 men and 321 women aged 50 to 60 demonstrated that high levels of depressive symptomatology (as measured by the depression sub-scale of the Minnesota Multiphasic Personality Inventory, MMPI) were predictive of increased risk for acute MI and mortality in both men and women over a 27 year period (Barefoot & Scholl, 1993). Furthermore, participants reporting greater depressive symptoms at baseline were more likely to have symptoms of angina pectoris and show evidence of ischemia on electrocardiograms. Finally, greater symptoms of depression were associated with poorer pulmonary functioning, an important indicator of CAD, even after controlling for other correlates of pulmonary function such as age, sex, systolic blood pressure, and cigarette smoking. Overall, this study indicates that evidence of depressive symptomatology between the ages of 50 and 60 is significantly associated with established disease indicators (e.g., angina), and predictive of increased risk for MI and mortality over a 27 year period.

An epidemiological study of 222 cardiac patients admitted for acute MI conducted by Lespérance and colleagues (1996) also found evidence linking a history of depression with the development of CAD. Firstly, 28% of patients reported having at least one episode of major depression before their first MI. Of all patients in the study, 16% were diagnosed as depressed at admission according to Beck Depression

Inventory (BDI) scores, a 21-item self-report questionnaire with scores of 10 or greater indicating at least mild depression, and the National Institute of Mental Health's Diagnostic Interview Schedule (DIS), an interview which provides psychiatric diagnoses based on DSM-III-R criteria. Compared to depressed patients without history of depression, patients with a history were more likely to be depressed in the hospital according to the DIS, and had higher BDI scores. Patients with a prior history of depression also showed greater evidence of heart dysfunction, as indicated by their greater likelihood of having a Killip Class 2 or higher. Finally, when patients were divided according to whether their in-hospital depression was recurrent or a first episode, patients with a recurrent depression were at significantly greater risk of mortality following 18-months (40%) as compared to those who were depressed for the first time (10%). Patients with recurrent depression also had marginally greater BDI scores than those with first time episodes (18.5 vs. 13.8), suggesting more severe depression in those with a prior history of the disorder.

Lastly, Freedland and colleagues (1992) reported that of 39 patients with recently diagnosed CAD who also met DSM-III criteria for major depression, 44% had a prior history of major depression. Furthermore, the severity of the depression was significantly greater in patients with a prior history of depression as compared to those with no prior history. Both the total score and total number of depressive symptoms endorsed on the BDI were significantly greater in patients with versus without a history of depression. Specifically, patients with a prior history of depression had a total score in the moderately severe range (20.7), whereas patients without a prior history of depression scored only in the mild depression range (11.5).

Taken together, the results from these studies suggest that pre-existing depression may heighten the risk for developing coronary problems, as well as increase the risk of developing depressive symptoms during hospitalization for coronary events.

While the evidence that MDD and depressive symptomatology precedes the onset of acute coronary syndromes is accumulating, we are still far short of proof that depression has a causal role in the pathogenesis of CHD. However, there is a solid literature linking depression with poorer post-MI prognosis and CHD outcome. For example, Carney and colleagues (Carney et al., 1988) found that of 52 patients undergoing diagnostic coronary angiography, 17% met diagnostic criteria for both CAD and MDD. Interestingly, 78% of CAD patients with depression reported having at least one major cardiac event (e.g., MI) in the following year, compared to only 35% of non-depressed CAD patients. Overall, the presence of MDD was found to be the single best predictor for the occurrence of cardiac events during the first 12 months following coronary angiography, and the predictive value of depression was independent of traditional risk factors such as the severity of coronary disease, smoking status, and left ventricular ejection fraction (LVEF). Therefore, the results of this study suggest that the presence of MDD in patients with CAD more than doubles the risk that a major cardiac event will occur within one year, and that the predictive value of depression appears to be independent of traditional indicators of disease outcome.

Depression has also been shown to increase the risk of re-infarction and mortality following MI (Frasure-Smith et al., 1993; Frasure-Smith et al., 1995; Frasure-Smith et al., 1995). Frasure-Smith and colleagues (1993) conducted a

prospective study to determine whether a diagnosis of MDD (according to the DIS) in patients hospitalized for MI would have an independent impact on cardiac mortality 6 months after discharge. Findings revealed that at follow-up, those patients who met criteria for MDD while hospitalized for their MI were at significantly greater risk of mortality as compared to patients who were not depressed. Interestingly, the impact of depression remained significant after controlling for other disease outcome indicators such as left ventricular dysfunction and previous history of MI. In a subsequent study, these researchers extended their follow-up period to 18 months post-discharge, and found that both a diagnosis of MDD in the hospital (as measured by the DIS) and depressive symptomatology (as measured by BDI scores) were significantly related to 18-month cardiac mortality (Frasure-Smith et al., 1995). Whereas only 6% of non-depressed patients had died by the follow-up assessment, 20% of patients who were diagnosed as depressed in the hospital had died. These researchers also observed a relationship between cardiac mortality, premature ventricular contractions (PVCs), and BDI scores. Patients with greater than 10 PVCs per hour who were also depressed according to the BDI were at substantially greater risk of mortality as compared to other patients. Interestingly, among patients with elevated PVCs and BDI scores, 5 out of 6 deaths observed at follow-up were due to fatal arrhythmias, pointing to a possible mechanism linking depression with poorer CHD outcome. Taken together, the results of these studies indicates that patients diagnosed with MDD at the time of admission for MI are at significantly greater risk of mortality over a 6 and 18 month period. The results of this study also demonstrate that BDI scores may also reliably predict mortality over the same period, indicating

that both the DIS and BDI may be used for in-hospital screening of patients who may be at risk for future cardiac events and/or mortality because of depression.

In addition to being associated with poorer-MI prognosis, MDD also appears to increase risk of mortality in patients with ventricular arrhythmias. Kennedy and colleagues (Kennedy, Hofer, Cohen, Shindledecker, & Fisher, 1987) evaluated 88 patients undergoing treatment for severe arrhythmias. After 18 months, 3 out of 4 patients (75%) who were depressed at discharge had died, compared to 12 of the 84 patients (14%) who were not depressed. These results are consistent with Frasure-Smith et al.'s (1995) finding that patients with elevated depressive symptomatology and elevated PVCs were at greater risk of mortality from arrhythmias. Taken together, these studies suggest an important link between MDD and poorer CAD outcome.

Panic Disorder and CAD

Like MDD, research has also documented a disproportionally high rate of panic disorder (PD) among both cardiology outpatients and patients with documented CAD. Panic disorder is characterized by recurrent panic attacks that consist of sudden episodes of intense fear or discomfort associated with several cognitive and somatic symptoms (American Psychiatric Association, 1994). Six of the 13 diagnostic symptoms of a panic attack are also cardinal features of CAD: chest pain, palpitations, sweating, shortness of breath, sensation of choking, and hot flushes (see Table 2 for a summary of diagnostic criteria). According to published reports, the

prevalence of PD in patients with documented CAD ranges from 6.5-53% (Fleet et al., 2000).

Table 2: Summary* of DSM-IV diagnostic criteria of Panic Disorder (PD):

A)	**Recurrent unexpected panic attacks (see below);**
B)	**Persistent concern about having additional attacks, including worry; about the implications of attack or its consequences**
C)	**Significant change in behavior as a result of the attacks.**
Panic Attack:	**A discrete period of intense fear or discomfort in which four or more of the following symptoms develop abruptly and reach a peak within 10 minutes:** **→ Palpitations or accelerated heart rate** **→ Sweating** **→ Trembling or shaking** **→ Shortness of breath (dyspnea)** **→ Choking** **→ Chest pain or discomfort** **→ Nausea or abdominal discomfort** **→ Feeling dizzy, unsteady, or faint** **→ Numbness or tingling sensations (parasthesias)** **→ Chills or hot flashes** **→ Derealization (feelings of unreality) or depersonalization** **→ Fear of losing control or going crazy** **→ Fear of dying**

***For complete diagnostic criteria, refer to the DSM-IV (APA, 1994).**

For example, Beitman and colleagues (1987) examined the prevalence of PD in 103 cardiology outpatients with atypical or non-anginal chest pain, 30 of which had documented CAD (Beitman et al., 1987). Results showed that 53% (n=16) of patients with documented CAD also met DSM-III criteria for PD. A similar study of 49 CAD patients presenting with atypical chest pain revealed that 27% met DSM-III criteria for PD (Basha et al., 1989). Finally, Fleet and colleagues (1996) examined the prevalence of PD in 441 consecutive patients presenting to an emergency department

with a chief complaint of chest pain. Results showed that of the 74 patients who also had documented CAD, 34% (n=25) met criteria for current PD (Fleet et al., 1996).

Besides the three aforementioned studies, only five studies (Chernen et al., 1995; Goldberg et al., 1990; Kane, Jr., Strohlein, & Harper, 1991; Katon et al., 1988; Morris, Baker, Devins, & Shapiro, 1997) have documented the presence of PD in different samples cardiology and/or CAD patients. Although these studies were not designed to establish the prevalence of PD in CAD patients, it can be estimated from their reports to be approximately 10-50%. A summary of the PD prevalence rates among CAD patients is presented in Table 3.

Clinical Significance of Panic Disorder in CAD Patients

No truly prospective study has examined the question of whether PD *per se* is a risk factor for CAD. However, two retrospective reports from the same research group claim that PD is associated with a higher risk of mortality from cardiovascular causes in patients without CAD. Coryell and colleagues (1982) examined mortality rates of psychiatric inpatients with probable PD 35 years after their index admission, and compared them to age-, period-, and gender-specific mortality rates for those living in the same state. Patients with probable PD had twice the expected mortality rates from cardiovascular causes. Specifically, among 113 former in-patients with probable PD, 12 patients died from circulatory disease, versus only 6 patients without probable PD (Coryell, Noyes, & Clancy, 1982).

In a subsequent study, Coryell and colleagues (1986) examined mortality rates of 155 outpatients with anxiety neurosis (a panic-like form of anxiety) 12 years after

Table 3:

Summary of Study Characteristics and PD Prevalence Rates:

Investigators [reference]	Participants	N [Entire sample]	N [CAD patients]	Setting	Measurement of CAD	Measurement of PD	Prevalence of PD in Entire Sample (%)	Prevalence Of PD in CAD patients (%)
Beitman et al. [5]	Cardiology outpatients with nonanginal chest pain	103	30	Cardiology clinic	Previous MI or positive cardiac catheterization	SCID	59 (57%)	16 (53%)
Basha et al. [6]	CAD outpatients with chest pain	49	49	University hospital	Cardiologist Interview, stress test, or positive angiogram	SCID	13 (27%)	13 (27%)
Fleet et al. [15]	Cardiology outpatients with chest pain	441	74	Emergency department (cardiology hospital)	Previous MI, bypass, angioplasty, positive angiogram, or positive stress test	ADIS-IV	108 (25%)	25 (34%)
Katon et al. [12]	Cardiologyoutpatients with chest pain	74	46	University hospital	Positive angiogram	DIS	15 (20%)	3 (6.5%)
Chernen et al. [16]	Cardiology outpatients referred for stress testing	30	18	Cardiology outpatient department	"Documented" history or positive stress test	ADIS-R	5 (17%)	2 (11%)
Morris et al. [17]	Cardiology outpatients	128	73	Thirteen outpatient cardiology clinics	Cardiologist diagnoses (tests not reported)	Questionnaire (DSM-IV criteria)	16 (12.5%)	10 (14%)
Kane et al. [18]	Patients referred to Digestive Disease Lab	278	68	General hospital	Chart reviews (tests not reported)	SADS-LA	104 (38%)	33 (49%)
Goldberg et al. [19]	Cardiology outpatients	310	44	Cardiology clinic	Cardiologist diagnoses (tests not reported)	Panic screening questionnaire (n=310) SCID (n=52)	104 (34%) with possible or definite PD 19 (6%)	 16 (36%)

PD = panic disorder; CAD = coronary artery disease; MI = myocardial infarction; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders-4th edition; SCID = Structured Clinical Interview for DSM; ADIS-IV = Anxiety Disorders Interview Schedule-4th edition; DIS = Diagnostic Interview Schedule; SADS-LA = Schedule of Affective Disorders and Schizophrenia-Lifetime Version Anxiety Disorders.

their index admission, and compared them to the age- and gender-matched mortality rates of those living in the same state. The relevant Iowa vital statistics predicted 1.8 male and 3.2 female deaths, and the actual number of deaths in the anxiety neurosis group was 4 men and 2 women. Of interest is that three of the four deaths in the male group were of cardiovascular disease (the fourth was due to suicide) (Coryell, Noyes, Jr., & House, 1986).

Since the publication of the Coryell reports, three prospective studies have found an association between self-reported panic-like anxiety and mortality from cardiovascular causes. The Northwick Park Heart Study (Haines, Imeson, & Meade, 1987) found that 1457 initially healthy men with high scores on the phobic anxiety subscale of the Crown-Crisp Index (Crown & Crisp, 1966) had a 3.77 relative risk of fatal coronary heart disease (95% CI: 1.64 to 8.64) as compared to men with low scores after a follow-up period of 6.7 years. Moreover, this association was maintained after controlling for traditional cardiovascular risk factors, such as resting blood pressure and smoking status.

Also using the phobic anxiety subscale of the Crown-Crisp Index, Kawachi et al. (1994a) prospectively examined the association between PD and cardiac mortality in a follow-up study of 33,999 male health professionals free of CHD at baseline. After 2 years, participants with the highest scores on the phobic anxiety scale had 2.45 (95% CI: 1.00 to 5.96) relative risk of fatal CHD death as compared to participants with the lowest scores (Kawachi et al., 1994a). Excess risk appeared to be specific to sudden cardiac death. Relative risks were adjusted for other cardiovascular risk factors, including body mass index, resting blood pressure, and

family history of heart disease. Kawachi and colleagues (1994b) also found a similar relationship between anxiety symptoms and risk of CHD death in the Normative Aging Study (Kawachi, Sparrow, Vokonas, & Weiss, 1994). Anxiety symptoms were assessed with 5 questions similar to the phobic scale of the Crown Index (e.g. "Do strange people or places make you afraid?"; "Do you often become suddenly scared for no good reason?"). Compared with men reporting no symptoms of anxiety, men reporting two or more symptoms had elevated risks of fatal CHD, particularly of sudden cardiac death (multivariate OR= 4.46; 95% CI: 0.92 to 21.6).

Finally, a recent study by Moser and Dracup (1996) indicated that high anxiety in patients hospitalized for an MI emerged as an independent predictor of post-MI complications. Specifically, patients reporting high levels of anxiety 48 hours after admission to hospital were 4.9 times more likely to have subsequent in-hospital complications (including acute ischemia, re-infarction, sustained ventricular tachycardia, ventricular fibrillation, and death) than those reporting low levels of anxiety. Taken together, the results of these studies suggest that anxiety may be important to CAD outcome.

Mechanisms Linking Mood and Anxiety Disorders to CAD Risk

Although there is considerable evidence linking mood and anxiety disorders to increased CAD risk, morbidity and mortality, research on the mechanisms which may be mediating this link is relatively immature. In studies to date, research has focused on primarily two mechanisms: (1) mental stress-induced myocardial ischemia and (2) dysregulation of the autonomic nervous system (ANS).

Myocardial Ischemia

Myocardial ischemia has been traditionally viewed as an imbalance between myocardial oxygen supply and demand (Cohn, 1992). Any factor which results in greater myocardial oxygen demand (e.g., increases in heart rate) or reduced oxygen supply (e.g., atherosclerotic obstruction) can therefore provoke ischemia. Myocardial ischemia exerts hemodynamic changes which are both systolic and disastolic in nature. These changes include increases in left ventricular end-diastolic pressure, decreases in cardiac output, greater diastolic tone (stiffness), and wall-motion abnormalities. The clinical manifestations of myocardial ischemia fall into two categories: symptomatic, (i.e., anginal) and asymptomatic (i.e., silent).

Risk for myocardial ischemia is particularly elevated in patients with documented CAD, and myocardial ischemia is a significant, independent predictor of future cardiac events (e.g., MI) (Hunziker, Gradel, Muller-Brand, Buser, & Pfisterer, 1998; Villella et al., 1995) and mortality (Deedwania & Carbajal, 1990; Gottlieb et al., 1988; Sheps et al., 2002) Results from both laboratory mental stress challenge and ambulatory electrocardiographic (ECG) studies confirm that myocardial ischemia can be induced by both exercise and mental stress challenges, and may occur at high or low levels of physical exertion in patients with CAD (Gabbay et al., 1996; Gullette et al., 1997). However, most ischemic episodes occur during sedentary activities and at relatively low heart rates (Cohn, 1992; Schang, Jr. & Pepine, 1977).

Because the majority of ischemic episodes occur at relatively low levels of physical exertion, investigators have hypothesized that these episodes might be the result of mental or emotional stress (Deedwania & Carbajal, 1991; Rozanski et al.,

1988). Both laboratory mental stress challenge and ambulatory ECG studies have found consistent, positive relationships between mental stress and ischemia in CAD patients.

Laboratory Studies of Mental Stress-Induced Ischemia

The development of a variety of sensitive non-invasive means for assessing myocardial ischemia among cardiac patients (e.g., radionuclide ventriculography (RV) and single-photon emission computed tomography (SPECT)) have permitted researchers to evaluate the extent to which mental stress can elicit myocardial ischemia (Krantz, Kop, Santiago, & Gottdiener, 1996; Fleet et al., 2000). RV and SPECT, which measure left ventricular regional wall-motion abnormalities and myocardial perfusion (blood flow) respectively, are used as markers of myocardial ischemia, which cannot be assessed directly (Pepine, 1992). Laboratory studies employing these techniques during various mental stress challenge tests (e.g., mental arithmetic, Stroop color-word, public speaking) have demonstrated that mental stress can elicit ischemia in 50% to 75% of CAD patients (Blumenthal et al., 1995; Burg, Jain, Soufer, Kerns, & Zaret, 1993; Deanfield et al., 1984; Gottdiener et al., 1994; Rozanski et al., 1988). In general, these studies indicate that unlike exercise-induced ischemia, mental stress-induced ischemia is usually asymptomatic (i.e., silent) (Gottdiener et al., 1994; Burg et al., 1993; Rozanski et al., 1988; Deanfield et al., 1984) and is rarely accompanied by ECG evidence of ischemia (i.e., ST-segment depressions) (Krantz et al., 1996; Rozanski et al., 1988). Finally, it also tends to occur

primarily among patients with a history of exercise-induced ischemia (Krantz et al., 1996; Blumenthal et al., 1995; Burg et al., 1993; Deanfield et al., 1984).

Ambulatory Studies of Mental Stress-Induced Ischemia

Laboratory studies of mental stress-induced ischemia demonstrate that under controlled conditions, mental stress challenge tests can reliably elicit myocardial ischemia. However, the ecological validity of many mental stress challenge tests (e.g., mental arithmetic, which does not represent a relevant stressor for most individuals), has been challenged by researchers (Jiang et al., 1996) Krantz et al., 1996). In addition, myocardial ischemia during daily life exhibits considerable within-subject variability in both frequency and duration over periods, days, weeks, and months that cannot be attributed to changes in clinical status (Nabel et al., 1988). This has lead researchers conduct ambulatory studies of mental stress experienced during daily life. In general, patients are equipped with Holter ECG monitors to measure myocardial ischemia, and are given self-monitoring diaries for the recording of their activities, physical symptoms, and emotions to determine what factors may be associated with ischemic episodes.

Studies using ambulatory Holter monitors in association with self-monitoring diaries have shown that mental stress (defined as the experience of negative emotions such as anxiety, tension, sadness, or anger) encountered during daily life can be a potent trigger of ischemic episodes (Freeman, Nixon, Sallabank, & Reaveley, 1987; Gottdiener et al., 1994; Gullette et al., 1997). For example, Freeman et al. (1987) examined CAD patients during a period of uncertainty (following coronary

angiography but prior to learning the results of the test) and subsequently during a less stressful period (after having had time to adjust to learning results of test). Results showed that ischemia was significantly more frequent during the period of high stress (uncertainty) compared to the subsequent less stressful period. Gabby et al. (1996) also reported positive associations between self-reported mental stress (intense anger) and myocardial ischemia, which was as potent a trigger of ischemia as strenuous physical exercise. Finally, a recent study by Guellette et al. (1997) demonstrated that mental stress during daily life (feelings of tension, frustration, and sadness) more than doubled the risk of ischemia occurring in the hour following the negative emotional experience. Taken together, ambulatory ECG studies show that mental stress may be a potent trigger of myocardial ischemia during daily life in CAD patients.

Clinical Significance of Mental Stress-Induced Ischemia

There is extensive research showing that patients exhibiting exercise-induced ischemia are more likely to suffer adverse clinical events, including mortality (Corbett et al., 1981; Fuller et al., 1981; Gibson et al., 1983; Gottlieb et al., 1988; Newman, Rerych, Upton, Sabiston, Jr., & Jones, 1980; Taliercio, Clements, Zinsmeister, & Gibbons, 1988). However, what is the prognostic significance of mental stress-induced ischemia with respect to cardiac morbidity and mortality? The long-term clinical implications of mental stress-induced ischemia in CAD patients has been demonstrated by several studies. Firstly, Jiang et al. (1996) found that the presence of mental stress-induced ischemia, as measured by RV in the laboratory

during various mental stress tests was associated with significantly higher rates of subsequent fatal and nonfatal cardiac events. It is noteworthy that the risk associated with mental stress-induced ischemia was independent of age, baseline LVEF, previous MI, and even predicted events over and above exercise-induced ischemia. A recent study by Sheps et al. (2002) provides additional evidence linking mental stress-induced ischemia to mortality in CAD patients. A group of 173 CAD patients were examined at baseline, where they underwent two mental stress challenges (public speaking, Stroop color-word), and after a three to four year follow-up period. At follow-up, there were 11 deaths, and the only predictor of mortality was the presence of new or worsening wall motion abnormalities (WMAs) during mental stress at baseline. Interestingly, five of 11 (44%) of those who died exhibited new or worsening WMAs in response to mental stress, compared to only 11 (18%) of the 162 survivors. After adjusting for resting LVEF, the odds ratio of the association between mortality and new or worsening WMAs during mental stress was 5.9, or nearly six times the risk of death.

Additional evidence supporting the predictive value of mental stress-induced ischemia was provided by Krantz and colleagues (1996) who assessed the prognostic value of mental stress-induced ischemic left ventricular WMAs in 79 patients with stable CAD. At a median follow-up of 3.5 years, new cardiac events were observed more frequently among the 44% of patients who exhibited mental stress-induced ischemia in the lab (induced via mental arithmetic and public speaking tasks) compared to only 23% of patients who did not exhibit mental stress-induced ischemia. Cardiac events experienced by patients exhibiting mental stress-induced

ischemia included coronary artery bypass graft surgury (CABG), myocardial infarction (MI), percutaneous transluminal coronary angioplasty (PTCA), and sudden death, though type of cardiac event did not differ between mental stress-positive and stress-negative patients. Finally, a study by Hunziker et al. (1998) demonstrated that the addition of mental stress testing to exercise (bicycle ergometry) testing was associated with more pronounced and earlier increases in blood pressure, rate-pressure product, peak stress heart rate, and greater decreases in LVEF (an important marker of ischemia). This study also showed that patients reported more intense symptoms with combined testing compared to exercise testing alone. These findings suggest that stress protocols using both mental and exercise stress challenges may improve symptom detection and non-invasive diagnosis of CAD. Taken together, these studies highlight the clinical significance of mental stress testing in diagnosing CAD and predicting future cardiac events.

Psychiatric Disorders and Myocardial Ischemia

As previously presented, DSM-IV mood and anxiety disorders appear to be the most common psychiatric disorders found in CAD patients, and there is robust evidence linking them to poor CAD prognosis. Despite a significant amount of research linking mental stress or "negative emotions" to myocardial ischemia, few if any laboratory studies have evaluated the impact of mental stress-induced ischemia in CAD patients with actual psychiatric disorders. Interestingly, only one study to date has published preliminary data demonstrating an association between a psychiatric disorder and mental stress-induced myocardial ischemia. Fleet et al. (2000) examined

whether panic attacks could induced myocardial perfusion defects in 49 CAD patients with and without panic disorder (PD). CAD patients with positive exercise stress tests (23 with PD & 26 controls) were submitted to an established panic challenge (one vital capacity inhalation of 35% carbon dioxide [CO2] and 65% oxygen [O2]) and were injected with a radioisotope tracer (Tc-99m-SESTAMIBI) upon inhalation. SPECT imaging was performed to assess the presence and severity of reversible myocardial perfusion defects (ischemia). Results showed that upon inhalation, 100% (n=23) of PD vs. 15% (n=4) of control patients experienced a panic attack. More importantly, 78% (n=18) of PD versus only 42% (n=10) of control patients exhibited reversible myocardial perfusion defects. It is interesting to note that even among those control patients who did demonstrate reversible myocardial perfusion defects, they were significantly less severe than those observed among PD patients. The results of this study, the first to document a link between panic symptomatology and myocardial ischemia in actual PD patients, suggest that CAD patients with a specific psychiatric disorder (PD) may be at greater risk for myocardial ischemia compared to non-PD CAD patients.

The results of mental stress studies to date suggest that negative emotions are potent triggers of myocardial ischemia, both in the lab and during daily life. The results of Fleet et al.'s study suggest that panic attacks may also confer risk for myocardial ischemia in PD patients with documented CAD. Because patients with mood and/or anxiety disorders by definition experience frequent daily episodes of emotional distress (e.g., anger, fear, sadness, panic), it is reasonable to hypothesize that CAD patients with comorbid mood and/or anxiety disorders would be at greater

risk for transient ischemic episodes during daily life compared to CAD patients with no psychiatric comorbidity.

Clearly, examining the degree to which CAD patients with psychiatric disorders experience ischemia relative to CAD patients without such disorders represents an important goal for mental stress-ischemia research.

Study Objective 1:

The first objective of the present study was to further elucidate the relationship between mental stress and the occurrence of transient myocardial ischemia in the daily lives of CAD patients. Specifically, this study examined the extent to which CAD patients with comorbid DSM-IV AXIS I mood (including MDD) and anxiety disorders (including PD with or without Agoraphobia, Generalized Anxiety Disorder, Social Phobia, Specific Phobia, Obsessive-Compulsive Disorder, and Post-Traumatic Stress Disorder) were at greater risk for ischemic episodes during daily life as compared to CAD patients without such disorders. Patients were instrumented for 48-hour ECG Holter monitoring and were required to complete a self-monitoring diary of their activities, emotions, and physical symptoms throughout the 48-hour monitoring period. The proportion of patients in each group (mood disorder vs. anxiety disorder vs. controls) displaying myocardial ischemia, as well as the frequency and duration of ischemic episodes during daily life were compared. For each episode of myocardial ischemia, diaries were examined to determine whether episodes were preceded by mental (e.g., negative emotions) or physical (e.g.,

exercise) stress, and to determine whether ischemic episodes were accompanied by chest pain (i.e., were anginal) or silent.

Specific Hypotheses:

It was hypothesized that a greater number of CAD patients with a comorbid mood or anxiety disorder would exhibit transient ischemic episodes during daily life compared to control patients. It was also hypothesized that CAD patients with a comorbid mood or anxiety disorder would exhibit a greater number of ischemic episodes, and of a longer duration compared to control patients. Finally, it was hypothesized that a greater number of ischemic episodes will be preceded by mental stress (i.e., negative emotions) as opposed to physical stress (i.e., exercise) in CAD patients with a comorbid mood or anxiety disorder compared to control patients.

Autonomic Nervous System Dysregulation

The second pathophysiological mechanism proposed to mediate the link between psychiatric disorders and increased CAD morbidity and mortality involves dysregulation of autonomic nervous system (ANS) functioning (Gorman & Sloan, 2000); Stein et al., 2000). Both basic heart rate and its modulation are primarily determined by alterations in cardiac autonomic activity (Aubert & Ramaekers, 1999). In healthy individuals, the role of the ANS in the beat-to-beat regulation of hemodynamic variables is thus essential to adequate cardiovascular functioning. Loss of normal ANS control of heart rate and cardiac rhythm has been shown to be important risk factors for adverse cardiovascular events. For example, among post-MI

patients, reduced beat-to-beat heart rate variability (HRV), a measure of cardiac autonomic innervation by the brain, is a strong predictor of sudden death and ventricular arrhythmias (Bigger, Jr. et al., 1992; Kleiger, Miller, Bigger, Jr., & Moss, 1987).

Heart Rate Variability (HRV)

In recent years, the analysis of HRV has been increasingly employed to study autonomic regulation of cardiac functioning. The beat of a healthy heart varies as a result of many factors, including exercise and mental stress. The intervals between normal sinus beats also vary periodically due to respiration, blood pressure changes, thermoregulatory processes, renin-angiotensen system activity, and circadian rhythms, which together represent the principal sources of HRV (Stein, Bosner, Kleiger, & Conger, 1994).

Heart rate also normally varies on a beat-to-beat basis due to parasympathetic innervation to the heart via the vagus nerve. With loss of vagal innervation, as is the case in patients with severe neuropathy or previous heart transplantation, there is marked attenuation or reduction of HRV. It is speculated that such reductions in parasympathetic innervation leave the heart exposed to uninhibited stimulation by the sympathetic nervous system. This in turn makes the heart vulnerable to arrhythmia and sudden death, and may also accelerate the progression of CAD (Gorman & Sloan, 2000; Ravenswaaij-Arts, Kollee, Hopman, Stoelinga, & van Geijn, 1993; Stys & Stys, 1998). It is via this mechanism that mental stress is thought to contribute to

increased cardiovascular morbidity and mortality in patients with established CAD (Kop et al., 2001).

Measurement of HRV

Through the use of ECG Holter recordings, HRV rhythms can be analyzed to provide sensitive, non-invasive measures of autonomic input to the heart. There are two approaches to the measurement of HRV: time domain analyses of the variation in normal R-R intervals (measured in milliseconds: ms), and frequency domain analyses which identify the "power" of spectral components that comprise the global variation in heart rate (measured in ms^2/hz). Time domain analyses address the question: "How much variability is there within a given period of time?" whereas frequency domain analyses address the question: "What are the underlying autonomic rhythms or frequencies that contribute to heart rate variations?". Time domain values are derived from performing simple statistical calculations on the set of interbeat intervals. Frequency domain values are derived using Fourier analysis to partition the total variance in heart rate into the variance accounted for by each of the underlying frequencies (Stein et al., 1994). Fourier analysis is a mathematical procedure used to determine the collection of sinewaves (differing in frequency and amplitude) that is necessary to make up the square-wave pattern under consideration.

Time domain HRV indices:

There are two classes of time domain variables, one based on interbeat intervals and the other based on comparisons of lengths of adjacent cycles. Those

based on interbeat intervals include SDNN (the standard deviation of all normal R-R [i.e., N-N] intervals, measured in milliseconds [ms]); SDANN (the standard deviation of the mean of the 5-minute intervals averaged over a 24-hour period, measured in ms); and ASDNN (the average of the standard deviations [SDs] of interbeat intervals for each 5-minute interval, measured in ms). Those based on comparisons of lengths of adjacent cycles includes pNN50 (the proportion of successive normal R-R interval differences that are > 50 ms, measured in percent); and rMSSD (the root mean-square successive difference of all normal R-R intervals, measured in ms). Whereas rMSSD and pNN50 are said to reflect primarily parasympathetically mediated changes in heart, the remaining time domain variables are said to be both sympathetically and parasympathetically mediated (Kleiger, Stein, Bosner, & Rottman, 1992).

Frequency domain indices:

Although both time and frequency domain measures have been used to assess HRV, the latter has increasingly become the method of choice among investigators (Malik & Camm, 1990; Malliani, Pagani, Lombardi, & Cerutti, 1991; Stein, Bosner, Kleiger, & Conger, 1994). Frequency domain measures of HRV are derived using spectral analysis, which yields information about the overall variance in heart rate resulting from periodic oscillations of heart rate at various frequencies. These variations allow for the mapping the ECG power spectra onto indices that reflect autonomic mediation of heart rate (Friedman & Thayer, 1998). The standard frequency domain components of HRV, all of which are measured in ms^2 include: High-frequency (HF) power (0.15 to 0.40 Hz), which is modulated by respiration and

is said to primarily reflect vagal tone (Akselrod et al., 1985); low-frequency (LF) power (0.04 to 0.15 Hz), which is associated with blood pressure regulation and said to reflect both sympathetic and parasympathetic tone (Akselrod et al., 1985); very-low frequency (VLF) power (0.0033-0.04 Hz), which is thought to be influenced by the thermoregulatory, peripheral vasomotor, and renin-angiotensin systems (Akselrod et al., 1985; Leisher et al., 1996) and reflects both sympathetic and parasympathetic activity; and ultra-low frequency (ULF) power ($1.5X10^{-5}$ to 0.0033 Hz), which is influenced by circadian and other long-term variations in heart rhythm and also reflects both sympathetic and parasympathetic activity. Total power (TP; $1.5X10^{-5}$ to 0.40 Hz) represents the total variation in the signal and is the sum of the HF, LF, VLF and ULF components. Finally, the ratio of LF:HF power is often calculated in order to cancel out the parasympathetic influence on the LF spectral component. This ratio provides a measure of the sympathovagal balance, where increased ratios are said to reflect a predominance of sympathetic over parasympathetic activity (Malliani, Lombardi, & Pagani, 1994).

Clinical Significance of Reduced HRV

Reduced HRV is recognized as an early marker of diabetic neuropathy (a complication of diabetes mellitus characterized by widespread degeneration of the small nerve fibres of both sympathetic and parasympathetic tracts) and as an independent predictor of ventricular arrhythmias and sudden death in patients with a history of MI (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). The Multicenter Post-

Infarction Project (MPIP) was the first major study to demonstrate an association between reduced HRV within two-weeks post-MI and increased risk of mortality over a 31-month follow-up period (Kleiger, Miller, Bigger, Jr., & Moss, 1987). Patients exhibiting an SDNN of less than 50 ms at two-weeks post-MI exhibited mortality rates which were 5.3 times greater than patients with an SDNN greater than 100 ms. The prognostic significance of reduced HRV in predicting post-MI mortality has been supported and replicated by numerous clinical studies (Bigger, Jr. et al., 1992; Copie et al., 1996; Fei, Copie, Malik, & Camm, 1996; Pipilis, Flather, Ormerod, & Sleight, 1991).

In addition to predicting mortality in post-MI patients, reduced HRV has also been shown to independently predict mortality at 1 year following elective angiography, and this in patients with no prior history of MI (Rich et al., 1988). A recent study by Lanza and colleagues (1997) investigated whether analysis of HRV could improve prediction of in-hospital cardiac events over and above Holter monitoring in 75 patients with stable angina. Results indicated that a total of 7 patients exhibited a major cardiac event (e.g., MI or death) in hospital, 6 of which also had myocardial ischemia during in-hospital Holter monitoring. Interestingly, results also showed that the LF:HF ratio, which reflects sympathovagal balance, was significantly higher among those patients who exhibited cardiac events, and was particularly higher among the 6 patients who also exhibited ischemia during Holter monitoring. These findings suggest that an imbalance of cardiac autonomic tone in favor of greater sympathetic activity further increases the risk of major cardiac events

among high-risk patients who also exhibit in-hospital ischemia, and this despite appropriate medical treatment (Lanza et al., 1997).

Interestingly, data emanating from the Framingham Heart Study has recently demonstrated a link between reduced HRV in patients initially free of CAD and increased risk for future cardiac events. Tsuji et al., (1996) collected ambulatory ECG recordings of 2501 men and women between the ages of 28 and 62 who were initially free of clinically detectable CAD from 1983 and 1987. After a mean follow-up period of 3.5 years, reduced HRV (both time and frequency domain measures) predicted increased risk for subsequent cardiac events, even after controlling for traditional cardiac risk factors such as cigarette smoking and hypertension (Tsuji et al., 1996). Taken together, the results of these studies and those demonstrating associations between reduced HRV and other clinically significant cardiac events (e.g., left ventricular dilatation (Dambrink et al., 1994), atrial fibrillation (van den Berg et al., 1997), and ventricular tachyarrhythmias (Valkama et al., 1995)) indicate the prognostic significance of reduced HRV among patients with CAD. In fact, the addition of HRV to current risk indicators such as LVEF and PVCs has been shown to improve predictive accuracy for coronary events 30 to 50% (Hohnloser, Klingenheben, Zabel, & Li, 1997).

Reduced HRV and Psychiatric Disorders

During periods of acute stress, it is well known that sympathetic activation leads to increased catecholamine release, which in turn increases heart rate. However, another factor influencing stress-induced tachycardia is the direct innervation from

the brain to the heart. Thus, the ability of the heart to respond to mental stress relies on both direct autonomic innervation and the effect of circulating catecholamines (Shapiro, Sloan, Horn, Myers, & Gorman, 1993). Interestingly, the results of several studies indicate that patients with certain psychiatric disorders, that is, mood and anxiety disorders, exhibit abnormally low HRV compared to non-psychiatric controls.

Depression and Reduced HRV:

Independent lines of research have provided evidence of reduced HRV among both depressed (non-CAD) psychiatric and depressed CAD patients. For example, among 300 healthy women who underwent 24 hour Holter monitoring, several symptoms relating to depression (e.g., inability to communicate anger to others and perceived social isolation) were related to multiple indices of reduced HRV (i.e., SDNN, VLF power, LF power and LF:HF ratio) (Horsten et al., 1999). In a similar study, Dalack and Roose (1990) reported that patients with major depression showed significantly reduced HRV and HF peaks, indicating decreased parasympathetic activity compared to control subjects. Finally, in a study which evaluated beat-to-beat QT variability, which is closely related to HRV, Yeragani et al. (2000) found evidence of increased QT variability in a sample of healthy patients with depression (DSM-III-R) (Yeragani et al., 2000). Increased QT variability, which represents time for repolarization of the ventricular myocardium, is also an important predictor of ventricular arrhythmias and like HRV, an indice of cardiac autonomic tone (Berger et al., 1997; Schwartz & Wolf, 1978). Therefore, there is evidence of reduced HRV

among non-cardiac depressed patients, lending support to previous studies suggesting a link between depression and cardiac morbidity.

However, to what extent does depression or depressive symptomatology influence HRV parameters among patients with established CAD? In studies examining the relationship between depressed mood (not actual DSM-IV-defined MDD) and HRV, there is robust evidence documenting a link between reduced HRV and depressive symptoms (Krittayaphong et al., 1997; Light, Kothandapani, & Allen, 1998; Light, Kothandapani & Allen, 1998; Sheffield et al., 1998). For example, in a study of 42 patients with documented CAD and recent exercise-induced myocardial ischemia, Krittayaphong et al. (1997) found evidence of significantly reduced SDNN and significantly increased resting heart rate among patients with high scores on the depression scale of the Minnesota Multiphasic Personality Inventory (MMPI-D). In a similar study of 41 patients with CAD, Sheffield et al. (1998) reported that patients with more severe depressive symptoms (BDI) exhibited significantly greater increases in heart rate and LF:HF ratio during a public speaking stressor compared to patients with less severe depression. The results of this study suggest that depressed mood may actually elicit sympathetic activation and/or inhibit vagal activity.

In studies of CAD patients who actually meet DSM-IV criteria for major depressive disorder, findings reveal a consistent pattern of reduced HRV indicating autonomic dysregulation. A recent study by Carney and colleagues (2001) found evidence of reduced HRV on all four frequency domain indices (ULF, VLF, LF, and HF) in a large sample of post-MI patients meeting DSM-IV criteria for major depression (n=380) compared to post-MI patients without major depression (n=424)

(Carney et al., 2001). Even after potential confounding variables (e.g., age, gender, diabetes, current cigarette smoking), all but one HRV index (HF) was significantly lower among depressed versus non-depressed patients. The results of a related study by the same research group also found that HRV was significantly reduced in depressed versus non-depressed patients with recently diagnosed CAD (Carney et al., 1995). A study by Stein et al. (2000), which controlled for the potential confounding effects of β-blockers also provided evidence of reduced HRV in depressed versus non-depressed patients with stable CAD (Stein et al., 2000). In this study, patients were classified as mildly depressed and moderately-to-severely depressed according to scores on the BDI. Results showed that resting heart rates were higher and all HRV indices but rMSSD and HF power were significantly lower among the moderately-to-severely depressed patients as compared to non-depressed patients. Results remained significant even after controlling for variables traditionally associated with HRV including age, gender, diabetes, current cigarette smoking, and previous MI. Finally, one prospective study recently reported that a diagnosis of depression 1-month post-MI was the best independent predictor of decreased SDNN during self-reported stress, which was assessed 18-months post-MI during 12-hour Holter monitoring (Thornton & Hallas, 1999). These findings are consistent with growing evidence linking depression and depressed mood with enhanced sympathetic reactivity to stress and reduced vagal activation, which can increase risk for adverse cardiac events in depressed individuals.

Panic-Anxiety, Anxiety Disorders and Reduced HRV:

The salience of tachycardia during panic attacks has long stimulated interest in investigating ANS disturbances in predisposing panic disorder (PD) patients to these episodes. It has been hypothesized that such autonomic instability is interpreted by the central nervous (CNS) as a source of persistent novel stimuli, which leads the CNS to respond to this stimuli with fear (Costello, 1971). A related hypothesis is that somatic variability leads to heightened perception of bodily sensations, which are then catastrophically misinterpreted (Anastasiades et al., 1990). Thus, the result of increased sympathetic activity and decreased vagal tone is poor control of heart rate, which can confer risk for tachycardia. To support these notions is evidence of reduced HRV, decreased cardiac vagal tone, and elevated sympathetic activity (heart rate) in patients with panic-like anxiety (Friedman & Thayer, 1998; George et al., 1989; Kawachi, Sparrow, Vokonas, & Weiss, 1995; Piccirillo et al., 1997; Yeragani et al., 1990; Yeragani et al., 1993).

In a large sample (n=581) of healthy patients exhibiting symptoms of phobic anxiety, Kawachi et al. (1995) found that patients with higher levels of phobic anxiety exhibited significantly higher resting heart rates and significantly lower HRV (SDNN) compared to patients without symptoms of phobic anxiety. In a similar study, Picirrillio and colleagues (1997) evaluated ANS activity via power spectral analysis of HRV among healthy volunteers both before and after sympathetic stress (tilt test). Results showed that in subjects reporting high state anxiety, resting HRV on all power spectral components was significantly lower, as was the LF:HF ratio during the tilt test (indicating greater parasympathetic activation to stress). These findings

suggest that individuals with high anxiety scores have baseline cardiac sympathetic hyperactivity, as well as lower HRV, compared to individuals with low anxiety.

Although research has documented a link between panic-like anxiety and reduced HRV, to what extent is actual PD associated with reduced HRV? Traditional views of PD posit that the disorder appears to be related to physiological changes resulting from sympathetic dysregulation, which is supported by studies linking PD to reduced HRV (Cohen, Matar, Kaplan, & Kotler, 1999; Klein, Cnaani, Harel, Braun, & Ben Haim, 1995; Yeragani et al., 1993; Yeragani, Berger, Songer, & Yeragani, 1997). For example, Yeragani et al. (1993) found evidence of decreased HF power and increased LF power in a sample of healthy (non-cardiac) PD patients compared to controls. These findings were replicated by Klein et al. (1995) and Yeragani et al. (1997), who reported that patients with PD exhibited significantly lower HF power at rest compared to non-PD patients. In a related study, spectral analysis of HRV was performed in PD patients both before and after isoproterenol infusion (a common panic-challenge test). Results indicated a significant increase in the LF:HF ratio in the PD patients following the isoproterenol challenge (Yeragani et al., 1995). Friedman et al. (1993) also found evidence of reduced HRV (using spectral analysis) and higher resting heart rate in PD patients compared to blood phobics (Friedman et al., 1993). This study also found that PD patients exhibited dominant sympathetic control of heart rate and lower vagal tone compared to blood phobics, suggesting that reduced HRV in PD can be distinguished from other anxiety disorders. Taken together, these findings indicate a consistent pattern of increased sympathetic and decreased parasympathetic tone in PD patients, suggesting that PD patients may be at increased

risk for poor control of heart rate (e.g., tachycardia & arrhythmias) compared to non-PD patients.

Although there is a robust link between panic-like anxiety, PD and reduced HRV, there are no studies to date evaluating HRV among patients with both PD and documented CAD. However, because reduced HRV has been consistently observed among individuals with panic-like anxiety, it is likely that PD patients *with* comorbid CAD would demonstrate even greater autonomic disturbances than patients without CAD due to their existing cardiac disease. It also possible that the increased risk for the development of CAD and subsequent morbidity and mortality in patients with panic-like anxiety (e.g., Coryell et al., 1982; 1986; Haines et al., 1987; Kawachi et al., 1994a; 1994b) could be due to such autonomic cardiac disturbances. One question which remains unanswered in the literature is whether HRV is also significantly reduced among patients with comorbid PD and CAD, as evidence of ANS dysregulation in such patients could have important implications for cardiac morbidity.

Study Objective 2:

The second objective of the present study was to extend previous research demonstrating an association between PD patients and reduced HRV to PD patients with documented CAD. Specifically, this study examined the extent to which CAD patients with comorbid PD exhibited significantly reduced HRV compared to CAD patients without comorbid PD (controls). Patients underwent 48-hour ECG Holter monitoring and the resulting time domain (ASDNN, SDNN, SDANN) and frequency

domain indices of HRV (HF, LF, VLF, ULF, TP, LF:HF ratio) were analyzed. Spectral analysis was used to examine frequency domain indices.

Anxiety Sensitivity: A Trait Marker of Dysregulated Autonomic Tone?

The HRV literature has demonstrated a consistent pattern of reduced HRV among both mood and anxiety disordered patients. What is less clear is what is underlying the observed association between reduced HRV in patients with these mood disturbances. That is, is there anything that patients with MDD and anxiety disorders might have in common that may predispose them to reductions in HRV, and therefore a dysregulation of cardiac autonomic tone, even before the onset of clinically detectable CAD?

According to the expectancy theory of Reiss and McNally (1985) and Reiss (1991), there are three fundamental fears that contribute to the development, maintenance and severity of a variety of fears or phobias: fear of negative evaluation or judgement by others, fear of injury or death, and anxiety sensitivity. Anxiety sensitivity (AS) has been conceptualized as an individual difference (trait) variable separate from anxiety which may predispose certain individuals to develop anxiety disorders ; Reiss & McNally, 1985; Reiss, Peterson, Gursky & McNally, 1986). AS, which is defined as "fear of fear" or fear of anxiety-related symptoms, is said to result from the belief that anxiety symptoms have harmful physical, social, or psychological consequences (Reiss & McNally, 1985). For example, fear of heart palpitations is based on the belief that tachycardia may be a warning sign for impending cardiac arrest. As a result of such beliefs, individuals with high AS will be hypervigilant to

bodily sensations and somatic changes to the extent that they become worried about feeling anxious. They may go on to interpret their anxiety as having the potential to lead to some unwanted consequence, such as a heart attack or mental illness. This in turn produces additional anxiety where a vicious circle develops in which life stressors produce anxiety, and then anxiety produces additional anxiety and so on. Therefore, individuals with high AS tend to have increased alertness to stimuli which signal the possibility of becoming anxious, tend to worry about the possibility of becoming anxious, and are generally highly motivated to avoid anxiety-provoking stimuli (Reiss et al., 1986). Over time, such chronic anxiety and "fear of fear" may contribute to feelings of helplessness, which is one of the major theories of depression (Seligman, 1992). Chronic anxiety may lead to feelings of helplessness when an individual in unable to predict when and where feared symptoms will occur, and believes that his or her mental and physical health or general sense of safety is beyond their control.

The Anxiety Sensitivity Index (ASI)

Anxiety sensitivity is assessed using the Anxiety Sensitivity Index (ASI; Peterson & Reiss, 1987, see appendix A). The ASI is a 16-item self-report questionnaire that specifies possible negative consequences to the experience of anxiety. Each item is rated on a five-point scale with total scores ranging from 0-64. Evidence demonstrates that there are at least three dimensions of AS: fear of somatic sensations (i.e., fear of heart palpitations stemming from the belief that palpitations may lead to a heart attack); phrenophobia (i.e., fear of losing "mental control" and/or

concentration difficulties stemming from the belief that these disturbances may lead to insanity or serious mental illness); and fear of observable anxiety symptoms (i.e., fear of blushing or shaking stemming from the belief that they will lead to rejection or ridicule from others) (Taylor, Koch, Woody, & McLean, 1996). Although there has been some debate as to whether the ASI represents a unitary or mutidimensional construct (Taylor et al., 1996; Zinbarg, Barlow, & Brown, 1997; Reiss et al., 1986; Peterson & Heilbronner, 1987; Taylor, Koch & Crockett, 1991), evidence to date suggests that the ASI is unifactorial, but measures different dimensions of AS (as outlined above) (Taylor, Koch, Woody, & McLean, 1996).

The ASI has demonstrated good test-retest reliability (α = .71 to .75; Reiss et al., 1986), split-half reliability, inter-item consistency and internal reliability (α = .82 to .91; Peterson & Heilbronner, 1987; Telch, Shermis, & Lucas, 1989; Taylor et al., 1991). A number of studies have also provided support for the ASI's construct validity. For example, the ASI has been shown to correlate highly to moderately with the Agoraphobic Cognitions Questionnaire (ACQ) (Chambless, Caputo, Bright, & Gallagher, 1984) and Body Sensations Questionnaire (BSQ; Chambless et al., 1984) which supports the claim that the ASI measures the fear of anxiety. Moreover, the ASI has been shown to distinct from both state and trait anxiety, and can predict fearfulness above and beyond that predicted by other anxiety measures (Reiss et al., 1986).

Anxiety Sensitivity in Patients with Depression and Anxiety Disorders

There has been much debate over the clinical validity of "pure" diagnostic categories or disorders (e.g., mood disorders or MDD specifically) because studies show that mood and anxiety disorders frequently co-occur (APA, 1994). Not only do mood and anxiety disorders share many symptoms (e.g., sleep and appetite disturbances, concentration difficulties, agitation, irritability), but research shows that anxiety and depression also share a similar genetic background (Kendler, Heath, Martin, & Eaves, 1987). Additional evidence of a shared etiology can be found in studies demonstrating the efficacy of selective serotonin reuptake inhibitors, SSRIs (e.g., Paroxetine) in relieving symptoms of both mood and anxiety disorders (Ninan, 2000; Ninan & Berger, 2001). The efficacy of such medications implicates the role of the neurotransmitter serotonin in the development of both mood and anxiety disorders. Thus, research suggests that there is a shared underlying psychopathology in patients with mood and anxiety disorders which likely represents some combination of somatic, neurochemical, affective and cognitive disturbances. One such underlying psychopathology may be the trait of AS.

Firstly, extensive research has demonstrated a link between high AS and anxiety disorders (Taylor et al., 1992; Otto, Pollack, Fava, Uccello, & Rosenbaum, 1995). Scores on the ASI have been found to be consistently elevated in patients with PD (e.g., Peterson & Reiss, 1987; Taylor et al., 1992), GAD, post-traumatic stress disorder (PTSD), social phobia, and obsessive-compulsive disorder (OCD) (Peterson & Reiss, 1992; Taylor et al., 1992). Normative data collected from 1,463 anxiety disorder patients indicates that mean ASI scores for different anxiety disorders are as

follows: 35.9 for PD patients with or without agoraphobia; 31.6 for PTSD patients; 26.1 for GAD patients; 25.4 for OCD patients; and 24.9 for social phobia patients. The mean normal ASI score is between 10-18 (SD=8.5) (Peterson & Reiss, 1992). Interestingly, a number of recent investigations have also demonstrated a similar association between high AS and depression (i.e., MDD) (Taylor et al, 1996; Otto et al., 1995). Otto and colleagues (1995) conducted two studies investigating the relationship between AS and MDD. In Study 1, a total of 15 patients with pure MDD (i.e., no co-morbid anxiety disorder) were found to have mean ASI scores of 25.3 (*SD*=12.5), which are comparable to scores observed in non-panic anxiety disorder patients (Peterson & Reiss, 1992). In Study 2, Otto et al. sought to replicate these findings with a larger sample (n=144) of depressed patients. They reported mean ASI scores of 25.2 (*SD*=11.9) for 63 patients with MDD and no co-morbid anxiety disorder; 28.5 (*SD*=12.2) for 53 patients with MDD and a comorbid non-panic anxiety disorder; and 31.2 (*SD*=13.0) for 28 patients with MDD and current or past PD. ASI scores for each of these diagnostic groups were significantly higher than those of the non-psychiatric control group (n=15, *M* = 15.3, *SD*=12.4). These findings were replicated by Taylor et al. (1996), who also found significantly elevated ASI scores among their sample of psychiatric patients. Specifically, they reported mean ASI scores of 31.4 (*SD*=9.6) for PD patients without MDD; 40.3 (*SD*=11.3) for PD patients with MDD; and 22.1 (*SD*=10.6) for MDD patients without PD. These authors went on to examine whether certain components of AS were more related to panic and anxiety versus more related to depression. Principal components analysis identified three dimensions of AS: fear of somatic sensations, phrenophobia (fear of

mental incapacity), and fear of publicly observable arousal symptoms. Interestingly, the authors found the relationship between panic-anxiety to be related to the AS dimensions of fear of somatic sensations and fear of publicly observable arousal symptoms. Conversely, the relationship between AS and depression appeared to be due to the dimension of phrenophobia as assessed by three items on the ASI: "It scares me when I am unable to keep my mind on a task," "When I cannot keep my mind on a task, I worry that I might be going crazy," and "When I am nervous, I worry that I might be mentally ill." The authors concluded that phrenophobia may be a depression-specific form of AS and suggests that AS is a construct which represents more than fear of fear or panic. What is interesting about these findings is that they provide evidence for a common link between anxiety and mood disorders. Not only does AS represent fear of fear, but it also appears to represent fear of insanity or mental incapacitation. The extent to which a person becomes concerned or worried about these symptoms is likely to depend on his or her beliefs about them in a similar manner as their beliefs about the implications of palpitations. The belief that mental or cognitive disturbances lead to insanity will make concentration or decision-making difficulties particularly distressing for an individual with a tendency to worry about the consequences of such symptoms. As such, these symptoms will produce considerable anxiety in susceptible individuals. Thus, the results of these studies demonstrate a clear pattern of high AS in different samples of depressed patients, and suggest a role for AS in depression that is comparable to non-panic anxiety disorders.

In sum, research to date suggests that AS may represent a shared underlying trait of in individuals with both mood and anxiety disorders was evidenced by high

ASI scores among such patients. However, to what extent could AS be underlying the relationship between mood and anxiety disorders and reduced HRV?

Anxiety Sensitivity and Dysregulated Cardiac Autonomic Tone

It has been suggested that having high AS or a lower threshold for activating fear is maladaptive such that it sustains the individual at an excessively high level of physiological arousal beyond what's required to maintain personal safety or survival (Logan & Goetsch, 1993). To support this claim is a robust body of evidence demonstrating a link between high state and trait anxiety and increased resting blood pressure levels (Henry & Grim, 1990). Interestingly a study by Pagotto et al. (1992) was also able to document a link between high AS and hypertension. Specifically, AS was assessed using the ASI in 20 hypertensive and 20 control patients and results showed that hypertensive patients exhibited significantly higher levels of AS compared to demographically-matched normotensive subjects (Pagotto, Fallo, Fava, Boscaro & Sonino, 1992). This study's design did not permit the authors to determine whether high AS is a cause or a consequence of hypertension, but provides evidence of an association between a dispositional variable (AS) and an objective disease state (hypertension). Given that dispositional (i.e., trait) variables typically emerge by late adolescence or early adulthood (Lau, Calamari, & Waraczynski, 1996), it is likely that the high AS observed in hypertensive patients preceded the development of hypertension. In fact, using the Childhood Anxiety Sensitivity Index (CASI) (Silverman, Fleisig, Rabian & Peterson, 1991), researchers have been able to document the presence of AS in children and adolescents (Rabian, Peterson, Richters,

& Jensen, 1993; Lau et al., 1996), suggesting that AS is indeed a dispositional variable which can emerge at a young age.

In addition to sustaining individuals at a high level of physiological arousal, it has also been suggested that high AS may predispose individuals to over-attend to physiological changes. The hypothesis that having an increased sensitivity to fear may also reduce the threshold for detecting or perceiving somatic changes has been supported by a recent study by Asmundson and colleagues (1997). These researchers demonstrated that chronic pain patients with high AS selectively attended to pain and injury-related stimuli (versus neutral stimuli) as compared to low AS patients (Asmundson, Kuperos, & Norton, 1997). Taken together, these findings point to an association between high AS and (1) risk for sustained high level of physiological arousal and (2) a hyper-sensitivity to any increases in such arousal.

Central Regulation of Emotion

The role of the ANS in emotion and anxiety in particular has received a great deal of attention in the literature. The James-Lange theory of emotion hypothesized that emotion was experienced as bodily sensations transported centrally via ANS afferents (James, 1884). Cannon (1927) refuted this hypothesis and postulated a role for the CNS in the etiology of emotion. Current theories have their roots in both of these theories, with some researchers arguing that AS arises from a catastrophic reaction to bodily physical and/or cognitive symptoms (Clark, 1986), while others believe that AS is the result of CNS abnormalities (Carr & Sheehan, 1984; Charney, Heninger, & Breier, 1984). Evidence in support of CNS influences stems from

research implicating the hypothalamus in the integration of emotional, somatic, endocrine and autonomic information from amydaloid and limbic structures (Aubert & Ramaekers, 1999). Moreover, there are two pathways by which the hypothalamus is linked to cardiovascular regulation: (1) via caudal projections which pass through the ventrolateral surface of the medulla and the lateral funiculus towards the intermediolateral nucleus of the spinal cord; and (2) via the dorsolateral hypothalamus which is linked to the dorsal vagal nucleus and medial nucleus tractus solaris whose descending fibres innervate sympathetic and parasympathetic preganglionic nuclei (Aubert & Ramaekers, 1999). Thus, HRV represents an important marker of emotionally-induced sympathetic arousal, where acute and/or chronic arousal disrupts sympathovagal balance via enhanced sympathetic outflow and simultaneous inhibition of neural activity in the dorsal vagal nucleus.

It is therefore possible that individuals with high AS, who experience chronic ANS hyper arousal due to their tendency to over-attend and hyper-react to bodily sensations and somatic changes, may from a very young age contribute to disruptions in ANS functioning. Specifically, high AS may over time lead to chronic sympathetic hyper arousal and vagal inhibition, thereby leading to dysregulations in cardiac autonomic tone and sympathovagal balance. However, the extent to which AS is related to cardiac autonomic tone and reduced HRV has not been investigated.

Study Objective 3:

The third objective of the present study was to examine the extent to which AS is related to dysregulated cardiac autonomic tone in CAD patients with mood and

anxiety disorders. Specifically, this study examined the extent to which CAD patients with Hi AS exhibited significantly reduced HRV compared to CAD patients with Lo AS. Anxiety sensitivity was assessed using the ASI and patients were divided into Hi and Lo AS groups based on cutoff scores on the ASI (Lo <11; Hi ≥ 11, Peterson & Reiss, 1992). Patients underwent 48-hour ECG Holter monitoring and the resulting time domain (ASDNN, SDNN, SDANN) and frequency domain (HF, LF, VLF, ULF, TP, LF:HF ratio) indices of HRV were analyzed. Spectral analysis was used to examine frequency domain indices.

METHODS

Participants

A total of 71 consecutive, eligible and consenting CAD patients with recent (< 6 months) positive nuclear exercise (treadmill) stress tests were recruited from the nuclear medicine service of the Montreal Heart Institute. A total of 59 (83%) patients were male and the sample had a mean age of 58.7 (SD = 7.4) years. For Study Objective 1, a total of 28 had a primary anxiety disorder diagnosis (n=15 with PD; n=5 with GAD, n=4 with social phobia, n=4 with specific phobia) and 20 had a primary mood disorder diagnosis (all with a diagnosis of major depressive disorder). No patients in the anxiety disorder group had a primary diagnosis of PTSD or OCD. For Study Objective 2, a total of 20 patients meeting diagnostic criteria for PD (with or without Agoraphobia) were compared to 22 patients with no current or lifetime history of psychiatric illness. For Study Objective 3, a total of 71 CAD patients were divided into Hi and Lo AS groups based on standard cutoffs (Lo = <11; Hi = ≥ 11, Peterson & Reiss, 1992) on the ASI. A total of 18 patients were classified as Lo AS and 41 patients were classified as Hi AS.

All patients underwent 48-hour ambulatory ECG monitoring and completed a self-monitoring diary of their emotions, activities, and physical symptoms. Holter monitoring was used to assess both the frequency and duration of transient ischemic episodes, as well as to sample HRV.

Inclusion/Exclusion Criteria

Inclusion Criteria:

Medically stable patients with documented CAD (documented by prior MI, coronary artery bypass graft surgery, CABG, percutaneous transluminal coronary angioplasty, PTCA, and/or at least 50% stenosis in 1 or more major coronary arteries, and/or previous evidence of reversible myocardial perfusion defects on exercise) between the ages of 18 and 69 were eligible to participate in the study. All patients had to have at least a mild to moderate reversible myocardial perfusion defect on the exercise stress test and have the cognitive and language ability to comprehend French or English sufficient to reliably complete self-report, interview, and diary assessments.

Objective 1:

Mood Disorder Groups: Must have met DSM-IV criteria (current) for one (or more) AXIS I mood (MDD, Dysthymia) disorder.

Anxiety Disorder Groups: Must have met DSM-IV criteria (current) for one or more anxiety disorder (PD with or without Agoraphobia, GAD, PTSD, OCD, Social Phobia, and/or Specific Phobia).

Control Group: Must not have met DSM-IV criteria (current or lifetime history) for any AXIS I disorder and have had BDI and ASI scores of less than 10.

Objective 2:

Panic Disorder Groups: Must have met DSM-IV criteria (current) for PD with or without Agoraphobia.

Control Group: Must not have met DSM-IV criteria (current or lifetime history) for any AXIS I disorder and have had BDI and ASI scores of less than 10.

Objective 3:

Hi AS Group: Scored ≥ 11 on the ASI.

Lo AS Group: Scored < 11 on the ASI.

Exclusion Criteria:

Patients were excluded if they had current or previous evidence of congestive heart failure (the inability of the heart to pump sufficient blood to meet the needs of the body), a recent (within 2 months) MI, CABG, or PTCA, another significant cardiac condition (including cardiomyopathy, valvular heart disease, arrhythmias, a pacemaker, left bundle-branch block, or Wolff-Parkinson-White syndrome), a resting blood pressure higher than 200/120 mmHg, a resting LVEF of less than 30%, a left main artery stenosis of 50% or greater, a serious pulmonary condition (e.g., chronic obstructive pulmonary disease), a severe systemic illness (e.g., cancer) or a noncardiac medical illness which could influence autonomic functioning (e.g., epilepsy). Patients were also excluded if they were or could have been pregnant, had a primary AXIS I psychiatric disorder other than mood or anxiety (e.g, schizophrenia, somatoform), had a substance abuse disorder (e.g., drug or alcohol), were current

regular users of benzodiazepine or antidepressant medication and could not stop temporarily for the study, were current users of psychotropic medication (e.g., neuroleptics), or demonstrated an apparent cognitive deficit such that they would have been unable to reliably complete the study.

Psychological Measures

Screening Interview

The Primary Care Evaluation of Mental Disorders (PRIME-MD):

The PRIME-MD (Spitzer et al., 1994) is a recently developed and validated screening tool designed to improve primary care physicians' recognition of the most common DSM-IV AXIS I (mood, anxiety, substance, somatoform) disorders in medical settings. It takes less than 10 minutes for physicians to administer and diagnose patients using this instrument, which consists of a one page (27-item) patient self-report questionnaire, followed by a 12 page structured interview that the physician uses to follow-up patient responses (see appendix B). The PRIME-MD has recently been made available in computer format, where questions are asked orally by the examiner, and was the format used in this study. This instrument was used to screen for the presence of AXIS I mood and anxiety disorders, and to screen out the presence of other AXIS I disorders, including substance abuse and somatoform disorders. Only patients with positive exercise tests who meet diagnostic criteria for one (or more) or no AXIS I mood or anxiety disorder were submitted to a structured interview (ADIS-IV) to confirm presence or absence of AXIS I disorder(s).

Self-Report Questionnaires

Anxiety Sensitivity Index (ASI):

The ASI (see appendix A) is a 16-item self-report questionnaire designed to measure patients' fear of anxiety symptoms (Reiss et al., 1986). This well-established instrument has become one of the most widely used instruments in anxiety and panic research. Scores on the ASI range from 0 to 64. The mean for sample of normal adults is between 10 and 18 (SD=8.5) (Peterson & Reiss, 1992). The ASI has a high degree of internal consistency and satisfactory test-retest reliability (Reiss et al., 1986; Peterson & Heilbronner, 1987; Telch et al., 1989; Taylor et al., 1991). It has also been translated and is currently being validated in Canadian French. For Study Objective 3, patients were classified into high and low AS groups using the following cutoff scores (Lo = <11; Hi = ≥ 11, Peterson & Reiss, 1992).

Beck Depression Inventory-II (BDI-II):

The BDI-II (see appendix C) is a 21-item self-report questionnaire designed to measure the intensity of depressive symptoms (Beck, Ward, Mendelsohn, Mock & Erbaugh, 1961). The BDI has been used extensively in studies examining the relationship between depressive symptoms, CAD, and cardiac events (Lesperance et al., 1996; Frasue-Smith et al., 1995b), and is considered the preferred questionnaire for measuring depressive symptoms in cardiac patients (Gotlib & Cane, 1989). Scores on the BDI range from 0 to 63, and scores of 10 or greater indicate at least moderate symptoms of depression (Frasure-Smith et al., 1995b). It has been translated and validated in Canadian French (Frasure-Smith et al., 1995a). Only patients with BDI

scores of 10 or greater (mood disorder group) or below 10 (control group) were submitted to further diagnostic screening.

Cook-Medley Hostility Scale (CMHO):

The CMHO (see appendix D) (Cook & Medley, 1954) contains 50 true or false questions derived from the MMPI (Smith & Fromm, 1985). This scale is thought to measure that aspect of hostility reflecting cynical and mistrusting attitudes towards others. It contains various subscales which assess hostile affect, hostile attitude, aggressive responding, cynicism, suspiciousness, and social avoidance. It has demonsrated high internal consistency (r=.86; Smith & Fromm, 1985), test-retest reliability (r=.84 to .85; Barefoot, Dahlstrom, & Williams, 1983; Shekelle, Gale, Ostfeld, & Paul, 1983), and good construct validity (Smith & Fromm, 1985). It has been empirically associated with a number of health outcomes, including hypertension, coronary heart disease, and cardiovascular reactivity in both retrospective and prospective studies (Houston, 1994). This scale was used to evaluate the relationship between HRV and hostility.

State-Trait Anxiety Inventory (STAI):

The STAI (see appendix E) (Spielberger, Gorsuch, & Lushene, 1970; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) is a 20-item scale designed to assess state and trait anxiety. Respondents indicate how they generally (trait) and presently (state) feel on a 4-point scale ranging from 1 (almost never) to 4 (almost always). Both scales of the STAI have demonstrated high internal consistency (r=.89

to .90), test-retest reliability (r=.73 to .86), and studies support its validity (Knight, Waal-Manning, & Spears, 1983).

This scale was used to evaluate the relationship between HRV and state and trait anxiety.

State-Trait Anger Inventory (STAXI):

The STAXI (see appendix F) (Speilberger, Jacobs, Russell, & Crane, 1983) is a 15-item scale designed to assess state and trait anger. Respondents indicate how they generally (trait) and presently feel on a 4-point scale ranging from 1 (almost never) to 4 (almost always). Both scales have shown high internal consistency (r=.84 to .93; Spielberger, 1980) and test-retest reliability (r=.91), and studies support its validity (Spielberger et al., 1983).

Diagnostic Interview

Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV): The ADIS-IV (see apppendix G) (DiNardo, Moras, Barlow, Rapee, & Brown, 1993) is a structured psychiatric interview for the diagnosis of DSM-IV mood and anxiety disorders. It also includes screening questions for alcohol and substance abuse disorders, as well as somatoform disorders. The DSM-III-R version of the interview (NiNardo & Barlow, 1988) displayed good inter-rater reliability for the diagnosis of AXIS I mood and anxiety disorders. Reliability data are not yet available for the updated DSM-IV version, however inter-rater reliability for the ADIS-IV should compare to the ADIS-R as diagnostic criteria for mood and anxiety disorders have not changed significantly

in the DSM-IV (APA, 1994). The interview was administered by telephone by a licensed clinical psychologist within 2 weeks of their initial screening interview. Phone administration of structured psychiatric interviews has been validated by several studies (e.g., Simon, Revicki & VonKorff, 1993; Wells, Burnam, Leake, & Robins, 1988). Only patients with positive nuclear exercise tests who met DSM-IV criteria for one (or more) or no mood or anxiety disorder (but not somatoform or substance abuse) on the ADIS-IV were be eligible to participate.

Mood, Activity and Symptom Diary:

During the 48-hours of ambulatory ECG monitoring, patients recorded their emotions, activities, and physiological symptoms in pocket-sized, structured diary booklets adapted from Hedges and colleagues (Hedges, Krantz, Contrada, & Rozanski, 1990). This structured diary system has been validated by several methods, including spouse or observer report, automated activity monitoring, and comparisons of home and work settings (Patterson et al., 1993). Patients were given careful instruction involving explicit definitions and modeling. Patients were prompted to make a random diary entry by a programmed auditory signal (JD-7 Random Reminder, Divilbiss Electronics) an average of 2 times per hour between 6am and midnight, excluding sleep hours, as well as when any significant interpersonal (e.g., argument) or cardiac (e.g., chest pain) event occurs (whenever activities, symptoms, or moods change). A sample diary page is presented in appendix H.

Nuclear Imaging Tests

Participants were recruited from consecutive patients referred for exercise stress single-photon emission computed tomography (SPECT) tests. Patients with recent (< 6 months) positive (evidence of exercise-induced reversible myocardial perfusion defects or ischemia) nuclear exercise (treadmill, Bruce protocol) stress tests were be submitted to diagnostic screening to determine the presence or absence of AXIS I disorders. Patients will be considered to have ischemia during exercise if they exhibit a myocardial perfusion defect compared to rest (baseline) as diagnosed by a nuclear cardiology physician according to standard medical practice.

Ambulatory ECG (Holter) Monitoring

Patients will be connected to an amplitude-modulated, 40 MG computer card-based, 3-channel SEER MC (Holter) 7-lead Ambulatory ECG recorder (Marquette Medical Systems Inc, Milwaukee, Wis) after skin preparation between 9am and 11am on the day of the Holter installation.

Myocardial Ischemia Assessment:

For each episode of ST-segment depression, the time of onset, duration, magnitude, and heart rate at onset of ischemia were recorded. Patients were monitored for 48 consecutive hours. ST-segment analyses was performed by an electrophysiology technician skilled in the interpretation of ECG data using the interpretation software package (the Multi-Parameter Analysis and Review System [MARS] Holter analysis and editing software) provided by Marquette Medical Systems, Inc, Milwaukee, Wis. Myocardial ischemia was defined as a horizontal or

downsloping ST-segment depression of 1mm (0.1 mV) or more for one minute or longer compared with resting baseline. The termination of an ischemic episode was determined at the time the ST-segment depression returned to less than 0.9 mm (0.9 mV) of the baseline for one minute or longer. If the ST-segments became re-depressed within 1 minute for at least one additional minute, the episodes were collapsed into one episode. ST-segment depressions associated with ventricular tachycardia or frequent ventricular beats were excluded from the analysis. Consensus regarding identification of ischemic episodes was reached for each Holter recording by two skilled electrophysiology technicians and the study cardiologist who were be blind to the patient's identity, psychiatric status, diary information, test scores, and clinical status.

Heart Rate Variability Assessment:

Time domain HRV indices based on interbeat intervals including SDNN (the SD of all normal R-R (i.e., N-N) intervals, measured in ms, SDANN (the SD of the mean of the 5-minute intervals averaged over a 24-hour period, measured in ms), and ASDNN (the average of the SDs of interbeat intervals for each 5-minute interval, measured in ms) will be measured.

Spectral analysis of frequency domain HRV indices were conducted by an electrophysiology technician skilled at HRV assessment using the MARS Holter analysis and editing software provided by Marquette Medical Systems, Inc, Milwaukee, Wis. The following standard frequency domain components of HRV, measured in ms and ms^2 were computed: high frequency (HF) power, the respiration-

mediated component of HRV between 0.15 and 0.40 Hz which is said to reflect vagal modulation of heart rate; low-frequency (LF) power, the component between 0.04 and 0.15 Hz and which reflects both sympathetic and parasympathetic activity; very-low frequency (VLF) power, the component between 0.0033 and 0.04 Hz and is said to also reflect both sympathetic and parasympathetic activity; ultra-low frequency (ULF) power, the component between 1.15×10^{-5} and 0.0033 Hz which is said to reflect circadian variation in heart rate and is influenced by both sympathetic and parasympathetic inputs (Akselrod et al., 1985). Total power (TP), which represents the total variation in heart rate or the sum of the HF, LF, VLF and ULF components (1.15×10^{-5} and 0.0033 Hz) was also computed. The ratio of low (sympathetic) to high (parasympathetic) (LF:HF) power, which is said to reflect sympathovagal balance, was also computed.

Spectral analysis of heart rate involves re-sampling and filtering the sequence of normal-to-normal (R-R) intervals to generate a uniformly based time series. Missing or "noisy" segments were replaced by linear interpolation from the surrounding signal. The average normal-to-normal interval was subtracted from the time series and fast Fourier transformed to extract the frequency components underlying the cyclic activity in the time series. Measurement of ULF and VLF power was based on *en bloc* analysis of the entire 48-hour recording (Rottman et al., 1990). For a more detailed description of spectral analysis of heart rate, please see Rottman et al. (1990).

Procedure

Consecutive patients referred for exercise SPECT imaging were recruited to complete an initial screening interview (PRIME-MD, medical history interview) and complete a battery of psychological questionnaires (ASI, BDI, CMHO, STAI, STAXI) on the day of their exercise stress test. A full-time research assistant sought patient consent (see appendix I) for the interview and questionnaires and conducted the PRIME-MD and medical history interview. Once nuclear exercise SPECT results were obtained (approximately 24-48 hours), patients meeting all initial eligibility criteria were contacted to schedule an appointment to conduct the ADIS-IV diagnostic interview by telephone. The interview was conducted by a licensed Doctoral Level, Clinical Psychologist to confirm the presence or absence of mood and/or anxiety disorder. The interview took between 15 minutes and 1.5 hours to complete, and was conducted within 2 weeks of the initial screening interview and exercise stress test.

Patients with a confirmed AXIS I mood (MDD, Dysthymia) and/or anxiety (PD with or without Agoraphobia, GAD, PTDS, OCD, Social Phobia, Specific Phobia), and patients without a current (or lifetime history) of psychiatric disorders were asked to participate in the 48-hour ambulatory (Holter) monitoring phase of the study. Ambulatory monitoring took place within approximately 4 weeks of the initial screening interview and exercise stress test. The cardiologists of all consenting patients were contacted to obtain written permission to install 48-hour ambulatory monitors.

Between 9am and 11am on the day of testing, patients were instrumented with an ambulatory (Holter) monitor (previously described) for 48-hour recording. Following an 8-minute calibration period, postural testing in 5 positions (supine, left lateral, right lateral, sitting, and standing for 2 minutes each) was performed. A 3 channel, 7-lead ECG Holter monitor was used for ECG recording to detect ST-segment variation and for HRV assessment.

Throughout the 48-hours of ambulatory ECG monitoring, patients recorded their emotions, activities, and physiological symptoms in a pocket-sized, structured self-monitoring diary. Patients were briefed in detail on the diary system, and were asked to complete several sample entries with the experimenter to ensure that they understood the procedure. Detailed instructions (see appendix J), including definitions of terms and examples of entries were provided. During the ambulatory ECG monitoring period, patients were prompted to make a random diary entry by a programmed auditory signal an average of 2 times per hour between 6am and midnight, excluding sleep hours, as well as when any significant interpersonal (e.g., argument) or cardiac (e.g., chest pain) event occurred (whenever activities, symptoms, or moods changed as per previous studies, e.g., Guelette et al. 1997). The auditory signal will be produced by a JD-7 Divilbiss Random Reminder (Divilbiss Electronics, Champain, Ill), a device with a belt that can be set to randomly beep at any 1 of 21 predetermined average frequencies per hour. Patients were instructed to rely on the Holter monitor's internal clock when entering time of day in the diary in order to ensure that diary entries correspond to monitor events. Each entry was made on a separate page which allowed for the recording of time of day; posture (reclining,

sitting, or standing); location; amount of mental and physical effort expended; emotions (including sadness, tension, anger, irritability, frustration, anxiety, fear, worry, "panicky", happiness, feeling in control); physiological symptoms (e.g., chest pain, shortness of breath, dizziness, nausea, sweating etc.); caffeine, alcohol, and tobacco consumption; and nitroglycerin use. Emotions and amount of effort (physical-mental) expended were be rated on 5-point intensity scales ranging from "not at all" to "very much".

Following the 48-hour monitoring period, patients returned all materials and diaries to the full-time research assistant. If data analysis indicated a significant myocardial defect or worsening of cardiac status, patients were referred to Dr. Denis Burelle, the study cardiologist and co-investigator, or to the patient's cardiologist. The research team obtained permission from the patient to communicate any pertinent findings to the patient's cardiologist or primary care physician in order for them to get appropriate and timely treatment

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Analytic Strategy and Statistical Analyses

Study Objective 1:

For baseline analyses, one-way analyses of variance (ANOVAs) and Chi-Square ($\chi 2$) analyses were conducted to examine differences between diagnostic groups on continuous (e.g., age, height, cardiovascular variables etc.) and dichotomous (e.g., hypertension, history of MI, smoking status, etc.) variables respectively. A series of one-way ANOVAs were conducted to examine differences between diagnostic group (mood disorder vs. anxiety disorder vs. controls) in the

number and duration of ischemic episodes exhibited during daily life. The proportion of patients in each group (mood disorder vs. anxiety disorder vs. controls) displaying myocardial ischemia was also assessed using Chi-Square ($\chi 2$) analyses for dichotomous variables. For each episode of myocardial ischemia, one-way ANOVAs were conducted to examine differences in the proportion of ischemic episodes that were preceded by mental stress versus by physical stress. To examine differences between self-reported chest pain and the number of chest pain episodes reported by each diagnostic group, Chi-Square ($\chi 2$) analyses and one-way ANOVA were conducted respectively. The α-level was set at 0.05 per comparison.

Study Objective 2:

For baseline analyses, one-way analyses of variance (ANOVAs) and Chi-Square ($\chi 2$) analyses were conducted to examine differences between diagnostic groups on continuous (e.g., age, height, cardiovascular variables etc.) and dichotomous (e.g., hypertension, history of MI, smoking status, etc.) variables respectively. A series of one-way ANOVAs were conducted to compare time and frequency domain HRV indices and other continuous variables for PD versus control patients. Analyses of covariance (ANCOVA) adjusted for variables that have previously been associated with HRV (current smoking, diabetes, and previous CABG) were conducted to examine differences between PD and control groups on HRV indices. The α-level was set at 0.05 per comparison.

Study Objective 3:

For baseline analyses, one-way analyses of variance (ANOVAs) and Chi-Square (χ_2) analyses were conducted to examine differences between diagnostic groups on continuous (e.g., age, height, cardiovascular variables etc.) and dichotomous (e.g., hypertension, history of MI, smoking status, etc.) variables respectively. A series of one-way ANOVAs were conducted to compare time and frequency domain HRV indices and other continuous variables for Hi versus Lo AS patients. Analyses of covariance (ANCOVA) adjusted for variables that have previously been associated with HRV (current smoking, diabetes, and previous CABG) were conducted to examine differences between Hi versus Lo AS groups on HRV indices. The α-level was set at .05 per comparison.

Power Analysis and Justification for the Sample Size

Sample size calculations were conducted using data from previous studies as per Cohen (1988) and specific calculations as per Shavelson (1988), Hayes (1973), and Levin (1975). For the main objective of the study (Objective 1), 18 patients per group are required to detect a significant difference between these 3 groups with a power of 0.8 conducting ANOVAs or χ^2 (two-sided) analyses with α= .05. Expecting 10% attrition and errors in experimental procedure (e.g., equipment failure, non-compliance etc), participation of at least 60 patients was sought (n=20 per group). This sample size was also adequate to conduct ANOVAs on number of ischemic episodes, duration of episodes, and severity of ST-segment depression that will detect differences between means of 0.5 SD (medium effect size) at α= .05 and β= .80.

RESULTS

Study Objective 1:

Myocardial Ischemia in Mood and Anxiety Disorder Patients

Participant Characteristics

To assess whether participants differed in age, height, weight, and body mass index (BMI) as a function of diagnostic group, a series of one-way analyses of variance (ANOVAs) were conducted for Mood Disorder, Anxiety Disorder, and control patients using mean age, height, weight, and BMI values. No group differences in were observed. Means and standard errors of age, height, weight, and BMI by diagnostic group are presented in Table 4.

Table 4: M (SE) of participants' age, height, weight and BMI as a function of diagnostic group:

	Anxiety Disorder n = 28	Mood Disorder n = 20	Control n = 23	*P*
Age (yrs)	57.9 (1.5)	58.9 (1.6)	59.6 (1.4)	.73
Height (cm)	166.4 (2.7)	168.7 (2.2)	171.3 (2.3)	.40
Weight (kg)	81.3 (3.2)	82.6 (3.5)	79.7 (2.4)	.82
BMI (kg/m^2)	29.5 (1.2)	29.0 (1.0)	27.5 (1.0)	.41

BMI = body mass index

Baseline Analyses

Demographics:

To assess whether participants differed in gender (% male), marital status (% married), living conditions (% living alone), employment status (% unemployed), and education history (% < 12 years of education) as a function of diagnostic group, a

series of Chi-square ($\chi 2$) analyses were conducted for Mood Disorder, Anxiety Disorder, and control patients. No group differences in were observed, with the exception that significantly more control patients than anxiety or mood disorder patients were male ($\chi 2$ (1,2)=7.53, $p<0.05$) . Proportions of patient demographic variables by diagnostic group are presented in Table 5.

Cardiac Risk Factors:

To assess whether participants differed in the proportion (%) with hypertension, cholesterol, diabetes, a positive family history of CAD, who currently smoked, and who currently consumed ≥ 3 alcoholic beverages per day as a function of diagnostic group, a series of Chi-square ($\chi 2$) analyses were conducted for Mood Disorder, Anxiety Disorder, and control patients. Significantly more anxiety disorder patients than mood disorder or control patients were current smokers ($\chi 2$ (1,2)=10.39, $p<0.01$) and consumed three or more alcoholic beverages per day ($\chi 2$ (1,2)=12.89, $p<0.01$). No other group differences in were observed. Proportions of cardiac risk factors by diagnostic group are presented in Table 5.

Cardiac Event History:

To assess whether participants differed in the proportion (%) with a history of myocardial infarction (MI), coronary artery bypass graft (CABG), or percutaneous transluminal coronary angioplasty (PTCA) as a function of diagnostic group, a series of Chi-square ($\chi 2$) analyses were conducted for Mood Disorder, Anxiety Disorder,

and control patients. No group differences in were observed. Proportions of cardiac events by diagnostic group are presented in Table 5.

Medication Profile:

To assess whether participants differed in the proportion (%) taking anti-ischemic medication (β-blockers, calcium-channel blockers, ACE-inhibitors), vasodilators (nitroglycerine), or aspirin (ASA) as a function of diagnostic group, a series of Chi-square ($\chi 2$) analyses were conducted for Mood Disorder, Anxiety Disorder, and control patients. No group differences in were observed. Proportions of cardiac medications by diagnostic group are presented in Table 5.

***Resting Stress Test Cardiovascular Values*:**

To assess whether there were baseline differences in resting (pre-exercise test) cardiovascular measures as a function of diagnostic group, a series of one-way ANOVAs was conducted for Mood Disorder, Anxiety Disorder, and control patients for the following cardiovascular measures: systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). No group differences in resting cardiovascular values were observed. Means and standard errors of baseline cardiovascular values by diagnostic group are presented in Table 5.

Table 5: Participants' demographics, cardiac risk factors, cardiac event history, medications, and resting cardiovascular values as a function of diagnostic group:

% (n)	Anxiety Disorder n = 28	Mood Disorder n = 20	Control n = 23	P
Demographics				
Gender (male)	71.4 (20)	80.0 (16)	100 (23)	**.02**
Marital status (married)	73.9 (17)	100 (16)	72.7 (16)	.07
Living alone	17.9 (5)	10.0 (2)	4.3 (1)	.31
Education (<12yrs)	32.1 (9)	50.0 (10)	34.8 (8)	.42
Employed	57.1 (16)	60.0 (12)	65.2 (15)	.84
Cardiac Risk Factors				
Hypertension	60.7 (17)	80.0 (16)	56.5 (13)	.23
Cholesterol	60.7 (17)	70.0 (14)	82.6 (19)	.23
Diabetes	10.7 (3)	30.0 (6)	26.1 (6)	.21
Family history CAD	78.6 (22)	78.9 (15)	65.2 (15)	.48
Smoker (current)	14.3 (4)	50.0 (10)	13.0 (3)	**.006**
≥3 alcoholic beverages/day	3.6 (1)	30.0 (6)	0 (0)	**.002**
Cardiac Event History				
MI	17.9 (5)	45.0 (9)	34.8 (8)	.12
CABG	28.6 (8)	30.0 (6)	21.7 (5)	.80
PTCA	32.1 (9)	60.0 (12)	43.5 (10)	.16
Medications				
Any anti-ischemic	85.0 (17)	78.6 (22)	73.9 (17)	.67
β-Blockers	50.0 (14)	55.0 (11)	56.5 (13)	.89
Ca-Channel Blockers	28.6 (8)	25.0 (5)	26.1 (6)	.96
ACE-inhibitors	32.1 (9)	40.0 (8)	43.5 (10)	.69
Vasodilators	42.9 (12)	45.0 (9)	47.8 (11)	.94
ASA	82.1 (23)	85.0 (17)	82.6 (19)	.96
M (SE) Resting Exercise Cardiovascular Values				
HR (bpm)	62.5 (1.9)	65.6 (2.0)	63.9 (1.8)	.54
SBP (mm Hg)	136.0 (3.4)	134.2 (4.6)	140.1 (4.6)	.61
DBP (mm Hg)	85.9 (1.9)	88.1 (4.3)	82.1 (2.6)	.36

CAD = coronary artery disease; MI = myocardial infarction; CABG = coronary artery bypass graft surgery; PTCA = percutaneous transluminal coronary angioplasty; Ca-Channel = calcium channel; ACE = angiotensin converting enzyme; ASA = acetylsalicylic acid (aspirin); HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Holter Analyses

A total of 21 ischemic episodes were recorded for 6 of the 71 patients assessed. Because so few patients exhibited transient ischemic episodes, there was insufficient power to make any meaningful comparisons between diagnostic groups. Thus, the differences reported below did not reach statistical significance. Nonetheless, a greater number of CAD patients with a comorbid anxiety disorder (4/28 or 14%) exhibited transient ischemic episodes relative to controls (2/23 or 9%). In addition, a greater number of episodes were recorded among patients with a comorbid anxiety disorder compared to controls. Only two of the 21 ischemic episodes occurred in control patients (mean = 1 episode each), while 19 episodes occurred in patients with a primary anxiety disorder (mean = 4.75 episodes each). There were no ischemic episodes exhibited by patients with a primary mood disorder. The mean total duration of ischemic episodes was 20 minutes in control patients and 127 minutes in anxiety disorder patients. All but three episodes (two in a control patient and one in an anxiety disorder patient) were asymptomatic (i.e., silent). Interestingly, diary analyses indicated that just under half (42%) of the ischemic episodes exhibited by anxiety disorder patients were preceded (within one hour of ischemia onset) by increases in mental stress (change in negative emotion) as compared to none of the episodes exhibited by control patients. In contrast, one of the two (50%) ischemic episodes exhibited by a control patient was preceded by physical exertion (exercise), compared to only 4 of the 19 (or 21%) of those exhibited by anxiety disorder patients. Four ischemic episodes exhibited by anxiety disorder patients were preceded by both mental and physical stress. A total of four episodes

(three in anxiety disorder patients and one in a control patient) were unrelated to either physical or mental stress (no identifiable cause). The number, percentage and duration of ischemic episodes, as well as descriptive data reported here are presented in Table 6.

Table 6: Summary of transient ischemic episode data as a function of diagnostic group:

	Anxiety Disorder n = 28	**Mood Disorder n = 20**	**Control n = 23**
Patients exhibiting ischemic episodes	4 (14%)	0	2 (9%)
Number of transient ischemic episodes	19	0	2
Mean (SD) duration of ischemic episodes (min)	127 (148)	0	20 (0)
Ischemic episodes preceded by physical stress	4/19 (21%)	0	1/2 (50%)
Ischemic episodes preceded by mental stress	8/19 (42%)	0	0
Ischemic episodes preceded by both physical & mental stress	4/19 (21%)	0	0
Ischemic episodes with no identifiable cause	3/19 (16%)	0	1/2 (50%)
Silent ischemic episodes	17/19 (90%)	0	2/2 (100%)

Although patients exhibited too few ischemic episodes to make a meaningful comparison between diagnostic groups, it is noteworthy that an analysis of diary entries indicated that significantly more patients with a primary mood disorder (70%, n=14/20) reported having at least one episode of chest pain or angina during the 48-hour Holter monitoring period compared to patients with a primary anxiety disorder (50%, n=14/28) and controls (30%, n=7/23). Patients with a primary mood disorder also reported significantly more episodes of chest pain (total = 89; mean = 4.45) compared to patients with a primary anxiety disorder (total = 49, mean = 1.75) and controls (total = 20; mean = 0.87). All but two (1%) chest pain reports were not

associated with ECG changes. These findings could not be attributed to the number of diary entries made by patients in each group, as the average number of diary entries was not significantly different between diagnostic groups. It is also noteworthy that five out the six patients who exhibited ischemia were taking ant-ischemic medication (three were taking β-blockers, one Ca-Channel blockers, and one ACE inhibitors). Thus, the majority (83%) or five out of six patients had ischemia despite taking anti-ischemic medication. The proportion of patients in each group reporting at least one episode of chest pain is presented in Figure 1. Means and standard errors of the number of chest pain episodes reported by diagnostic group is presented in Figure 2. The number of diary entries made by each diagnostic group is presented in Figures 3.

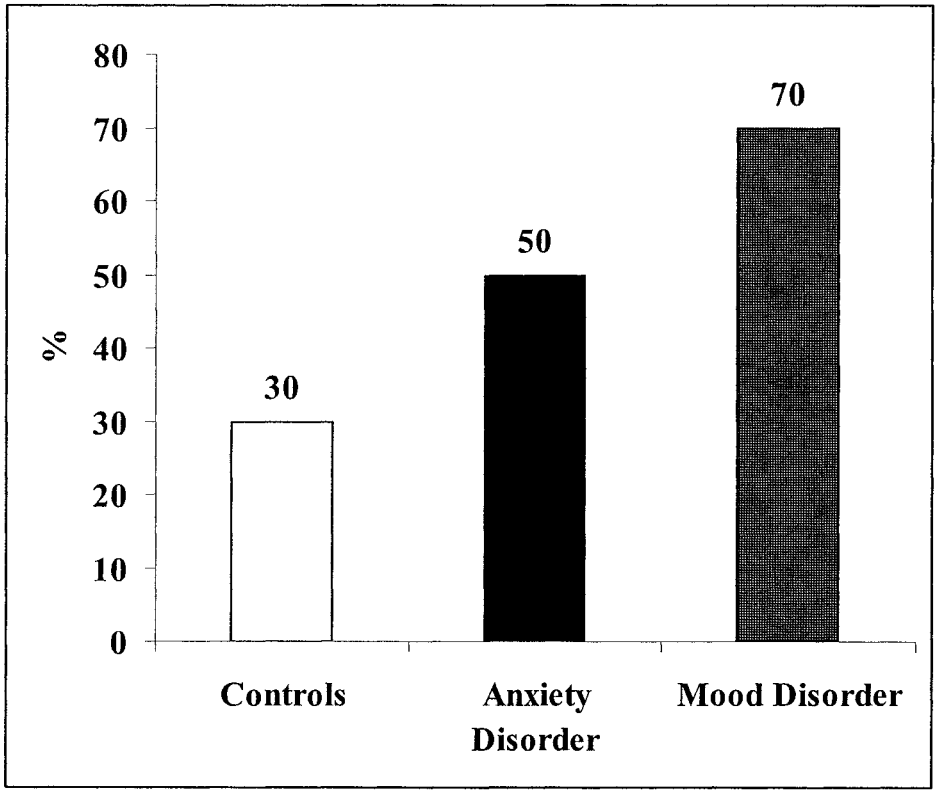

Figure 1: Proportion (%) of patients in each diagnostic group reporting at least one episode of chest pain

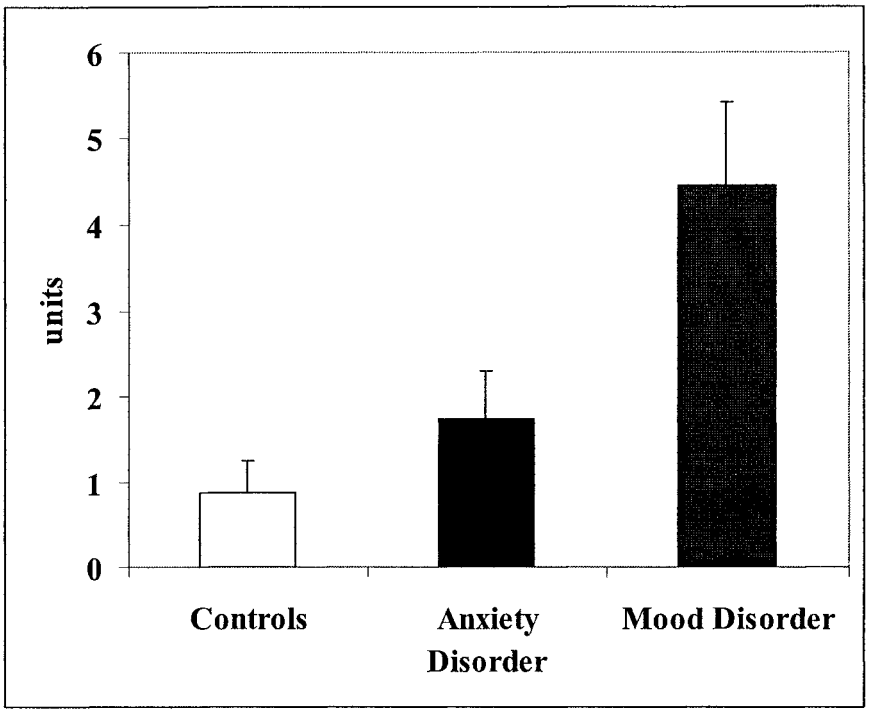

Figure 2: **M (SE) of the number of chest pain episodes reported by diagnostic group**

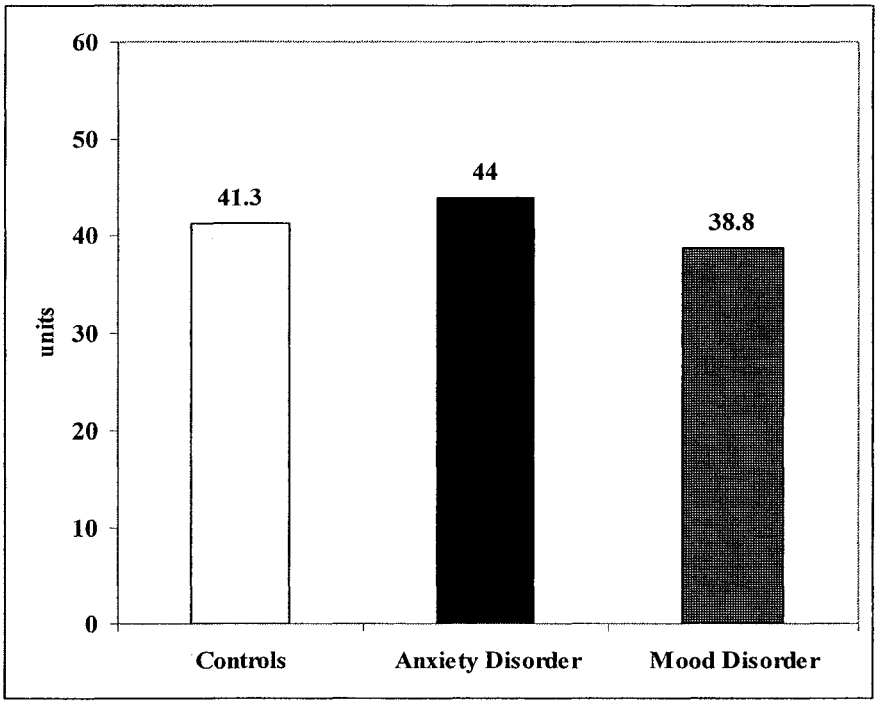

Figure 3: **Mean number of diary entries made by diagnostic group**

Study Objective 2 :

HRV in PD versus Control Patients with CAD

Participant Characteristics

To assess whether participants differed in age, height, weight, and body mass index (BMI) as a function of diagnostic group, a series of one-way analyses of variance (ANOVAs) were conducted for PD and control patients using mean age, height, weight, and BMI values. No group differences in were observed. Means and standard errors of age, height, weight, and BMI by diagnostic group are presented in Table 7.

Table 7: M (SE) of participants' age, height, weight and BMI as a function of diagnostic group (panic disorder versus controls):

	Panic Disorder n = 20	Control n = 22	p
Age (yrs)	55.9 (1.8)	59.4 (1.5)	.14
Height (cm)	170.7 (2.4)	170.9 (2.4)	.96
Weight (kg)	85.5 (3.5)	79.3 (2.5)	.16
BMI (kg/m²)	29.4 (1.0)	27.5 (1.0)	.19

BMI = body mass index

Baseline Analyses

Demographics:

To assess whether participants differed in gender (% male), marital status (% married), living conditions (% living alone), employment status (% unemployed), and education history (% < 12 years of education) as a function of diagnostic group, a series of Chi-square ($\chi 2$) analyses were conducted for PD and control patients. No

group differences in were observed. Proportions of patient demographic variables by diagnostic group are presented in Table 8.

Cardiac Risk Factors:

To assess whether participants differed in the proportion (%) with hypertension, cholesterol, diabetes, a positive family history of CAD, who currently smoked, and who currently consumed ≥ 3 alcoholic beverages per day as a function of diagnostic group, a series of Chi-square ($\chi 2$) analyses were conducted for PD and control patients. No group differences in were observed. Proportions of cardiac risk factors by diagnostic group are presented in Table 8.

Cardiac Event History:

To assess whether participants differed in the proportion (%) with a history of myocardial infarction (MI), coronary artery bypass graft (CABG), or percutaneous transluminal coronary angioplasty (PTCA) as a function of diagnostic group, a series of Chi-square ($\chi 2$) analyses were conducted for PD and control patients. No group differences in were observed. Proportions of cardiac event(s) by diagnostic group are presented in Table 8.

Table 8: Participants' demographics, cardiac risk factors, cardiac event history, medications, and resting cardiovascular values in panic disorder patients and controls:

% (n)	Panic Disorder n = 20	Control n = 22	p
Demographics			
Gender (male)	80.0 (16)	100.0 (22)	**.04**
Marital status (married)	73.3 (11)	76.2 (16)	.57
Living alone	25.0 (5)	.5 (1)	.07
Education (<12yrs)	50.0 (10)	31.8 (7)	.19
Employed	60.0 (12)	63.6 (14)	.53
Cardiac Risk Factors			
Hypertension	65.0 (13)	54.5 (12)	.35
Cholesterol	70.0 (14)	81.8 (18)	.30
Diabetes	10.0 (2)	27.3 (6)	.15
Family history CAD	80.0 (16)	68.2 (15)	.30
Smoker (current)	25.0 (5)	13.6 (3)	.29
≥ 3 alcoholic beverages/day	10.0 (2)	0 (0)	.22
Cardiac Event History			
MI	33.3 (6)	34.6 (8)	.55
CABG	38.9 (7)	22.7 (5)	.22
PTCA	38.9 (7)	40.9 (9)	.58
Medications			
Any anti-ischemic	80.0 (16)	72.7 (16)	.43
β-Blockers	55.0 (11)	54.5 (12)	.61
Ca-Channel Blockers	35.0 (7)	22.7 (5)	.30
ACE-inhibitors	35.0 (7)	40.9 (9)	.47
Vasodilators	40.0 (8)	50.0 (11)	.37
ASA	75.0 (15)	81.8 (18)	.44
M (SE) Resting Exercise Cardiovascular Values			
HR (bpm)	66.2 (2.5)	63.9 (1.8)	.45
SBP (mm Hg)	137.1 (4.7)	138.7 (4.6)	.81
DBP (mm Hg)	87.6 (2.2)	82.2 (2.8)	.14

CAD = coronary artery disease; MI = myocardial infarction; CABG = coronary artery bypass graft surgery; PTCA = percutaneous transluminal coronary angioplasty; Ca-Channel = calcium channel; ACE = angiotensin converting enzyme; ASA = acetylsalicylic acid (aspirin); HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Medication Profile:

To assess whether participants differed in the proportion (%) taking anti-ischemic medication (β-blockers, calcium-channel blockers, ACE-inhibitors), vasodilators (nitroglycerine), or aspirin (ASA) as a function of diagnostic group, a series of Chi-square ($\chi 2$) analyses were conducted for PD and control patients. No group differences in were observed. Proportions of cardiac medication by diagnostic group are presented in Table 8.

***Resting Stress Test Cardiovascular Values*:**

To assess whether there were baseline differences in resting (pre-exercise test) cardiovascular measures as a function of diagnostic group, a series of one-way ANOVAs was conducted for PD and control patients for the following cardiovascular measures: resting systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). No group differences in resting cardiovascular values were observed. Means and standard errors of baseline cardiovascular values by diagnostic group are presented in Table 8.

HRV Analyses

To assess the relationship between diagnostic group (panic disorder versus controls) and HRV, a series of one-way ANOVAs were conducted for time (ASDNN, SDANN, SDNN) and frequency (HF, LF, VLF, ULF, TP, LF:HF ratio) domains indices of HRV. The analysis yielded a significant main effect for the LF:HF ratio ($F(1,40) = 5.35$, $p < 0.05$) indicating a significantly lower LF:HF ratio for panic

disorder patients as compared to controls. This suggests greater parasympathetic control of heart rate (or less sympathetic modulation of heart rate) among panic disorder patients with CAD compared to controls. No other main effects were observed. Means and standard errors of time and frequency domain indices of HRV by diagnostic group are presented in Table 9. The significant main effect for the LF:HF ratio is presented in Figure 4.

Table 9: M (SE) of time and frequency domain indices of heart rate variability for panic disorder patients and controls:

	Panic Disorder n = 20	**Control n = 22**	**p**
Time domain indices			
ASDNN (ms)	48.1 (2.6)	51.2 (4.4)	.56
SDANN (ms)	103.7 (6.1)	111.1 (6.9)	.43
SDNN (ms)	117.5 (6.2)	125.6 (7.8)	.43
Frequency domain indices			
HF power (ms^2)	126.2 (18.1)	106.2 (20.9)	.48
LF power (ms^2)	326.6 (45.6)	388.6 (72.2)	.48
VLF power (ms^2)	729.1 (88.1)	987.4 (192.7)	.24
ULF power (ms^2)	318.9 (40.6)	497.4 (109.3)	.14
Total power (ms^2)	1511.0 (173.9)	1788.9 (372.0)	.52
LF:HF ratio	2.8 (0.26)	4.1 (0.47)	**.03**

In order to rule out the effects of potential confounding baseline characteristics which are known to influence HRV, a series of one-way ANCOVAs were conducted using current smoking, diabetes, and history of CABG surgery as covariates. Results showed that the significant main effect for the LF:HF ratio ($F(1,37) = 6.19$, $p < 0.05$) indicating a significantly lower LF:HF ratio among panic disorder patients remained significant, even after controlling for important confounds. Thus, the significantly lower LF:HF ratio observed among panic disorder patients

relative to controls cannot be explained by greater smoking, comorbid diabetes, or history of CABG surgery. Means and standard errors of time and frequency domain indices of HRV by diagnostic group are presented in Table 10.

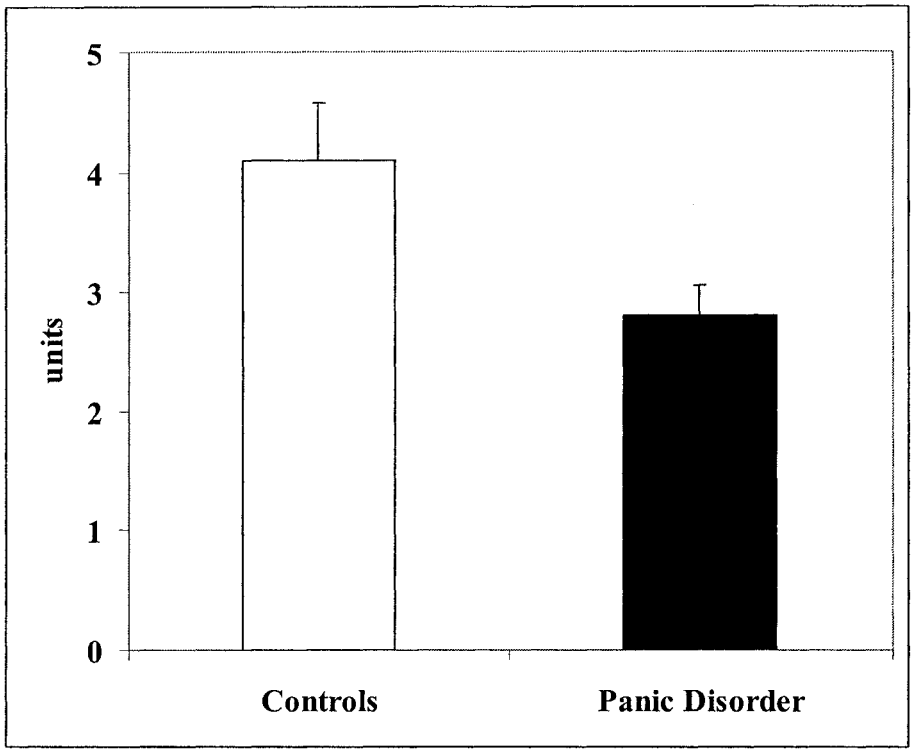

Figure 4: M (SE) of LF:HF ratio in panic disorder patients and controls

For comparison, a series of one-way ANOVAs were conducted to assess the relationship between major depressive disorder (MDD) and time and frequency domain HRV indices. Interestingly, no significant associations were observed. Means and standard errors of time and frequency domain HRV indices for patients with a primary diagnosis of MDD are presented in Table 11. Thus, results suggest that parasympathetic control of heart rate may be specific to panic disorder relative to MDD.

Table 10: M (SE) of time and frequency domain indices of heart rate variability for panic disorder patients and controls controlling for current smoking, diabetes, and history of coronary artery bypass graft surgery:

	Panic Disorder n = 20	Control n = 22	p
Time domain indices			
ASDNN (ms)	48.1 (2.6)	51.2 (4.4)	.51
Smoker			.61
Diabetes			.08
CABG			.16
SDANN (ms)	103.7 (6.1)	111.1 (6.9)	.14
Smoker			.17
Diabetes			**.04**
CABG			.51
SDNN (ms)	117.5 (6.2)	125.6 (7.8)	.18
Smoker			.35
Diabetes			**.05**
CABG			.43
Frequency domain indices			
HF power (ms^2)	126.2 (18.1)	106.2 (20.9)	.49
Smoker			.37
Diabetes			.07
CABG			.31
LF power (ms^2)	326.6 (45.6)	388.6 (72.2)	.38
Smoker			.99
Diabetes			**.05**
CABG			.09
VLF power (ms^2)	729.1 (88.1)	987.4 (192.7)	.25
Smoker			.47
Diabetes			.17
CABG			.15
ULF power (ms^2)	318.9 (40.6)	497.4 (109.3)	.17
Smoker			.27
Diabetes			.27
CABG			.23
Total power (ms^2)	1511.0 (173.9)	1788.9 (372.0)	.49
Smoker			.60
Diabetes			.19
CABG			.26
LF/HF ratio	2.8 (0.26)	4.1 (0.47)	**.02**
Smoker			.12
Diabetes			.62
CABG			.61

CABG = coronary artery bypass graft

Table 11: M (SE) of time and frequency domain indices of heart rate variability for patients with major depressive disorder and controls:

	MDD n = 26	Control n = 22	p
Time domain indices			
ASDNN (ms)	46.0 (2.2)	51.2 (4.4)	.28
SDANN (ms)	101.1 (4.1)	111.1 (6.9)	.20
SDNN (ms)	113.9 (20.1)	125.6 (7.8)	.17
Frequency domain indices			
HF power (ms^2)	100.7 (15.7)	106.2 (20.9)	.83
LF power (ms^2)	311.7 (38.8)	388.6 (72.2)	.33
VLF power (ms^2)	675.7 (64.5)	987.4 (192.7)	.11
ULF power (ms^2)	298.3 (30.3)	497.4 (109.3)	.07
Total power (ms^2)	1386.5 (137.0)	1788.9 (372.0)	.27
LF/HF ratio	3.77 (0.50)	4.14 (0.47)	.61

Study Objective 3:

HRV in Hi AS versus Lo AS Patients

When participants were divided into Hi and Lo AS groups based on cutoff scores of < 11 (Lo AS) and ≥ 11 (Hi AS), a total of 21 participants were in the Lo AS group (mean ASI score = 5.3, SD = 3.0) and a total of 50 participants were in the Hi AS group (mean ASI score = 22.8, SD = 9.5). This suggests that AS groups were adequately distinct.

Participant Characteristics

To assess whether participants differed in age, height, weight, and body mass index (BMI) as a function of AS group, a series of one-way analyses of variance (ANOVAs) were conducted for Hi and Lo AS patients using mean age, height, weight, and BMI values. Participants in the Hi AS group were significantly taller ($F(1,62) = 5.32$, $p < 0.05$) and had a significantly higher BMI ($F(1,62) = 4.89$, p

<0.05) compared to Lo AS participants. The higher BMI observed in Hi AS participants may be due to the fact that Hi AS participants were also significantly taller. No other group differences in were observed. Means and standard errors of age, height, weight, and BMI by AS group are presented in Table 12.

Table 12: M (SE) of participants' age, height, weight and BMI as a function of anxiety sensitivity group:

	Lo AS n = 21	Hi AS n = 50	p
Age (yrs)	57.6 (1.7)	59.2 (1.0)	.41
Height (cm)	173.7 (1.1)	166.5 (1.9)	**.02**
Weight (kg)	79.8 (2.7)	81.7 (2.3)	.64
BMI (kg/m²)	26.6 (.84)	29.5 (.78)	**.03**

BMI = body mass index

Baseline Analyses

Demographics:

To assess whether participants differed in gender (% male), marital status (% married), living conditions (% living alone), employment status (% unemployed), and education history (% < 12 years of education) as a function of AS, a series of Chi-square ($\chi 2$) analyses were conducted for Hi and Lo AS patients. No group differences in were observed. Proportions of patient demographic variables by diagnostic group are presented in Table 13.

Table 13: Participants' demographics, cardiac risk factors, cardiac event history, medications, and resting cardiovascular values in Hi versus Lo anxiety sensitivity (AS) patients:

% (n)	Lo AS n = 21	Hi AS n = 50	p
Demographics			
Gender (male)	95.2 (21)	78.0 (39)	.07
Marital status (married)	80.0 (16)	80.5 (33)	.61
Living alone	9.5 (2)	12.0 (6)	.56
Education (<12yrs)	28.6 (6)	42.0 (21)	.21
Employed	66.7 (14)	58.0 (29)	.34
Cardiac Risk Factors			
Hypertension	52.4 (11)	70.0 (35)	.13
Cholesterol	76.2 (16)	68.0 (34)	.35
Diabetes	14.3 (3)	24.0 (12)	.28
Family history CAD	71.4 (15)	75.5 (37)	.47
Smoker (current)	9.5 (2)	30.0 (15)	.06
≥3 alcoholic beverages/day	0.0 (0)	14.0 (7)	.08
Cardiac Event History			
MI	28.6 (6)	32.0 (16)	.50
CABG	14.3 (3)	32.0 (16)	.10
PTCA	42.9 (9)	44.0 (22)	.57
Medications			
Any anti-ischemic	66.7 (14)	84.0 (42)	.10
β-Blockers	52.4 (11)	54.0 (27)	.55
Ca-Channel Blockers	23.8 (5)	28.0 (14)	.48
ACE-inhibitors	33.3 (7)	40.0 (20)	.40
Vasodilators	28.6 (6)	52.0 (26)	.06
ASA	85.7 (18)	82.0 (41)	.50
M (SE) Resting Exercise Cardiovascular Values			
HR (bpm)	64.3 (2.1)	63.6 (1.3)	.77
SBP (mmHg)	136.3 (5.3)	137.0 (2.6)	.89
DBP (mmHg)	84.9 (4.6)	85.4 (1.4)	.88

CAD = coronary artery disease; MI = myocardial infarction; CABG = coronary artery bypass graft surgery; PTCA = percutaneous transluminal coronary angioplasty; Ca-Channel = calcium channel; ACE = angiotensin converting enzyme; ASA = acetylsalicylic acid (aspirin); HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Cardiac Risk Factors:

To assess whether participants differed in the proportion (%) with hypertension, cholesterol, diabetes, a positive family history of CAD, who currently smoked, and who currently consumed ≥ 3 alcoholic beverages per day as a function of AS group, a series of Chi-square ($\chi 2$) analyses were conducted for Hi and Lo AS patients. No group differences in were observed. Proportions of cardiac risk factors by diagnostic group are presented in Table 13.

Cardiac Event History:

To assess whether participants differed in the proportion (%) with a history of myocardial infarction (MI), coronary artery bypass graft (CABG), or percutaneous transluminal coronary angioplasty (PTCA) as a function of AS, a series of Chi-square ($\chi 2$) analyses were conducted for Hi and Lo AS patients. No group differences in were observed. Proportions of cardiac event(s) by diagnostic group are presented in Table 13.

Medication Profile:

To assess whether participants differed in the proportion (%) taking anti-ischemic medication (β-blockers, calcium-channel blockers, ACE-inhibitors), vasodilators (nitroglycerine), or aspirin (ASA) as a function of AS, a series of Chi-square ($\chi 2$) analyses were conducted for Hi and Lo AS patients. No group differences in were observed. Proportions of cardiac medication by diagnostic group are presented in Table 13.

***Resting Stress Test Cardiovascular Values*:**

To assess whether there were baseline differences in resting (pre-exercise test) cardiovascular measures as a function of AS, a series of one-way ANOVAs was conducted for Hi and Lo AS patients for the following cardiovascular measures: resting systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). No group differences in resting cardiovascular values were observed. Means and standard errors of baseline cardiovascular values by diagnostic group are presented in Table 13.

HRV Analyses

To assess the relationship between anxiety sensitivity group (Hi versus Lo) and HRV, a series of one-way ANOVAs were conducted for time (ASDNN, SDANN, SDNN) and frequency (HF, LF, VLF, ULF, TP, LF:HF ratio) domains indices of HRV. The analysis yielded significant main effects for the following time domain HRV indices: ASDNN ($F(1,69) = 4.73$, $p < 0.05$), SDANN ($F(1,69) = 4.04$, $p < 0.05$), and SDNN ($F(1,69) = 4.74$, $p < 0.05$), and for the following frequency domain HRV indices: LF ($F(1,69) = 6.22$, $p < 0.01$), VLF ($F(1,69) = 6.98$, $p < 0.01$), ULF ($F(1,69) = 7.8$, $p < 0.01$), and TP ($F(1,69) = 4.78$, $p < 0.05$), indicating significantly lower ASDNN, SDANN, SDNN, LF power, VLF power, ULF power, and TP among Hi AS patients compared to Loi AS patients. Though not significant, means were in the expected direction indicating lower HF power in Hi versus Lo AS patients. These findings suggest that a general tendency to be sensitive to anxiety symptoms is associated with significant reductions in HRV, reflecting abnormalities in cardiac

autonomic tone. No other main effects were observed. Means and standard errors of time and frequency domain indices of HRV by AS group are presented in Table 14. The significant main effects for ASDNN, SDANN, and SDNN are presented in Figures 5-7. The significant main effects for LF, VLF, ULF, and TP are presented in Figures 8-11.

Table 14: M (SE) of time and frequency domain indices of heart rate variability for Hi and Lo anxiety sensitivity patients:

	Lo AS n = 21	**Hi AS n = 50**	**p**
Time domain indices			
ASDNN (ms)	54.7 (4.5)	46.1 (12.4)	**.03**
SDANN (ms)	119.9 (7.5)	102.9 (4.5)	**.05**
SDNN (ms)	134.3 (8.2)	115.7 (4.4)	**.03**
Frequency domain indices			
HF power (ms^2)	128.4 (21.9)	105.2 (11.9)	.32
LF power (ms^2)	468.3 (73.8)	296.1 (32.4)	**.01**
VLF power (ms^2)	1082.4 (197.7)	684.5 (52.4)	**.01**
ULF power (ms^2)	537.8 (112.1)	312.8 (23.5)	**.007**
Total power (ms^2)	2045.9 (377.2)	1390.7 (114.0)	**.03**
LF:HF ratio	4.1 (0.58)	3.3 (0.26)	.13

In order to rule out the effects of potential confounding baseline characteristics which are known to influence HRV, a series of one-way ANCOVAs were conducted using current smoking, diabetes, and history of CABG surgery as covariates. Results showed that the significant main effects for LF power ($F(1,66) = 3.72$, $p < 0.05$), VLF power ($F(1,66) = 4.06$, $p < 0.05$), and ULF power ($F(1,66) = 4.67$, $p < 0.05$) indicating significantly lower LF, VLF, and ULF power among Hi AS patients remained significant, even after controlling for important confounds. Thus, the significantly lower LF, VLF and ULF power observed among Hi AS patients

relative to Lo AS patients cannot be explained by greater smoking, comorbid diabetes, or history of CABG surgery. However, the significant main effects for ASDNN, SDANN, SDNN, and TP were no longer significant after controlling for smoking, comorbid diabetes, and history of CABG (all p's >0.05). Means and standard errors of time and frequency domain indices of HRV by AS group are presented in Table 15.

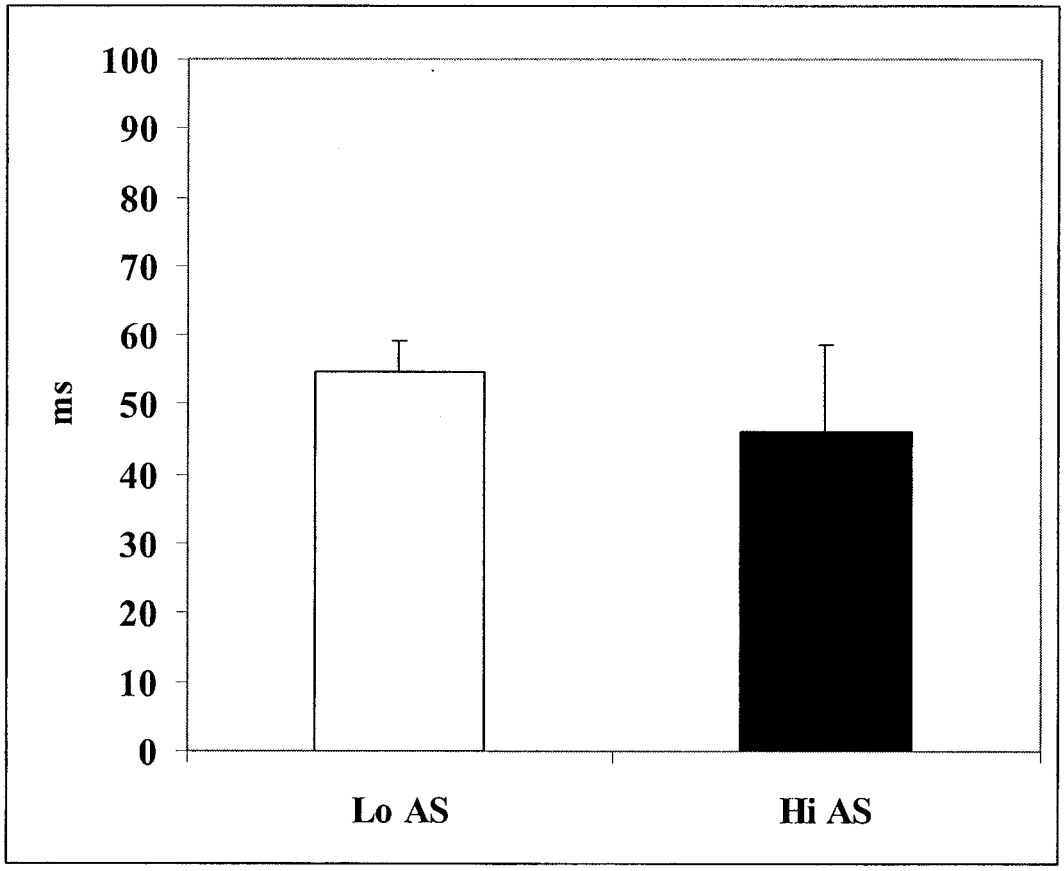

Figure 5: M (SE) of ASDNN in Hi versus Lo anxiety sensitivity (AS) patients

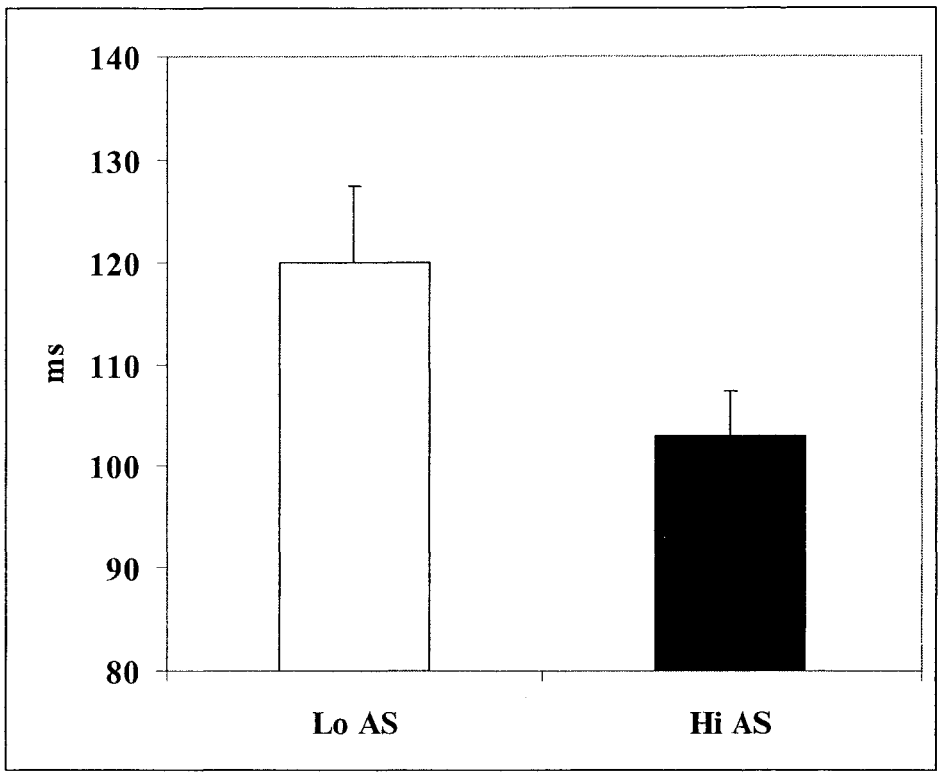

Figure 6: M (SE) of SDANN in Hi versus Lo anxiety sensitivity (AS) patients

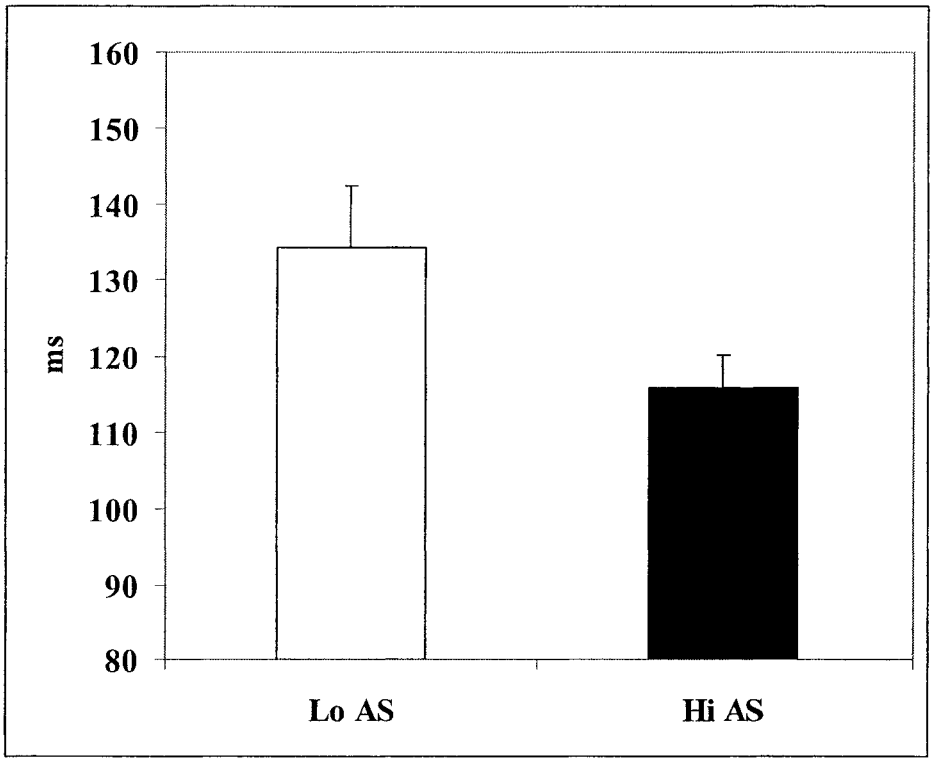

Figure 7: M (SE) of SDNN in Hi versus Lo anxiety sensitivity (AS) patients

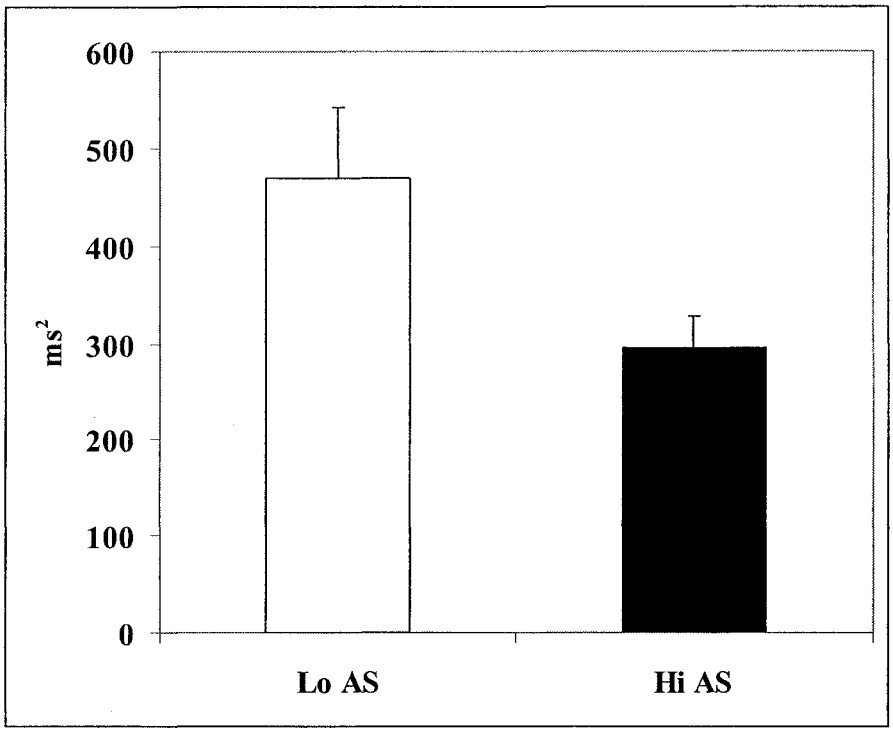

Figure 8: **Means and standard deviations of LF power in Hi versus Lo anxiety sensitivity (AS) patients**

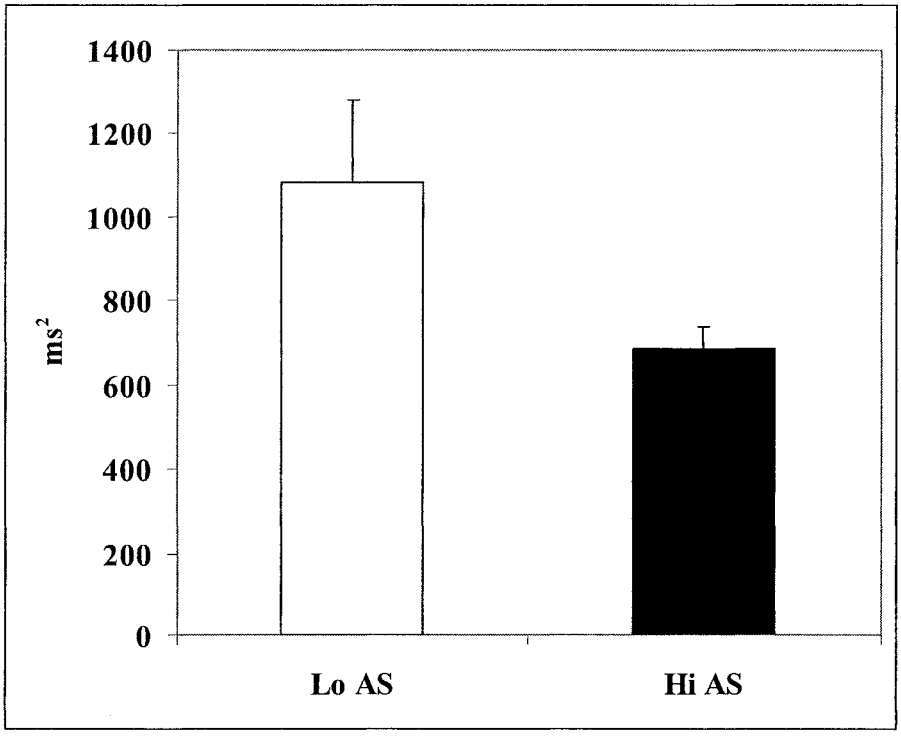

Figure 9: **M (SE) of VLF power in Hi versus Lo anxiety sensitivity (AS) patients**

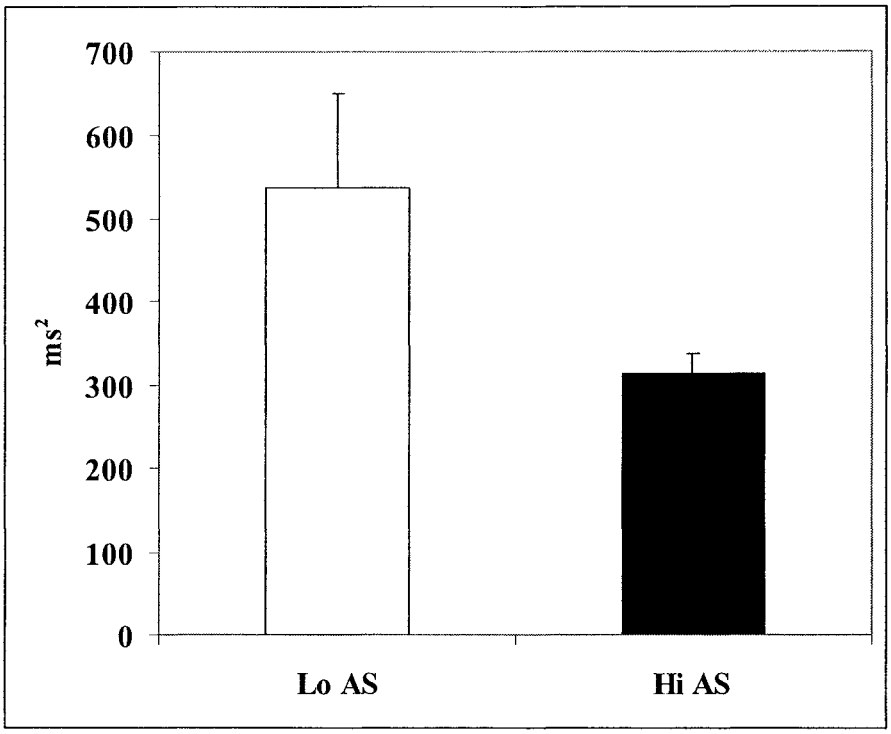

Figure 10: M (SE) of ULF power in Hi versus Lo anxiety sensitivity (AS) patients

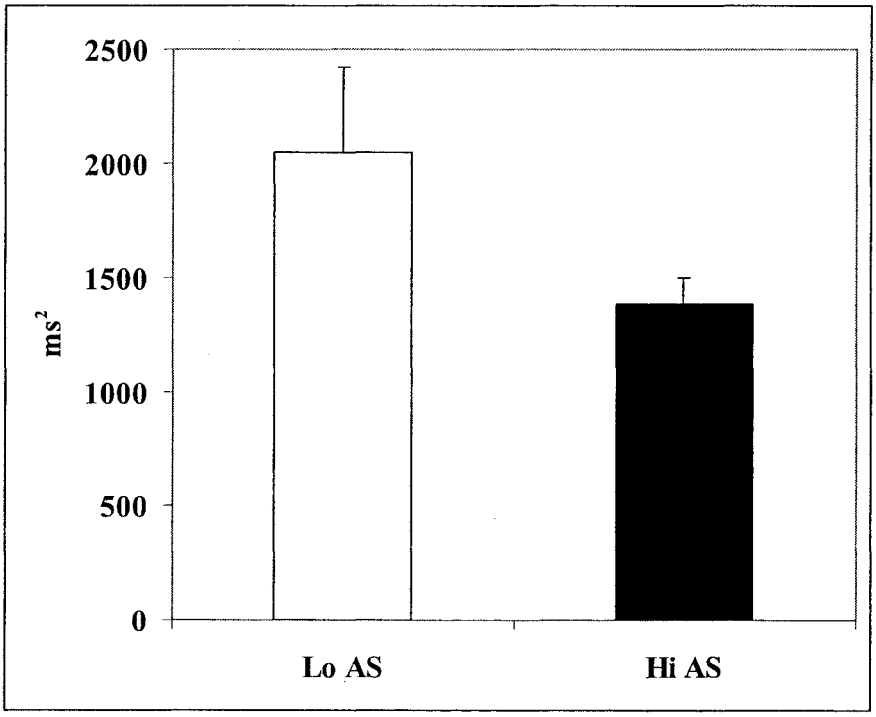

Figure 11: M (SE) of Total power in Hi versus Lo anxiety sensitivity (AS) patients

Table 15: M (SE) of time and frequency domain indices of heart rate variability for Hi and Lo anxiety sensitivity (AS) patients controlling for current smoking, diabetes and history of coronary artery bypass graft surgery:

	Lo AS n = 21	Hi AS n = 50	p
Time domain indices			
ASDNN (ms)	54.7 (4.5)	46.1 (12.4)	.13
Smoker			.53
Diabetes			**.005**
CABG			**.05**
SDANN (ms)	119.9 (7.5)	102.9 (4.5)	.08
Smoker			.70
Diabetes			**.002**
CABG			.33
SDNN (ms)	134.3 (8.2)	115.7 (4.4)	.07
Smoker			.89
Diabetes			**.001**
CABG			.22
Frequency domain indices			
HF power (ms^2)	128.4 (21.9)	105.2 (11.9)	.74
Smoker			.52
Diabetes			**.009**
CABG			.13
LF power (ms^2)	468.3 (73.8)	296.1 (32.4)	**.05**
Smoker			.72
Diabetes			**.004**
CABG			.06
VLF power (ms^2)	1082.4 (197.7)	684.5 (52.4)	**.05**
Smoker			.44
Diabetes			**.03**
CABG			.07
ULF power (ms^2)	537.8 (112.1)	312.8 (23.5)	**.03**
Smoker			.25
Diabetes			.08
CABG			.12
Total power (ms^2)	2045.9 (377.2)	1390.7 (114.0)	.11
Smoker			.55
Diabetes			**.03**
CABG			.12
LF/HF ratio	4.1 (0.58)	3.3 (0.26)	.09
Smoker			.76
Diabetes			.59
CABG			.95

CABG = coronary artery bypass graft

For comparison, a series of one-way ANOVAs were conducted to assess the relationship between the three major diagnostic groups in this study (primary anxiety disorder, primary mood disorder, controls) and time and frequency domain HRV indices. Although 52% (n=26) of the Hi AS group had a primary anxiety disorder and 32% (n=16) had a primary mood disorder, no significant associations were observed between having an anxiety or mood disorder per se and reduced HRV, suggesting that trait AS may be more important to HRV than syndromal diagnostic categories. Means and standard errors of time and frequency domain HRV indices for patients in each diagnostic group are presented in Table 16.

Table 16: M (SE) of time and frequency domain indices of heart rate variability for mood disorder, anxiety disorder, and control patients:

	Mood Disorder n = 20	**Anxiety Disorder n = 28**	**Control n = 23**	**p**
Time domain indices				
ASDNN (ms)	45.7 (2.8)	49.5 (2.3)	50.3 (4.3)	.60
SDANN (ms)	102.2 (4.0)	110.9 (7.9)	109.3 (6.8)	.66
SDNN (ms)	114.7 (4.3)	124.0 (7.4)	123.5 (7.8)	.60
Frequency domain indices				
HF power (ms^2)	94.6 (16.2)	130.3 (17.6)	105.1 (20.0)	.36
LF power (ms^2)	307.6 (47.7)	352.0 (49.9)	375.3 (70.3)	.72
VLF power (ms^2)	682.6 (79.8)	762.7 (77.0)	954.2 (187.1)	.31
ULF power (ms^2)	299.7 (37.3)	353.2 (32.7)	480.7 (105.8)	.16
Total power (ms^2)	1384.5 (166.0)	1605.5 (165.3)	1732.9 (359.9)	.63
LF:HF ratio	3.78 (0.62)	3.04 (0.25)	3.99 (0.47)	.25

In order to assess the relative significance of AS as compared to other psychological variables, a series of one-way ANOVAs were conducted to assess the relationship between trait hostility (CMHO), depression (BDI), trait anger (STAXI) and state and trait anxiety (STAI) and time and frequency domain HRV indices using

median splits of questionnaire scores for each variable. Interestingly, no significant associations were observed. These findings also suggest that trait AS in particular may be more important for HRV than other psychological trait variables like hostility, trait anxiety, and trait anger. Means and standard errors of time and frequency domain HRV indices for patients with hi versus lo hostility, depression, trait anger and state and trait anxiety are presented in Tables 17-21.

Table 17: M (SE)of time and frequency domain indices of heart rate variability for patients with hi and lo Cook Medley Hostility (CMHO) Inventory scores:

	Lo CMHO n = 34	**Hi CMHO n = 33**	**p**
CMHO score	16.4	27.1	
Time domain indices			
ASDNN (ms)	46.6 (2.4)	50.5 (2.9)	.31
SDANN (ms)	107.0 (5.4)	106.5 (5.6)	.95
SDNN (ms)	119.8 (5.3)	120.7 (5.9)	.90
Frequency domain indices			
HF power (ms^2)	105.5 (15.6)	114.7 (13.7)	.66
LF power (ms^2)	309.9 (42.8)	375.1 (45.6)	.30
VLF power (ms^2)	737.5 (79.2)	863.0 (126.2)	.40
ULF power (ms^2)	363.7 (55.9)	393.6 (58.9)	.71
Total power (ms^2)	1393.2 (167.7)	1752.5 (230.9)	.21
LF:HF ratio	3.47 (0.34)	3.74 (0.41)	.62

Table 18: M (SE)of time and frequency domain indices of heart rate variability for patients with hi and lo Beck Depression Inventory (BDI) scores:

	Lo BDI n = 35	Hi BDI n = 36	p
BDI Score	3.4	20.6	
Time domain indices			
ASDNN (ms)	50.7 (3.0)	46.7 (2.2)	.28
SDANN (ms)	114.0 (6.2)	102.0 (4.8)	.13
SDNN (ms)	127.6 (6.4)	115.1 (4.9)	.12
Frequency domain indices			
HF power (ms^2)	116.9 (15.2)	107.4 (14.9)	.66
LF power (ms^2)	379.9 (60.0)	315.1 (41.1)	.33
VLF power (ms^2)	901.3 (127.9)	705.9 (65.0)	.17
ULF power (ms^2)	438.2 (71.1)	322.3 (29.9)	.13
Total power (ms^2)	1722.1 (244.6)	1450.8 (142.2)	.34
LF:HF ratio	3.65 (0.34)	3.47 (0.38)	.72

Table 19: M (SE) of time and frequency domain indices of heart rate variability for patients with hi and lo trait anger (STAXI) scores:

	Lo Trait Anger n = 31	Hi Trait Anger n = 35	p
Trait Anger score	23.1	37.8	
Time domain indices			
ASDNN (ms)	50.2 (3.3)	46.4 (2.0)	.32
SDANN (ms)	110.5 (5.9)	103.4 (5.2)	.37
SDNN (ms)	124.2 (6.3)	116.3 (5.1)	.33
Frequency domain indices			
HF power (ms^2)	116.7 (16.3)	102.9 (13.6)	.51
LF power (ms^2)	361.5 (53.2)	317.7 (36.6)	.49
VLF power (ms^2)	899.2 (142.1)	688.5 (58.0)	.16
ULF power (ms^2)	441.3 (79.8)	308.9 (25.0)	.10
Total power (ms^2)	1683.4 (271.1)	1423.7 (122.6)	.37
LF:HF ratio	3.62 (0.38)	3.58 (0.39)	.92

Table 20: M (SE) of time and frequency domain indices of heart rate variability for patients with hi and lo state anxiety (STAI) scores:

	Lo State Anxiety n = 27	Hi State Anxiety n = 32	p
State Anxiety score	25.1	43.5	
Time domain indices			
ASDNN (ms)	49.6 (3.1)	48.4 (2.5)	.77
SDANN (ms)	107.5 (7.3)	109.1 (4.8)	.86
SDNN (ms)	121.0 (7.5)	122.4 (4.8)	.88
Frequency domain indices			
HF power (ms^2)	112.0 (15.4)	109.6 (16.6)	.92
LF power (ms^2)	339.9 (48.7)	362.2 (43.1)	.73
VLF power (ms^2)	852.2 (142.3)	783.8 (84.3)	.67
ULF power (ms^2)	430.6 (86.0)	340.3 (36.3)	.31
Total power (ms^2)	1601.6 (262.7)	1577.3 (175.6)	.94
LF:HF ratio	3.55 (0.40)	3.98 (0.41)	.46

Table 21: M (SE) of time and frequency domain indices of heart rate variability for patients with hi and lo trait anxiety (STAI) scores:

	Lo Trait Anxiety n = 30	Hi Trait Anxiety n = 31	p
Trait Anxiety score	28.7	49.0	
Time domain indices			
ASDNN (ms)	50.5 (3.2)	46.5 (2.1)	.30
SDANN (ms)	111.9 (7.1)	103.7 (4.1)	.32
SDNN (ms)	125.1 (7.2)	116.9 (4.2)	.33
Frequency domain indices			
HF power (ms^2)	113.1 (15.1)	104.5 (16.3)	.70
LF power (ms^2)	355.9 (48.9)	330.2 (41.4)	.67
LF power (ms^2)	900.3 (141.2)	702.3 (64.3)	.20
ULF power (ms^2)	449.0 (82.3)	303.1 (22.8)	.09
Total power (ms^2)	1678.5 (268.6)	1440.1 (135.9)	.43
LF:HF ratio	3.71 (0.40)	3.72 (0.41)	.98

DISCUSSION

There is considerable evidence linking mood and anxiety disorders and negative emotions to increased CAD risk, morbidity and mortality. However, research on the mechanisms that may be mediating this association is relatively immature. Mental stress-induced myocardial ischemia and dysregulation of the autonomic nervous system (ANS) are two mechanisms which have been proposed to link mood and anxiety disorders to CAD risk, morbidity and mortality. The present study sought to further explore this proposed association by evaluating the extent to which CAD patients with mood and anxiety disorders exhibit mental stress-induced ischemia during daily life, and the extent to which CAD patients with anxiety sensitivity (a trait variable underlying both mood and anxiety syndromes) is related to dysregulated cardiac autonomic tone (reduced HRV).

Mental Stress-Induced Myocardial Ischemia

Mental stress studies to date suggest that negative emotions are potent triggers of myocardial ischemia, both in the lab and during daily life. There is also evidence suggesting that panic attacks may also confer risk for myocardial ischemia in PD patients with documented CAD. Because patients with mood and/or anxiety disorders by definition experience frequent daily episodes of emotional distress (e.g., anger, fear, sadness, panic), this first objective of the present study was to examine the extent to which CAD patients with comorbid mood and/or anxiety disorders would be at greater risk for transient ischemic episodes (assessed using 48-hour Holter monitor)

during daily life compared to CAD patients with no psychiatric comorbidity. It was hypothesized that a greater number of CAD patients with a comorbid mood or anxiety disorder would exhibit transient ischemic episodes during daily life compared to control patients. It was also hypothesized that patients with a comorbid mood or anxiety disorder would exhibit a greater number of ischemic episodes and of a longer duration compared to control patients. Finally, it was hypothesized that a greater number of ischemic episodes would be preceded by mental stress (i.e., negative emotions) as opposed to physical stress (i.e., exercise) in CAD patients with a comorbid mood or anxiety disorder compared to control patients.

Surprisingly, only six out of the 71 patients tested exhibited transient myocardial ischemia during Holter monitoring, which was too few to conduct meaningful statistical analyses. Nonetheless, results showed that a greater number of CAD patients with a comorbid anxiety disorder (4/28 or 14%) exhibited transient ischemic episodes compared to controls (2/23 or 9%). Additionally, of all ischemic episodes recorded, the majority (19/21 or 90%) occurred in patients with a comorbid anxiety disorder. Anxiety disorder patients also exhibited a greater number of ischemic episodes (mean = 4.75 vs. 1) and of a longer duration (127 min. vs. 20 min.) relative to controls. Even though results did not reach statistical significance, they are consistent with hypotheses and suggest that CAD with a comorbid anxiety disorder may be at greater risk for transient ischemic episodes during daily life relative to CAD patients with no psychiatric comorbidity. Surprisingly, no ischemic episodes were recorded among patients with a primary mood disorder, which may suggest that CAD patients with a comorbid anxiety versus mood disorder may be at greater risk

for ischemia during daily life. However, because too few patients in each group exhibited ischemia, there is insufficient evidence to draw that conclusion.

The results also show that a significant proportion (42%) of ischemic episodes observed in anxiety disorder patients were preceded by mental stress (i.e., increased feelings of tension, nervousness and stress). This finding is consistent with those reported by Guellette et al. (1997), who found that increased feelings of tension and frustration in particular more than doubled the risk of ischemia occurring the following hour. Of the two episodes observed in control patients, one was preceded by physical stress (exercise) and the other had no identifiable cause. Interestingly, neither of the two episodes recorded among control patients were preceded by mental stress. Though not statistically significant, these results suggest that CAD patients with a comorbid anxiety disorder experience more negative emotions and may be at greater risk for mental stress-induced ischemia relative to CAD patients with no psychiatric comorbidity. However, because so few patients demonstrated ischemia (8% of the total sample), these findings are only preliminary and these interpretations speculative.

It was surprising that so few patients exhibited transient ischemic episodes, which ultimately affected statistical power and may explain why results did not reach significance. There are a number of possible explanations of why so few patients exhibited ischemia. First, this was the first ambulatory mental-stress study to evaluate myocardial ischemia during daily life which did not temporarily withdraw anti-ischemic medication 48-hours before and for the duration of the ambulatory period. All patients were maintained on their anti-ischemic medication, including β-blockers,

Ca-channel blockers, ACE-inhibitors and vasodilators (nitroglycerine) whose prescriptions did not differ between diagnostic groups. However, 79% (n=56/71) of the sample was taking some form of anti-ischemic medication, including 53% (n=38/71) who were on β-blockers which are known to protect against both physical and mental stress-induced ischemia (Wong & Freedman, 1997). It is therefore possible that anti-ischemic medication effectively protected against mental stress-induced ischemia for the majority of "potential" episodes. In fact, previous findings of mental stress-induced ischemia during daily life have been observed primarily in patients either not taking β-blockers (e.g., Wong & Freedman, 1997), or in patients whose anti-ischemic medication had been temporarily withdrawn for the duration of the study (Gottdiener et al., 1994; Krantz et al., 1994; Stone et al., 1999). The decision not to withdraw anti-ischemic medication was taken in order to examine for the first time the extent to which mental stress was associated with transient myocardial ischemia over and above the protective effects of medication. Maintaining patients on their regular medication was also done to conduct a study which would be more reflective of clinical reality in that the study population (patients with documented CAD) is typically taking appropriate cardiac medication. Findings of significant mental stress-induced ischemia despite being maintained on cardiac medication would have emphasized the importance of negative emotions in cardiac morbidity. Interestingly, five out of the six patients who exhibited ischemia were on anti-ischemic medication (mostly β-blockers), three of which had an anxiety disorder. Among anxiety disorder patients exhibiting mental stress-induced ischemic episodes, 11 out of 19 episodes occurred in patients who were medicated. Therefore, the

patients in this study exhibited ischemia (and mental stress-induced ischemia) despite being on anti-ischemic medication, suggesting that negative emotions can induce ischemia in appropriately medicated CAD patients. Though the findings reported here did not reach significance, they suggests a preliminary trend towards greater risk for ischemia in CAD patients with anxiety disorders, and that relative to physical stress, mental stress may be a more potent or relevant trigger of myocardial ischemia among CAD patients with a comorbid anxiety disorder relative to CAD patients with no psychiatric comorbidity.

A second possible explanation for why so few patients exhibited ischemia may have been related to the relative insensitivity of Holter monitors to detect myocardial ischemia compared to more sensitive imagining techniques (e.g., SPECT) (DiMarco & Philbrick, 1990; Crawford et al., 1999). All patients in the current study exhibited at least mild-moderate ischemia during exercise using SPECT imaging, so all patients were "ischemic" and therefore at reasonable risk for transient episodes during daily life. An examination of the number of episodes of chest pain (angina) reported by patients reveals that a far greater number of patients reported experiencing chest pain, though no ischemia was detected on the Holter monitor. In fact, 35 out of the 71 patients tested or 49% of the total sample reported experiencing at least one episode of chest pain over the 48-hour monitoring period, but only 6 patients (or 8%) exhibited ischemia. This finding could be interpreted as reflecting an over-reporting bias on the part of some patients (due to symptom misperception) or the failure of the Holter to detect some ischemic episodes. Unfortunately, both interpretations are equally plausible. Holter monitoring has its limitations, most of

which are related to its sensitivity to detect cardiac events including ST-segment depressions (DiMarco and Philbrick, 1990; Crawford et al., 1999) and ventricular arrhythmias (Kinlay et al., 1996; Safe & Maxwell, 1990). In addition, the majority of chest pain episodes were reported by CAD patients with a psychiatric comorbidity who are known to over-report or "complain" about physical symptoms (McHugh & Vallis, 1986; Costa, Fleg, McCrae & Lakatta, 1982). However, the overall number of chest pain episodes reported is consistent with previous studies examining the prevalence of chest pain (angina) in CAD patients, suggesting that the chest pain episodes reported in the present study are in line with typical rates of angina in CAD patients (e.g., Freedman & Wong, 1998; Krantz et al., 1994). More research is needed to clarify this question, which cannot be answered by the current study.

Although there are a number of plausible explanations to explain why so few patients exhibited ischemia, we cannot exclude the possibility that mental stress-induced ischemia during daily life is simply not a significant risk factor for the majority of appropriately medicated CAD patients. We also cannot exclude the possibility of Type II error, given the surprisingly few patients that exhibited ischemia. In fact, considering the present results, a sample size of 71 and three diagnostic groups, a calculation of the actual power of this study was approximately .35, significantly less than the planned .80. One explanation for the present findings is that the sample size was too small (Stevens, 1986), which affected the power of the study; even though a sample size estimate was calculated according to standard statistical practice. Taking the present results into consideration, a re-calculation of the sample size estimate suggests that a minimum of 150 patients would have been

needed to detect a significant difference in the number of ischemic episodes exhibited by each group (maintaining α at 0.05 and a power of .80). Therefore, a much larger sample of patients would need to be tested in order to determine whether the trend observed here can reach statistical significance.

Objective 1 Limitations and Suggestions for Future Research

This study objective was limited by the following factors: First, the self-report nature of the structured diary used to measure mental stress (negative emotions), physical activities, and chest pain is necessarily subjective. Although the diary has been used extensively in previous ambulatory studies accurately and reproducibly (Hedges et al., 1990), it is possible that the negative emotions and chest pain reported were biased (or over-reported). However, it is equally possible that negative emotions and chest pain episodes were either not reported or under reported and that our data underestimate relations between various triggers of ischemia (e.g., mental stress), chest pain, and actual ischemic episodes. Though subjectivity is an unavoidable limitation, it nevertheless represents patients' perceptions which are often more important to health behavior and clinical care. Furthermore, it is often how a patient interprets his or her symptoms which can lead to increased anxiety, arousal, and symptom exacerbation. The fact that patients were prompted to make diary entries an average of two times per hour during waking hours (approximately 28 hours total), and that the average number of diary entries was 42 over the 48-hour monitoring period suggests that patients reliably completed the diary.

This study objective was also limited by the fact that ambulatory measurements were taken over a 48-hour period, which is a very restricted period of time in which to experience negative emotions and record a significant number of ischemic events. However, 48-hour Holter monitoring is technologically the maximum amount of time recordings can be taken, and has become the standard assessment period in ambulatory ischemia studies. Thus, even though it has its limitations, the current design allows us to compare our findings with existing literature.

A third limitation of the present objective is that because mental stress-induced ischemia (our primary variable of interest) typically occurs at very low heart rates and blood pressure, it is less readily detectable by Holter electrocardiographic monitors relative to more sensitive imaging techniques (e.g., SPECT). Therefore, the use of Holter monitoring to measure ischemia during daily life may have limited our ability to detect a significant number of ischemic episodes, particularly those which may have been induced by mental stress. Furthermore, because this study relied on ambulatory techniques to assess ischemia, the occurrence of study variables was based on observation and was not under experimental control.

This study was also limited by the heterogeneity of the anxiety disorder group, which included patients with several anxiety disorders (including panic disorder (PD), generalized anxiety disorder, social anxiety disorder, and post-traumatic stress disorder). Although inclusion criteria for the mood disorder group were any primary mood disorder diagnosis, it was actually comprised of all major depressive disorder (MDD) patients. Therefore, the fact that the anxiety disorder group was comprised of

patients with different anxiety disorders (though the majority had primary PD), it may be difficult to generalize findings to a specific anxiety disorder. Though this was not the objective of the study, future studies may want to compare ambulatory ischemia in specific diagnostic groups (e.g., MDD versus PD) in order to achieve greater generalizability.

In retrospect, a final major limitation of the present study may have been our decision not to withdraw anti-ischemic medication before and for the duration of the study. Unlike previous ambulatory studies, we wanted to conduct a study which would be more reflective of clinical reality by maintaining CAD patients on their prescribed cardiac medication. Thus, investigating the impact of having an additional comorbid psychiatric disorder on ambulatory ischemia while patients are off medication would not have been very ecologically valid, given that most patients are taking appropriate cardiac medication. However, given that this was the first study to investigate the impact of actual comorbid psychiatric disorders on ischemia during daily life, it may have been more appropriate to conduct an initial study with medications withdrawn, and a subsequent study with medications maintained. Future research should consider this study design in order to more adequately test the impact of comorbid mood and anxiety disorders on ambulatory ischemia, and the extent to which medication is really cardio protective in these patients.

Overall, the fact that so few patients exhibited ischemia (8% of the total sample) suggests that future studies may need to test a larger sample of subjects in order to ensure adequate statistical power. Although our sample size was comparable to previous ambulatory studies, the fact we did not withdraw anti-ischemic

medication may have resulted in a significant loss of potentially ischemic subjects. In addition, future studies may want to compare the relative effectiveness of different ambulatory monitoring techniques, such as Holter versus cardiac event recorders, which are hand-held devices that are applied to the chest by patients when cardiac symptoms (e.g., chest pain) occurs. A recent study by Kinlay et al. (1996) found that cardiac event recorders provided superior data and were more cost-effective than Holter monitors for the recording of arrhythmias. Additional controlled trials are needed to determine if the same is true for the measurement of myocardial ischemia.

Dysregulation of the Autonomic Nervous System

The second pathophysiological mechanism proposed to mediate the link between psychiatric disorders and increased CAD morbidity and mortality involves dysregulation of ANS functioning. In recent years, the analysis of HRV has been employed to study cardiovascular autonomic responses, which is a technique that provides a window into the relative contributions of sympathetic and parasympathetic activity in heart rate modulation. Loss of normal ANS control of heart rate and cardiac rhythm has been shown to confer risk for cardiac morbidity and mortality, including ventricular arrhythmias and sudden death among post-MI patients.

HRV in panic disorder patients and controls

The results of several studies indicate that patients with certain psychiatric disorders exhibit abnormally low HRV compared to non-psychiatric controls. Independent lines of research have provided evidence of reduced HRV among both

depressed (non-CAD) psychiatric and depressed CAD patients. Several studies have also found evidence of reduced HRV among non-cardiac patients with panic-like anxiety and PD. Although reduced HRV has been consistently observed among individuals with PD, no studies have evaluated HRV among PD patients with documented CAD, who may be at even greater risk for autonomic disturbances due to their existing cardiac disease. The second objective of the present study was to examine ANS disturbances in CAD patients with comorbid PD. Specifically, we examined the extent to which CAD patients with comorbid PD exhibited significantly reduced HRV (assessed using 48-hour Holter monitoring) compared to CAD patients without comorbid PD.

The results showed that although there were no differences on individual HRV components (time or frequency indexes) between PD patients and controls, CAD patients with PD exhibited significantly lower LF:HF ratios compared to CAD patients without PD. This difference remained significant even after controlling for variables known to influence HRV (current cigarette smoking, diabetes, history of CABG). The LF:HF ratio is said to reflect sympathovagal balance, with higher ratios representing a predominance of sympathetic over parasympathetic activity and lower ratios representing a predominance of parasympathetic control over heart rate. Thus, the present finding of lower ratios among PD patients suggests that PD patients with CAD show dominant parasympathetic control over heart rate and/or depressed sympathetic activity under baseline (ordinary daily life) conditions. These findings are consistent with those reported by McCraty and colleagues, who found that the SDNN index, TP and VLF were significantly lower in non-cardiac PD patients

relative to controls over a 24-hour ambulatory period (McCraty, Atkinson, Tomasino & Stuppy, 2002). These findings, like those observed in our study, suggest that sympathetic activity is depressed in PD patients during ordinary daily life, leading to a relative predominance of vagal control of heart rate under baseline conditions.

One interpretation of the present findings is that PD patients demonstrate baseline parasympathetic predominance over heart rate and respond to stress (or perceived stress) via parasympathetic withdrawal rather than via direct increases in sympathetic activity. The present findings are consistent with previous reports that suggest parasympathetic withdrawal rather than increased sympathetic activity is the mechanism by which PD patients respond to panic challenges (e.g., lactate infusion and hyperventilation) (George, Nutt, Walker et al., 1989). It has been argued that panic challenges such as lactate infusion facilitate the expression of sympathetic activity without direct sympathetic excitation by depressing parasympathetic or vagal tone (George et al., 1989). This argument is consistent with the clinical observation that administration of lactate causes symptoms that mimic those exhibited during parasympathetic blockade (e.g., tachycardia) but without concurrent increases in plasma norepinephrine levels. This supports the notion that parasympathetic withdrawal from a previously heightened state of activation, rather than increased sympathetic activity, may be responsible for mental stress-induced cardiac events (e.g., ischemia, arrhythmias) (George et al., 1989). The fact that mental stress-induced cardiac events typically occur at low HR's and BP's further supports the hypothesis that mental stress may exert a greater influence over parasympathetic activity, whereas physical stress may exert a greater influence over sympathetic activity.

It is therefore possible that it is PD patients' dominant parasympathetic control over heart rate that may account for their high sensitivity to any increases in sympathetic arousal. Usual increases or variations in sympathetic arousal, while within the range of "normal reactivity" for most individuals may be experienced as uncomfortably (and dangerously) large for PD patients. Such baseline parasympathetic predominance may also play a role in the origin of panic attacks as this dysfunction in autonomic balance may explain the higher resting HR's and exaggerated BP's and HR responses to standing (Weissman, Shear, Kramer-Fox et al., 1987), Valsalva's maneuver (Weissman et al., 1987), and pharmacological panic challenges (e.g., CO^2 inhalation) (Fleet et al., 2000; Charney, Heninger, & Brier, 1984; Nutt, 1986) in PD patients.

The second possible interpretation of the current findings is that PD patients, due to their exaggerated sensitivity to somatic symptoms (particularly cardiovascular symptoms) may persistently and mistakenly perceive danger in the absence of any real threat. It is possible that this hyper vigilance to threat, over time, could lead to chronic activation of the sympathetic nervous system, leading to subsequent shift in autonomic balance favouring parasympathetic activation to compensate for chronic sympathetic hyperactivity. This may explain why the current findings are in contrast to those reported in studies of non-cardiac PD patients, who demonstrate baseline sympathetic hyperactivity (e.g., Yeragani et al., 1997; 1993; Klein et al., 1995; Friedman et al., 1993). However, these studies were conducted in non-cardiac PD patients, who may have a pattern of ANS dysregulation that is distinct from PD patients with established CAD. It is also possible that a shift towards parasympathetic

control of heart rate only occurs after chronic sympathetic dysregulation, and may be the mechanism underlying autonomic imbalances observed in patients with PD. Conducting a study of initially healthy (non-cardiac) PD patients over an extended period of time and examining changing patterns of ANS activity to see if there is any relationship between shifts in autonomic balance and the development of CAD would help provide important insights into this hypothesis.

It was surprising that PD and non-PD patients did not differ on any of the HRV variables under investigation. It was expected that consistent with previous studies, PD patients with CAD, like PD patients without CAD, would exhibit significantly lower HRV (indicating greater risk for arrhythmias) on both time and frequency domain indices compared to controls. Although the differences did not reach statistical significance, they were in the expected direction indicating lower HRV for SDANN and SDNN indices as well as for LF, VLF, ULF, and TP relative to controls. Interestingly, HF power was greater (though not significantly) in PD patients compared to controls, indicating greater parasympathetic control of heart rate among PD patients. It was also surprising that contrary to previous studies, no significant differences were observed among CAD patients with MDD relative to controls on any of the HRV indices assessed. At least two recent studies (Carney et al., 2001; Stein et al., 2000) did find evidence of decreased HRV (on both time and frequency domain indices) among patients with MDD and comorbid CAD. However, these studies differed from the present study on a number of important methodological details. First, Stein et al. (2000) discontinued patients' cardiac medication for the duration of the study, which may have contributed to their positive

findings via the induction of a rebound effect as a result of the discontinuation of β-blockers. Second, although Carney et al. (2001) found evidence of reduced HRV in their sample of CAD patients with MDD, their study included over 800 subjects whereas our analysis only included 48 (26 with MDD). Thus, the power created by their sample size may have contributed to their significant findings (and unfortunately, no effect sizes were reported). Furthermore, an examination of the absolute adjusted (for age, sex, diabetes, current cigarette smoking) HRV values for depressed versus not depressed patients on log transformed ULF and VLF power indices were 8.52 (depressed) versus 8.66 (not depressed) and 6.32 (depressed) versus 6.59 (not depressed) respectively. Although these differences reached statistical significance (p's < 0.05), they do not represent very large absolute differences and may be of questionable clinical significance. Finally, the results of studies linking reduced HRV to MDD in CAD patients (e.g., Carney et al., 2001; Stein et al., 2000; Thornton & Hallas, 1999) point to a consistent pattern of enhanced sympathetic reactivity to stress and reduced vagal activation, unlike the present study which found evidence of predominant parasympathetic tone in PD patients with PD.

Overall, the present findings suggest that PD patients with CAD show a predominance of parasympathetic tone, which may be the primary mechanism underlying ANS disturbances in PD patients with established CAD, and that this mechanism may be specific to PD relative to MDD. Future studies should compare HRV and cardiac autonomic tone in PD versus MDD patients with established CAD in order to more adequately explore this hypothesis.

Objective 2 Limitations and Suggestions for Future Research

The present findings must be interpreted with caution in light of some important methodological limitations. First, the sample size was modest with 42 subjects (n=20 with PD) and was comprised of primarily men (90%). The primarily male sample reflects the disproportionately male cardiac population from which our sub-sample was drawn. Thus, the results reported here may not be generalizable to women with comorbid CAD and PD. Given the increasing prevalence of CAD among women, and the disproportional rate of PD among women relative to men (APA, 1994), future studies should strive to include equal proportions of men and women in order to increase the generalizability of results.

A second limitation of the present study is that the majority (75%, n=15) of PD patients had a comorbid psychiatric disorder, including GAD (30%, n=6), specific phobia (30%, n=6), dysthymia (20%, n=4), social phobia (15%, n=3), minor depression (10%, n=2), and MDD (10%, n=2), and just under half (45%, n=9) had more than one comorbid diagnosis. Although the majority (75%, n=15) of patients were diagnosed as having a primary diagnosis of PD according to DSM-IV criteria, the fact that so many patients also had a comorbid psychiatric disorder could have influenced the results. It is therefore possible that findings of greater parasympathetic control of heart rate under ordinary daily life conditions could have been in part due to the impact of having one or more of the above comorbid diagnoses. However, clinical reality is such that the existence of pure diagnostic categories is a rare occurrence in clinical practice, so the findings reported here are in line with psychiatric prevalence rates (APA, 1994). Furthermore, the comorbidity rates in this

study are consistent with comorbidity rates reported in previous studies examining HRV in non-cardiac PD patients (e.g., Tucker, Adamson, Miranda et al., 1997). The majority of comorbid diagnoses were related anxiety disorders, which share many core symptoms with PD (e.g., sympathetic arousal, avoidance behaviour) and is typical among clinical populations. Thus, aiming to study "pure" diagnostic categories may be clinically invalid given the high rate of comorbid diagnoses.

Because this study relied on ambulatory electrocardiographic measurements of autonomic changes, we were not able to control for the potential confounding effect of breathing frequency that is known to impact HRV variables (Stein et al., 1994). In addition, the use of ambulatory techniques to assess autonomic changes implies that the occurrence of study variables was based on observation and was not under experimental control. This is an avoidable trade-off in ambulatory studies of HRV, but permits a longer and more naturalistic assessment of study variables. Future studies could combine both ambulatory and laboratory designs which would permit examination of ANS responses to physical and psychological challenge under both controlled and naturalistic conditions. Finally, the measurement of HRV is an indirect measure of cardiac autonomic tone, as direct measures of neural activity are not feasible during ambulatory studies. This may have limited precision in the measurement of HRV variables. Developments in digital ambulatory ECG recording devices may provide an opportunity to improve the acquisition and measurement of HRV variables in future studies.

HRV in Hi versus Lo anxiety sensitivity patients

The HRV literature has demonstrated a consistent pattern of reduced HRV among both mood and anxiety disordered patients. What has been less clear is what could be underlying the relationship between reduced HRV in patients with these psychiatric disturbances. One such underlying psychopathology may be the trait of AS, which is common among both anxiety and mood disorder patients and is characterized by high sensitivity or "reactivity" to somatic symptoms and a strong desire to minimize the cognitive and physical manifestations of anxiety. High AS may be contribute to disruptions in ANS functioning via (1) a propensity to perceive events and bodily sensations as more intense and "stressful", leading to an overall increase in the number of stressful experiences, and (2) a tendency to over-react emotionally (exaggerated fear response) and physiologically (exaggerated sympathetic arousal) to the symptoms of anxiety caused by these experiences. Thus, high AS may contribute to ANS disturbances through chronic sympathetic hyper arousal and vagal inhibition. Because no studies to date had investigated the relationship between AS and HRV, the third objective of the present study was to examine the extent to which AS is related to reduced HRV in CAD patients with mood and anxiety disorders. Using the ASI, patients were divided into Hi and Lo AS groups and underwent 48-hour ECG Holter monitoring to assess both time and frequency domain indices of HRV.

The results indicated that Hi AS patients exhibited significantly lower ASDNN, SDANN, SDNN, LF power, VLF power, ULF power, and TP compared to Lo AS patients. Though not significant, means were in the expected direction

indicating lower HF power in Hi versus Lo AS patients. Variables known to be associated with reduced HRV (current cigarette smoking, diabetes, history of CABG) were compared in Hi versus low AS patients and were entered into an ANCOVA. Hi AS patients still demonstrated significantly reduced LF, VLF and ULF power relative to Lo AS patients, but the time domain indices (ASDNN, SDANN, SDNN) and TP no longer emerged as significant. These findings suggest that a general tendency to be sensitive to anxiety symptoms is associated with significant reductions in HRV, even after controlling for important confounds. The relative contributions of sympathetic and parasympathetic activity to these HRV indices are difficult to specify precisely. Hi AS patients showed decreased LF, VLF, and ULF but not HF or TP after covariate adjustment. LF, VLF and ULF power are all influenced by both sympathetic and parasympathetic systems, whereas HF is largely thought to reflect parasympathetic tone (Stein et al. 1994). However, the majority of evidence linking HF power to parasympathetic activity emanates from studies of healthy (non-cardiac) humans and animals (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Stein (1999) reported that among cardiac patients, HF power is influenced by non-respiratory sinus arrhythmia, which may exaggerate the magnitude of HF power but may not reflect vagal modulation of HR in the usual sense. There is also evidence to suggest that VLF power may also reflect parasympathetic activity (Taylor, Carr, Myers et al. 1997), a variable that did remain significant even after controlling for important confounding variables. Although it is not possible to conclude that reduced HRV in CAD patients with Hi AS is due to decreased parasympathetic modulation, increased sympathetic

modulation, or both, the present findings do suggest disturbances in cardiac autonomic regulation among Hi AS patients relative to Lo AS patients that cannot be attributable to typical confounders.

It is important to consider the clinical significance of the present findings. In the Cardiac Arrhythmia Pilot Study (CAPS), which assessed HRV in CAD patients 1 year after MI, a VLF power of $< 600ms^2$ identified patients at a 4.4 relative risk of mortality over the next 2 years (Bigger, Fleiss, Rolnitzky, & Steinman, 1993). In the present study, 54% (n=27/50) of patients in the Hi AS group exhibited a VLF power of $< 600ms^2$, compared to only 33% (n=7/21) of the Lo AS group. This suggests that CAD patients with Hi AS may have a nearly 2-fold increased risk for mortality that may be attributable to low HRV relative to CAD patients with Lo AS. Given that a full 32% of Hi AS patients have a history of MI, this finding highlights the clinical significance of this study. This finding is consistent with the percentage of moderately-to-severe depressed patients (47%) who exhibited a VLF below this cutoff in Stein et al.'s study of depressed CAD patients (2000). Although AS was not measured in this study, it is possible that their findings of reduced HRV in depressed patients may have been due to patients' underlying AS, which has been shown to be disproportionately high among depressed patients (Taylor et al., 1996; Otto et al., 1995). Future studies examining HRV among depressed CAD patients should include measures of AS in order to determine the relative contribution of underlying trait AS to the associations observed between MDD and reduced HRV. Nonetheless, the present findings suggest that the lower HRV in the Hi AS patients may have important prognostic significance and warrants further investigation.

Interestingly, HRV was not related to any other psychological variable studied, including having a diagnosable anxiety disorder or mood disorder, or having high depression, hostility, state anxiety, trait anxiety, or trait anger scores. These findings suggest that the trait of AS, rather than having a psychiatric disorder per se is associated with significant reductions in HRV and abnormalities in cardiac autonomic tone. These findings also suggest that trait AS in particular and not high depression scores, trait anxiety, trait hostility, or trait anger is associated with reduced HRV, pointing to a unique association between AS and dysregulated ANS activity.

Why would trait AS be related to reduced HRV, and therefore dysregulated cardiac autonomic tone, where other trait variables typically associated with CAD morbidity and mortality were not? With respect to depression scores, these findings are in contrast to Krittayaphong et al.'s study (1997), who found that CAD patients with higher depression scores had lower HRV (SDNN) compared to patients with lower depression scores. However, this study used the depression (D) scale of the Minnesota Multiphasic Personality Inventory (MMPI) and dichotomized patients based on a median split on the D-scale, whereas we used standard cutoffs ($\geq$ 10) on the BDI to measure depression. The fact that we used different scales and cutoffs could account for our disparate findings. Krittayaphong et al.'s findings were also limited to lower SDNN, as they did not assess frequency domain indices of HRV. It they had measured a wider range of HRV variables, it is possible that no positive findings would have been reported.

With respect to hostility, the study by Sloan, Shapiro, Bigger et al. (1994) that found evidence of reduced HRV and vagal modulation among men with high trait

hostility was conducted in a sample of normal, healthy (non-cardiac) men. The fact that our study was conducted in a population with established CAD, and who were maintained on standard cardiac medication, may account for our negative findings.

There are also a number of theoretical reasons why AS in particular may predispose individuals to disturbances in cardiac autonomic tone. It has been argued that having high AS or a lower threshold for activating fear may sustain individuals at an excessively high level of physiological arousal beyond what's required to maintain personal safety or survival (Logan & Goetsch, 1993). This hypothesis has been supported by studies linking high state and trait anxiety to increased resting BP levels and hypertension (Pagotto et al., 1992; Henry & Grim, 1990). Given that AS is a trait or dispositional variable that typically emerges by late adolescence or early adulthood (Lau et al., 1996), the effects of this sustained physiological arousal may be experienced over a period of several years. This chronic hyper arousal may contribute to cardiac autonomic disturbances and may help explain the higher risk for the development and progression of CAD in initially-healthy individuals with panic-like anxiety. This hypothesis is supported by studies linking panic-like anxiety (which is conceptually similar to AS) and increased cardiac morbidity and mortality in longitudinal studies (Coryell et al., 1982; 1986; Haines et al., 1987; Kawachi et al., 1994a; 1994b).

It has also been suggested that high AS may predispose individuals to over-attend to physiological changes, leading to an increased sensitivity or reduced threshold for detecting somatic changes. This hyper sensitivity to somatic changes may result in a greater-than-expected number of "stressful" events experienced over a

lifetime, increasing wear and tear on the cardiovascular system. This hypothesis has been supported by a study showing that chronic pain patients with high AS selectively attend to pain and injury-related stimuli (versus neutral stimuli) relative to low AS patients (Asmundson et al., 1997).

Finally, central theories of emotion have argued that AS may be the result of CNS abnormalities (Charney et al., 1984; Carr & Sheehan, 1984), citing studies linking the hypothalamus, which integrates emotional, somatic, endocrine and autonomic information from the amygdala and limbic structures to cardiovascular regulation (Aubert & Ramaekers, 1999). There is also evidence from positron emission tomography (PET) studies on PD patients suggesting abnormalities in limbic structures (Reiman, Raichle, Butler, Herscovitch & Robbins, 1984). In addition, a study involving electrical stimulation of limbic structures in cats (Klevans & Gebber, 1970) reported finding evidence of altered barorecptor responses in experimental animals, further supporting a link between limbic system function and cardiac activity. The involvement of limbic structures in ANS control lends support to the hypothesis that anatomical brain structures may be implicated in physiological abnormalities. Thus, HRV may represent an important marker of emotionally-induced sympathetic arousal, where acute and/or chronic arousal disrupts sympathovagal balance via enhanced sympathetic outflow and simultaneous inhibition of neural activity in the dorsal vagal nucleus. It is therefore possible that individuals with high AS, who experience chronic ANS hyper arousal due to their tendency to over-attend and hyper-react to bodily sensations and somatic changes may from a very young age contribute to disturbances in ANS functioning. As such, high AS may over time lead

to chronic sympathetic hyper arousal and vagal inhibition, thereby leading to dysregulations in cardiac autonomic tone and sympathovagal balance. This may the mechanism by which patients with high anxiety and AS may be at increased risk for cardiac morbidity associated with these disruptions in cardiac autonomic tone: namely ventricular arrhythmias and sudden death. The results of the present study demonstrating reduced HRV among CAD patients with high AS suggest that this subgroup of cardiac patients may be at increased risk for arrhythmias and sudden death compared to CAD patients with Lo AS. In order to determine the actual fate of Hi AS CAD patients, it would be of interest to conduct a follow-up study to evaluate cardiac morbidity and mortality.

Objective 3 Limitations and Suggestions for Future Research

The present findings must be interpreted with caution in light some important study limitations. First, the cell sizes of Hi and Lo AS groups were not equal, with disproportionately more patients in the Hi AS group (n=50/71). The sample was also comprised of primarily men (84%), which reflects the disproportionately male cardiac population from which our sub-sample was drawn. Thus, the results reported here may not be generalizable to women with comorbid CAD and Hi AS. Given the increasing prevalence of CAD among women, future studies should strive to include equal proportions of men and women in order to increase the generalizability of results.

Second, although all of the patients in the study had CAD documented by previous CABG, PTCA, MI or SPECT exerice-induced myocardia ischemia, recent

angiograms were not available for all patients. Although one study found no relationship between any index of HRV and the severity of CAD (Pai, Hu & Ting, 1995), another study did find an association between a vagally modulated index of HRV and CAD severity (Hayano, Yamada, Mukai et al., 1991). Therefore, the relationship between CAD severity and HRV is unclear. Although it is possible that there was a difference in the severity of CAD between Hi and Lo AS patients, an examination of baseline medical and demographic differences between the two groups would suggest this is not the case.

Third, the results of the present study may be limited by the self-report and therefore subjective nature of the ASI from which patient groups were derived. Although the ASI has demonstrated very good statistical properties and has been used extensively in previous studies, it is possible that self-reports of AS were biased. However, subjectivity is unavoidable when using self-report questionnaires and it is often patients' interpretations of their symptoms which are more important determinants of health behaviour than the presence of symptoms alone.

Because this study relied on ambulatory electrocardiographic measurements of autonomic changes, we were not able to control for the potential confounding effects of breathing frequency which are known to impact HRV variables (Stein et al., 1993). In addition, the use of ambulatory techniques to assess autonomic changes implies that the occurrence of study variables was based on observation and was not under experimental control. This is an avoidable trade-off in ambulatory studies of HRV, but permits a longer and more naturalistic assessment of study variables.

Finally, the measurement of HRV is an indirect measure of cardiac autonomic tone, as direct measures of neural activity are not feasible during ambulatory studies. This may have limited precision in the measurement of HRV variables. In addition, because of the capabilities of current electrocardiographic technology, we were not able to determine the relative contributions of sympathetic and parasympathetic activity to the low frequency HRV variables found to be reduced in Hi AS patients. This would have help shed light on the debate as to whether AS is associated with disturbances in primarily sympathetic or parasympathetic activation. However, the fact that several HRV variables were significantly reduced does suggest a clear pattern of cardiac autonomic dysregulation in CAD patients with Hi AS which may place them at increased risk for associated cardiac morbidity. Developments in digital ambulatory ECG recording devices may provide an opportunity to improve the acquisition and measurement of HRV variables in future studies.

Study Implications and Conclusions

The present study investigated the relationship between two pathophysiological mechanisms thought to mediate the link between anxiety and mood disorders and negative emotions and increased risk for CAD morbidity and mortality. These mechanisms include: (1) mental stress-induced myocardial ischemia and (2) dysregulation of the ANS.

The results of the present study showed, though not significantly, that CAD with a comorbid anxiety or mood disorder exhibited a greater number of ischemic episodes during daily life, and for a longer duration compared to CAD patients with

no history of psychiatric illness. The majority of ischemic episodes exhibited by CAD patients with comorbid psychiatric disorders were preceded by mental as opposed to physical stress, tentatively suggesting an increased risk for mental stress-induced ischemia in CAD patients with comorbid anxiety and mood disorders relative to matched controls. In order to support this hypothesis, a study with a greater number of subjects in which cardiac medications are withdrawn for the duration of the study is recommended.

The present study also found that PD patients with CAD show a predominance of parasympathetic tone (even after controlling for important confounds), and may be the primary mechanism underlying ANS disturbances in PD patients with established CAD. Finally, this study also found a significant relationship between reduced HRV and trait AS, even after controlling for important confounds. Specifically, reduced HRV (LF, VLF and ULF) was observed in CAD patients with Hi versus Lo AS. These findings indicate that a general tendency to be sensitive to anxiety symptoms is associated with significant reductions in HRV, and therefore important disruptions in cardiac autonomic regulation.

In conclusion, the present findings raise the question of whether early identification and treatment of AS might increase HRV and thereby reduce risk associated with dysregulated cardiac autonomic tone. There is some evidence showing that treating PD (which is highly correlated with AS) with SSRI's (e.g., Paroxetine) may increase HRV in non-cardiac PD patients (Tucker et al., 1997; Rechlin, 1994). The extent to which either pharmacotherapy (SSRI's) or psychotherapy (e.g., cognitive-behavioral therapy) can increase HRV in PD or high

anxiety sensitive patients with documented CAD has not yet been studied and may be an interesting avenue for future research. However, because this is the first study to report associations between AS and reduced HRV, these findings need to be replicated with a larger sample before concluding that a relationship between AS and dysregulated autonomic tone exists and warrants intervention.

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Appendix A:

Anxiety Sensitivity Index (ASI)

ID: ☐☐☐☐ Date: ☐☐ Jour ☐☐ Mois ☐☐ Année

Index de sensibilité à l'anxiété

Instructions: Veuillez encercler le choix de réponse qui décrit le mieux vote degré d'accord avec les items suivants. Si un des items ne vous concerne pas (ex: "Cela me fait peur lorsque je me sens trembler", pour quelqu'un qui n'a jamais ressenti ce malaise) répondez en pensant à la façon dont vous vous seriez senti dans une telle situation, sinon répondez selon votre expérience

	très peu	un peu	quelquefois	beaucoup	énormément
1. Il est important pour moi de ne pas paraître nerveux (euse)	0	1	2	3	4
2. Quand je ne peux me concentrer sur une tâche, je m'inquiète de devenir fou (folle)	0	1	2	3	4
3. Cela me fait peur quand je me sens trembler	0	1	2	3	4
4. Cela me fait peur quand je pense m'évanouir	0	1	2	3	4
5. Il est important pour moi de rester en contrôle de mes émotions	0	1	2	3	4
6. Cela me fait peur quand mon coeur bat rapidement	0	1	2	3	4
7. Cela m'embarasse quand mon estomac "crie"	0	1	2	3	4
8. Cela me fait peur quand j'ai des sensations de nausée	0	1	2	3	4
9. Quand je m'aperçois que mon coeur bat rapidement, je m'inquiète que je pourrais avoir une "Crise de coeur" (infarctus)	0	1	2	3	4
10. Cela me fait peur quand je deviens essoufflé(e)	0	1	2	3	4
11. Quand mon estomac est à l'envers, je m'inquiète que je pourrais être malade	0	1	2	3	4
12. Cela me fait peur quand je suis incapable de me concentrer sur une tâche	0	1	2	3	4
13. Les gens remarquent quand je me sens tout (e) tremblant (e)	0	1	2	3	4
14. Les sensations corporelles inhabituelles me font peur	0	1	2	3	4
15. Quand je me sens nerveux (se), je m'inquiète que je pourrais avoir une maladie mentale	0	1	2	3	4
16. Cela me fait peur quand je suis nerveux (se)	0	1	2	3	4

ID: ☐☐☐☐ Date: ☐☐ Jour ☐☐☐ Mois ☐☐ Année

Anxiety sensitivity index

Circle the one phrase that best represents the extent to which you agree with the item. If any of the items concern something that is not part of your experience (e.g., "It scares me what I feel shaky" for someone who has never trembled or had the "shakes"), answer on the basis of how you think you might feel if you had such an experience. Otherwise, answer all items on the basis of your own experience

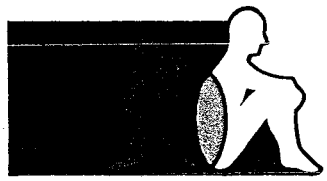
		very little	a little	some	much	very much
1	It is important to me not to appear nervous	0	1	2	3	4
2	When I cannot keep my mind on a task, I worry that I might be going crazy	0	1	2	3	4
3	It scares me when I feel "shaky"	0	1	2	3	4
4	It scares me when I feel faint	0	1	2	3	4
5	It is important to me to stay in control of my emotions	0	1	2	3	4
6	It scares me when my heart beats rapidly	0	1	2	3	4
7	It embarrasses me when my stomach growls	0	1	2	3	4
8	It scares me when I am nauseous	0	1	2	3	4
9	When I notice that my heart is beating rapidly, I worry that I might have a heart attack	0	1	2	3	4
10	It scares me when I become short of breath	0	1	2	3	4
11.	When my stomach is upset, I worry that I might be seriously ill	0	1	2	3	4
12.	It scares me when I am unable to keep my mind on a task	0	1	2	3	4
13.	Other people notice when I feel shaky	0	1	2	3	4
14.	Unusual body sensations scare me	0	1	2	3	4
15.	When I an nervous, I worry that I might be mentally ill	0	1	2	3	4
16.	It scares me when I am nervous	0	1	2	3	4

Appendix B:

Prime-MD interview (paper version)

Prime·MD*

ÉVALUATION PRIMAIRE DES TROUBLES MENTAUX



GUIDE DU CLINICIEN

mis à jour - DSM-IV†

INSTRUCTIONS

1. **Les instructions qui vous sont destinées sont en caractères gras. Les questions que vous posez ou les déclarations que vous faites au(à la) patient(e) sont imprimées normalement.**

2. **Pour chaque module, posez les questions dans l'ordre indiqué, à moins qu'il ne vous soit demandé de passer à une autre question, ou de quitter le module. Important: passez toujours à la question suivante, à moins qu'on ne vous donne une consigne différente.**

3. **Les diagnostics sont encadrés et en italiques.**

4. **Quand vous devez quitter un module, explorez le suivant (selon les réponses du[de la] patient[e]), ou passez directement à la dernière page (résumé).**

NOM DU(DE LA) PATIENT(E): _____

PRÉSENTATION DE LA DÉMARCHE AU(À LA) PATIENT(E):

Permettez-moi de consulter vos réponses et, si nécessaire, de vous poser quelques questions à propos des symptômes que vous avez signalés. Je prendrai des notes pendant notre entretien.

UTILISATION DES MODULES DU GUIDE DU CLINICIEN

Utilisez les modules dans l'ordre selon lequel ils apparaissent dans le Guide du clinicien: (tr. de l'humeur, tr. anxieux, tr. liés à l'alcool, tr. de l'alimentation et tr. somatoformes).

Choisissez les modules sur la base des réponses du(de la) patient(e) au questionnaire, comme suit:

Au moins 3 des questions 1–15: Troubles somatoformes	La question 16: Tr. de l'alimentation	La question 17 ou 18: Tr. de l'humeur	La question 19, 20 ou 21: Tr. anxieux	Au moins 1 des questions 22–25: Tr. liés à l'alcool

Vous pouvez utiliser tout module non suggéré par le questionnaire si vous avez d'autres raisons de soupçonner un diagnostic dans ce module.

PRIME-MD a été mis au point par Robert L. Spitzer, M.D., Janet B.W. Williams, D. Serv. Soc., Kurt Kroenke, M.D., Mark Linzer, M.D., Frank Verloin deGruy III, M.D., Steven R. Hahn, M.D., et David Brody, M.D., grâce à une subvention sans restriction à l'éducation accordée par Pfizer Inc.

Pour informations aux fins de recherche, prière d'écrire à l'adresse suivante: Biometrics Research Department, New York State Psychiatric Institute, 722 West 168th Street, Unit 74, New York, NY 10032 (Docteurs Spitzer et Williams).

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QUESTIONNAIRE DESTINÉ AU(À LA) PATIENT(E)

mis à jour - DSM-IV†

NOM: _____ SEXE: ☐ M. ☐ F. ÂGE: _____ DATE: _____

INSTRUCTIONS: Ce questionnaire aidera votre médecin à mieux comprendre vos problèmes. Votre médecin peut vous poser d'autres questions à ce sujet. Veuillez, s.v.p., répondre à toutes les questions suivantes:

*Pendant le **MOIS ÉCOULÉ**, avez-vous **SOUVENT** souffert...*

	Oui	Non
1. de maux d'estomac?	☐	☐
2. de douleurs au dos?	☐	☐
3. de douleurs dans les bras, les jambes ou les articulations (genoux, hanches etc.)?	☐	☐
4. (Femmes) de douleurs menstruelles ou de problèmes de règles?	☐	☐
5. de douleurs ou de problèmes pendant les rapports sexuels?	☐	☐
6. de maux de tête?	☐	☐
7. de douleurs dans la poitrine?	☐	☐
8. de vertiges?	☐	☐
9. de malaises?	☐	☐
10. de palpitations?	☐	☐
11. de difficultés à respirer?	☐	☐
12. de constipation, de selles molles, ou de diarrhée?	☐	☐
13. de nausées, de flatulence ou d'indigestion?	☐	☐
14. de fatigue, ou d'un manque d'énergie?	☐	☐
15. de difficultés à dormir?	☐	☐
16. d'un besoin irrépressible de manger?	☐	☐
17. d'une perte d'intérêt ou de plaisir dans vos activités habituelles?	☐	☐
18. d'un sentiment d'abattement, de dépression ou de désespoir?	☐	☐
19. de tension nerveuse, d'angoisse ou d'agacement?	☐	☐
20. de soucis à propos de tout et de rien?	☐	☐

*Pendant le **MOIS ÉCOULÉ**...*

	Oui	Non
21. avez-vous eu une crise d'angoisse ou une soudaine panique?	☐	☐
22. avez-vous songé à réduire votre consommation d'alcool?	☐	☐
23. quelqu'un s'est-il plaint de votre consommation d'alcool?	☐	☐
24. vous êtes-vous senti(e) coupable ou irrité(e) à ce sujet?	☐	☐
25. avez-vous pris, en une seule journée, au moins 5 verres de bière, de vin ou de spiritueux?	☐	☐

Globalement, vous diriez que votre santé est plutôt:

- excellente. ☐
- très bonne. ☐
- bonne. ☐
- assez bonne. ☐
- mauvaise. ☐

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MODULE 1: TROUBLES DE L'HUMEUR

DÉPRESSION MAJEURE

Pendant les 2 dernières semaines, avez-vous eu un (ou plusieurs) des problèmes suivants presque chaque jour:

1. De la difficulté à vous endormir, à rester endormi(e), ou au contraire une tendance à trop dormir? **Oui** **Non**

2. De la fatigue ou un manque d'énergie? **Oui** **Non**

3. Un manque ou un excès d'appétit? **Oui** **Non**

4. Un manque d'intérêt ou de plaisir dans vos activités habituelles? **Oui** **Non**

5. Un sentiment d'abattement, de dépression ou de désespoir? **Oui** **Non**

6. Une mauvaise opinion de vous-même—l'impression que vous êtes un(e) raté(e)—ou que vous n'êtes pas à la hauteur, à vos yeux ou à ceux de votre famille? **Oui** **Non**

7. De la difficulté à vous concentrer, p.ex. pour lire ou regarder la TV? **Oui** **Non**

8. Une tension ou une agitation telles que vous n'avez pas cessé de vous lever et de bouger?
   Si NON: Avez-vous eu, au contraire, l'impression de parler ou de bouger si lentement que votre entourage aurait pu s'en apercevoir?
   Considérez la réponse globale comme positive si l'une ou l'autre des réponses partielles est OUI, ou si vous observez une agitation ou un ralentissement psychomoteurs pendant l'interview. **Oui** **Non**

9. Au cours des 2 dernières semaines, avez-vous souhaité mourir ou pensé vous faire du mal? **Oui** **Non**
   Si OUI: Dites-m'en plus à ce sujet.

10. **Avez-vous obtenu au moins 5 OUI aux questions 1–9 (dont un à la question 4 ou 5)?** **Oui** → ***Trouble dépressif majeur*** **Passez à la question 12** **Non**

RÉMISSION PARTIELLE D'UNE DÉPRESSION MAJEURE

11. À un moment donné, avez-vous été beaucoup plus déprimé(e), ou avez-vous eu encore moins d'intérêt ou de plaisir dans vos activités habituelles, que maintenant?
Si OUI: À ce moment-là, aviez-vous plusieurs des problèmes que je viens de citer, comme de la difficulté à dormir ou à vous concentrer, de la fatigue, un manque d'appétit, et une perte d'intérêt pour le monde extérieur?
La réponse ne doit être considérée positive que si, dans le passé, le(la) patient(e) a probablement eu au moins 5 des symptômes 1 à 9, et présente actuellement une humeur dépressive ou une perte d'intérêt ou de plaisir.

Oui → *Rémission partielle d'une dépression majeure* — Non

DYSTHYMIE

12. Ces 2 dernières années, vous êtes-vous senti(e) déprimé(e), ou avez-vous eu moins d'intérêt ou de plaisir dans vos activités?
Considérer la réponse comme positive, seulement si le(la) patient(e) répond OUI également à: Cela a-t-il été le cas plus de 1 jour sur 2 pendant les 2 dernières années?

Oui — Non → Passez à la question 14

13. Ces 2 dernières années, ces problèmes vous ont-ils rendu le travail, l'entretien de la maison ou les contacts avec les autres, plus difficiles?

Oui → *Dysthymie* / Passez à la question 16 — Non

DÉPRESSION MINEURE

14. **Avez-vous diagnostiqué une dépression majeur (y compris «rémission partielle») aux questions 10 ou 11?**

Oui → Passez à la question 16 — Non

15. **Le(la) patient(e) a-t-il répondu OUI à 2 (au moins) des questions 1–9 (dont la question 4 ou 5)?**

Oui → *Trouble dépressif mineur* — Non → Quittez ce module

TROUBLE BIPOLAIRE

16. Un médecin vous a-t-il déjà dit que vous étiez maniaco-dépressif(ve) ou vous a-t-il déjà prescrit du lithium?
Si OUI: Quand? Pourquoi?

Oui → Possibilité de *trouble bipolaire* — Non

DÉPRESSION SECONDAIRE À UNE MALADIE PHYSIQUE OU À LA PRISE D'UN MÉDICAMENT OU D'UNE DROGUE

17. **Les symptômes actuels sont-ils probablement dûs aux effets biologiques d'une maladie physique, d'un médicament ou d'une drogue?**

Oui / (Pas certain) → Possibilité de *trouble dépressif dû à une maladie physique, à un médicament ou à une drogue* / Quittez ce module — Non → Quittez ce module

MODULE 2: TROUBLES ANXIEUX

TROUBLE PANIQUE

Si le(la) patient(e) a répondu NON à la question 21 (du questionnaire destiné au[à la] patient[e]), passez à la question 33.

18. Vous avez indiqué que vous avez eu une attaque d'anxiété ce mois-ci. Cela s'est-il déjà produit auparavant? **Oui** **Non** → **Passez à la question 33**

19. L'attaque arrive-t-elle quelquefois par surprise? **Si nécessaire, précisez:** C'est-à-dire quand vous ne vous attendez pas à vous sentir mal à l'aise ni nerveux(se)? **Oui** **Non** → **Passez à la question 33**

20. Craignez-vous grandement d'avoir une autre attaque ou qu'il y ait quelque chose qui cloche en vous? **Répondez OUI si cette crainte a déjà existé.** **Oui** **Non** → **Passez à la question 33**

Pensez à la dernière attaque grave que vous avez subie.

Passez à la question 32 dès que le(la) patient(e) a confirmé l'apparition de 4 des symptômes suivants pendant sa dernière attaque:

Avez-vous:

21. ☐ eu de la peine à respirer?
22. ☐ ressenti des palpitations?
23. ☐ ressenti une douleur ou une pression dans la poitrine?
24. ☐ transpiré abondamment?
25. ☐ eu l'impression de suffoquer?
26. ☐ eu des bouffées de chaleur ou des frissons?
27. ☐ eu de la nausée, un poids sur l'estomac, ou l'impression que vous alliez avoir la diarrhée?
28. ☐ eu une impression de vertige, d'instabilité ou que vous alliez perdre connaissance?
29. ☐ senti des picotements ou un engourdissement dans certaines parties de votre corps?
30. ☐ ressenti des tremblements?
31. ☐ eu peur de mourir?

32. **Avez-vous obtenu des réponses positives à 4 (au moins) des questions 21 à 31?** **Oui** → *Trouble panique* **Non** → *Trouble anxieux non spécifié par ailleurs*

ANXIÉTÉ GÉNÉRALISÉE

33. Pendant le mois écoulé, vous êtes-vous senti(e) nerveux(se), anxieux(se) ou irritable plus d'un jour sur deux? **Oui** **Non** → Passez à la question 44

Au cours du mois écoulé, avez-vous été souvent préoccupé(e) par un de ces problèmes:

34. ☐ Une telle agitation qu'il vous était difficile de rester assis(e)?

35. ☐ Une fatigabilité marquée?

36. ☐ Des tensions, des courbatures ou des douleurs musculaires?

37. ☐ Des difficultés d'endormissement, des réveils fréquents ou prématurés?

38. ☐ De la peine à vous concentrer, p.ex. pour lire ou regarder la TV?

39. ☐ Une plus grande facilité à être contrarié(e) ou irrité(e)?

40. **Avez-vous obtenu des réponses positive à 3 (au moins) des questions 34 à 39?** **Oui** **Non** → Passez à la question 44

41. Au cours du mois écoulé, ces problèmes vous ont-ils rendu le travail, l'entretien de la maison ou les contacts avec les autres plus difficiles? **Oui** **Non** → *Tr. anxieux non spécifié par ailleurs*; Passez à la question 45

42. Au cours des 6 derniers mois, vous êtes-vous fait beaucoup de souci pour diverses raisons?
Considérer la réponse comme positive seulement si le(la) patient(e) répond aussi OUI à: Cela a-t-il été le cas plus d'un jour sur deux pendant les 6 derniers mois? **Oui** **Non** → *Tr. anxieux non spécifié par ailleurs*; Passez à la question 45

43. Lorsque vous avez de telles préoccupations, constatez-vous que vous ne pouvez vous arrêter d'y penser? **Oui** → *Anxiété généralisée*; Passez à la question 45 **Non** → *Tr. anxieux non spécifié par ailleurs*; Passez à la question 45

44. **Avez-vous diagnostiqué un trouble panique ou un trouble anxieux non spécifié par ailleurs?** **Oui** **Non** → Quittez ce module

ANXIÉTÉ SECONDAIRE À UNE MALADIE PHYSIQUE OU À LA PRISE D'UN MÉDICAMENT OU D'UNE DROGUE

45. **Les symptômes anxieux actuels sont-ils probablement secondaires aux effets biologiques d'une maladie physique ou de la prise d'un médicament ou d'une drogue?**

Oui → *Possibilité de trouble anxieux dû à une maladie physique, un médicament ou un toxique* (Pas Certain); Quittez ce module **Non** → Quittez ce module

MODULE 3: TROUBLES LIÉS À L'ALCOOL

ABUS/DÉPENDANCE

Section A

En répondant à votre questionnaire, vous avez indiqué que:

Si le(la) patient(e) a répondu OUI à la question 22 du QP:	...vous pensez que vous devriez réduire votre consommation d'alcool. Pourquoi?
Si le(la) patient(e) a répondu OUI à la question 23 du QP:	...quelqu'un s'est plaint de votre consommation d'alcool. Qui? Pourquoi?
Si le(la) patient(e) a répondu OUI à la question 24 du QP:	...vous vous sentez coupable ou irrité(e) par votre consommation d'alcool. Pourquoi?
Si le(la) patient(e) a répondu OUI à la question 25 du QP:	....vous avez pris au moins 5 verres d'alcool en une seule journée au cours du mois écoulé. Combien de fois avez-vous bu autant au cours des 6 derniers mois? Cela vous a-t-il occasionné des difficultés?

Section B

Évaluez les questions 46 à 50 en 1) posant chaque question au(à la) patient(e); 2) considérant les réponses données ci-dessus; ou 3) vous basant sur des informations complémentaires à propos du(de la) patient(e), obtenues, par exemple, d'un membre de sa famille.

46. Un médecin vous a-t-il déjà suggéré d'arrêter de boire de l'alcool en raison d'un problème de santé?
Considérer la réponse comme positive si le(la) patient(e) a continué à boire pendant les 6 mois qui ont suivi la suggestion du médecin. **Oui** **Non**

Une des choses suivantes vous est-elle arrivée <u>à plus d'une reprise</u> dans les 6 derniers mois:

47. Avez-vous abusé de l'alcool ou eu la «gueule de bois» au travail, à l'école ou alors que vous assumiez d'autres responsabilités? **Oui** **Non**

48. Avez-vous manqué ou commencé en retard votre travail, l'école, ou d'autres charges en raison d'un abus d'alcool ou d'une «gueule de bois»? **Oui** **Non**

49. Avez-vous rencontré des difficultés relationnelles après avoir bu? **Oui** **Non**

50. Avez-vous conduit après avoir pris plusieurs verres ou en ayant trop bu? **Oui** **Non**

51. **Avez-vous obtenu au moins 1 OUI aux questions 46 à 50, OU la section A révèle-t-elle un problème d'alcool important au cours des 6 derniers mois?**

Oui → *Alcoolisme probable* / Quittez ce module

Non → Quittez ce module

MODULE 4: TROUBLES DE L'ALIMENTATION

BOULIMIE, COMPULSION ALIMENTAIRE

52. Mangez-vous souvent, en 2 heures environ, ce que la plupart des gens considéreraient comme une grande quantité de nourriture? **Oui** **Non** → Quittez ce module

53. Quand vous mangez ainsi, avez-vous souvent le sentiment de ne pas pouvoir contrôler la nature ou la quantité des aliments? **Oui** **Non** → Quittez ce module

54. Cela est-il arrivé, en moyenne, 2 fois par semaine au moins au cours des 3 derniers mois? **Oui** **Non** → Quittez ce module

55. Vous faites-vous souvent vomir, ou prenez-vous plus que le double de la dose recommandée de laxatifs pour éviter de d'engraisser après avoir mangé ainsi? **Oui** **Non** → Passez à la question 57

56. Cela vous est-il arrivé, en moyenne, au moins 2 fois par semaine, au cours des 3 derniers mois? **Oui** → *Boulimie, type expulsion* → Quittez ce module **Non**

57. Jeûnez-vous souvent—sans rien manger—pendant au moins 24 heures—ou faites-vous de l'exercice pendant plus d'une heure pour éviter d'engraisser après avoir mangé ainsi? **Oui** **Non** → *Trouble alimentaire compulsif* → Quittez ce module

58. Cela vous est-il arrivé, en moyenne, au moins 2 fois par semaine au cours des 3 derniers mois? **Oui** → *Boulimie, type sans expulsion* → Quittez ce module **Non** → *Trouble alimentaire compulsif* → Quittez ce module

MODULE 5: TROUBLES SOMATOFORMES

TROUBLE MULTISOMATOFORME

59. **Parmi les symptômes physiques cochés dans le questionnaire destiné au(à la) patient(e) (questions 1 à 15), y en a-t-il au moins trois de nature somatoforme: absence d'une cause physique adéquate pour expliquer leur gravité et l'incapacité qui en découle, en dépit d'un bilan raisonnable?**
Note: Si un trouble dépressif majeur ou un trouble panique est également présent, les symptômes physiques qui relèvent de ces entités ne sont pas considérés comme somatoformes (par exemple, les palpitations ou la dyspnée pour le trouble panique ou la fatigue et l'insomnie pour la dépression majeure).

Oui → **Non** → **Quittez ce module**

60. **Ce(cette) patient(e) a-t-il(elle) éprouvé ces symptômes mal expliqués pendant au moins quelques années?**

Oui → *Trouble multisomatoforme*

Non → *Trouble somato-forme non spécifié par ailleurs*

RÉSUMÉ

Patient(e): _____ **N° de dossier:** _____

Médecin: _____ **Date:** _____

RÉSUMÉ DES DIAGNOSTICS

Vérifiez tous les diagnostics posés dans chaque module. Les codes CIM-9 apparaissent entre parenthèses.

☐ Aucun diagnostic

Troubles de l'humeur

☐ Trouble dépressif majeur (296.20)
☐ Rémission partielle d'un trouble dépressif majeur (296.25)
☐ Dysthymie (300.4)
☐ Trouble dépressif mineur (311)
☐ Trouble bipolaire (diagnostic provisoire) (Si confirmé: 296.50)
☐ Trouble dépressif dû à une maladie physique, à un médicament ou à une drogue (diagnostic provisoire)
(Si confirmé, et dû à une maladie physique: 293.83)
(Si confirmé, et dû à un médicament ou à une drogue: 292.84)

Troubles anxieux

☐ Trouble panique (300.01)
☐ Anxiété généralisée (300.02)
☐ Trouble anxieux non spécifié par ailleurs (300.00)
☐ Trouble anxieux dû à une maladie physique, à un médicament ou à une drogue (diagnostic provisoire)
(Si confirmé et dû à une maladie physique: 293.89)
(Si confirmé et dû à un médicament ou à une drogue: 292.89)

Troubles lié à l'alcool

☐ Alcoolisme probable
(Si abus d'alcool confirmé: 305.00)
(Si dépendance à l'alcool confirmée: 303.90)

Troubles de l'alimentation

☐ Trouble alimentaire compulsif (frénésie alimentaire) (307.50)
☐ Boulimie, type à expulsion (307.51)
☐ Boulimie, type sans expulsion (307.51)

Troubles somatoformes

☐ Trouble multisomatoforme (300.7)
☐ Trouble somatoforme non spécifié par ailleurs (300.7)

Appendix C:

Beck Depression Inventory-II (BDI-II)

BDI®-II

Date: _____
année / mois / jour

Nom _____ Situation de famille ___ ☐ marié(e) ☐ vivant maritalement ☐ divorcé(e) ☐ veuf(ve) ☐ séparé(e) ☐ célibataire

Âge ____ Sexe ___ ☐M ☐F Profession _____ Niveau d'études _____

Consigne: Ce questionnaire comporte 21 groupes d'énoncés. Veuillez lire avec soin chacun de ces groupes puis, dans chaque groupe, choisissez **l'énoncé** qui décrit le mieux comment vous vous êtes senti(e) **au cours des deux dernières semaines, incluant aujourd'hui.** Encerclez alors le chiffre placé devant l'énoncé que vous avez choisi. Si, dans un groupe d'énoncés, vous en trouvez plusieurs qui semblent décrire également bien ce que vous ressentez, choisissez celui qui a le chiffre le plus élevé et encerclez ce chiffre. Assurez-vous bien de ne choisir qu'**un seul** énoncé dans chaque groupe, y compris le groupe n° 16 (modifications dans les habitudes de sommeil) et le groupe n° 18 (modifications de l'appétit).

1 Tristesse
0 Je ne me sens pas triste.
1 Je me sens très souvent triste.
2 Je suis tout le temps triste.
3 Je suis si triste ou si malheureux(se), que ce n'est pas supportable.

2 Pessimisme
0 Je ne suis pas découragé(e) face à mon avenir.
1 Je me sens plus découragé(e) qu'avant face à mon avenir.
2 Je ne m'attends pas à ce que les choses s'arrangent pour moi.
3 J'ai le sentiment que mon avenir est sans espoir et qu'il ne peut qu'empirer.

3 Échecs dans le passé
0 Je n'ai pas le sentiment d'avoir échoué dans la vie, d'être un(e) raté(e).
1 J'ai échoué plus souvent que je n'aurais dû.
2 Quand je pense à mon passé, je constate un grand nombre d'échecs.
3 J'ai le sentiment d'avoir complètement raté ma vie.

4 Perte de plaisir
0 J'éprouve toujours autant de plaisir qu'avant aux choses qui me plaisent.
1 Je n'éprouve pas autant de plaisir aux choses qu'avant.
2 J'éprouve très peu de plaisir aux choses qui me plaisaient habituellement.
3 Je n'éprouve aucun plaisir aux choses qui me plaisaient habituellement.

5 Sentiments de culpabilité
0 Je ne me sens pas particulièrement coupable.
1 Je me sens coupable pour bien des choses que j'ai faites ou que j'aurais dû faire.
2 Je me sens coupable la plupart du temps.
3 Je me sens tout le temps coupable.

6 Sentiment d'être puni(e)
0 Je n'ai pas le sentiment d'être puni(e).
1 Je sens que je pourrais être puni(e).
2 Je m'attends à être puni(e).
3 J'ai le sentiment d'être puni(e).

7 Sentiments négatifs envers soi-même
0 Mes sentiments envers moi-même n'ont pas changé.
1 J'ai perdu confiance en moi.
2 Je suis déçu(e) par moi-même.
3 Je ne m'aime pas du tout.

8 Attitude critique envers soi
0 Je ne me blâme pas ou ne me critique pas plus que d'habitude.
1 Je suis plus critique envers moi-même que je ne l'étais.
2 Je me reproche tous mes défauts.
3 Je me reproche tous les malheurs qui arrivent.

9 Pensées ou désirs de suicide
0 Je ne pense pas du tout à me suicider.
1 Il m'arrive de penser à me suicider, mais je ne le ferais pas.
2 J'aimerais me suicider.
3 Je me suiciderais si l'occasion se présentait.

Verso

_____ Sous-total, page 1

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10 Pleurs

0 Je ne pleure pas plus qu'avant.
1 Je pleure plus qu'avant.
2 Je pleure pour la moindre petite chose.
3 Je voudrais pleurer mais je n'en suis pas capable.

11 Agitation

0 Je ne suis pas plus agité(e) ou plus tendu(e) que d'habitude.
1 Je me sens plus agité(e) ou plus tendu(e) que d'habitude.
2 Je suis si agité(e) ou tendu(e) que j'ai du mal à rester tranquille.
3 Je suis si agité(e) ou tendu(e) que je dois continuellement bouger ou faire quelque chose.

12 Perte d'intérêt

0 Je n'ai pas perdu d'intérêt pour les gens ou pour les activités.
1 Je m'intéresse moins qu'avant aux gens et aux choses.
2 Je ne m'intéresse presque plus aux gens et aux choses.
3 J'ai du mal à m'intéresser à quoi que ce soit.

13 Indécision

0 Je prends des décisions toujours aussi bien qu'avant.
1 Il m'est plus difficile que d'habitude de prendre des décisions.
2 J'ai beaucoup plus de mal qu'avant à prendre des décisions.
3 J'ai du mal à prendre n'importe quelle décision.

14 Dévalorisation

0 Je pense être quelqu'un de valable.
1 Je ne crois pas avoir autant de valeur ni être aussi utile qu'avant.
2 Je me sens moins valable que les autres.
3 Je sens que je ne vaux absolument rien.

15 Perte d'énergie

0 J'ai toujours autant d'énergie qu'avant.
1 J'ai moins d'énergie qu'avant.
2 Je n'ai pas assez d'énergie pour pouvoir faire grand-chose.
3 J'ai trop peu d'énergie pour faire quoi que ce soit.

16 Modifications dans les habitudes de sommeil

0 Mes habitudes de sommeil n'ont pas changé.

1a Je dors un peu plus que d'habitude.
1b Je dors un peu moins que d'habitude.

2a Je dors beaucoup plus que d'habitude.
2b Je dors beaucoup moins que d'habitude.

3a Je dors presque toute la journée.
3b Je me réveille une ou deux heures plus tôt et je suis incapable de me rendormir.

17 Irritabilité

0 Je ne suis pas plus irritable que d'habitude.
1 Je suis plus irritable que d'habitude.
2 Je suis beaucoup plus irritable que d'habitude.
3 Je suis constamment irritable.

18 Modifications de l'appétit

0 Mon appétit n'a pas changé.

1a J'ai un peu moins d'appétit que d'habitude.
1b J'ai un peu plus d'appétit que d'habitude.

2a J'ai beaucoup moins d'appétit que d'habitude.
2b J'ai beaucoup plus d'appétit que d'habitude.

3a Je n'ai pas d'appétit du tout.
3b J'ai constamment envie de manger.

19 Difficulté à se concentrer

0 Je parviens à me concentrer toujours aussi bien qu'avant.
1 Je ne parviens pas à me concentrer aussi bien que d'habitude.
2 J'ai du mal à me concentrer longtemps sur quoi que ce soit.
3 Je me trouve incapable de me concentrer sur quoi que ce soit.

20 Fatigue

0 Je ne suis pas plus fatigué(e) que d'habitude.
1 Je me fatigue plus facilement que d'habitude.
2 Je suis trop fatigué(e) pour faire un grand nombre de choses que je faisais avant.
3 Je suis trop fatigué(e) pour faire la plupart des choses que je faisais avant.

21 Perte d'intérêt pour le sexe

0 Je n'ai pas noté de changement récent dans mon intérêt pour le sexe.
1 Le sexe m'intéresse moins qu'avant.
2 Le sexe m'intéresse beaucoup moins maintenant.
3 J'ai perdu tout intérêt pour le sexe.

Sous-total, page 2

Sous-total, page 1

Score total

BDI-II

Date:

Name: _____ Marital Status: _____ Age: _____ Sex: _____

Occupation: _____ Education: _____

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness

0 I do not feel sad.
1 I feel sad much of the time.
2 I am sad all the time.
3 I am so sad or unhappy that I can't stand it.

2. Pessimism

0 I am not discouraged about my future.
1 I feel more discouraged about my future than I used to be.
2 I do not expect things to work out for me.
3 I feel my future is hopeless and will only get worse.

3. Past Failure

0 I do not feel like a failure.
1 I have failed more than I should have.
2 As I look back, I see a lot of failures.
3 I feel I am a total failure as a person.

4. Loss of Pleasure

0 I get as much pleasure as I ever did from the things I enjoy.
1 I don't enjoy things as much as I used to.
2 I get very little pleasure from the things I used to enjoy.
3 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings

0 I don't feel particularly guilty.
1 I feel guilty over many things I have done or should have done.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6. Punishment Feelings

0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.

7. Self-Dislike

0 I feel the same about myself as ever.
1 I have lost confidence in myself.
2 I am disappointed in myself.
3 I dislike myself.

8. Self-Criticalness

0 I don't criticize or blame myself more than usual.
1 I am more critical of myself than I used to be.
2 I criticize myself for all of my faults.
3 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes

0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10. Crying

0 I don't cry anymore than I used to.
1 I cry more than I used to.
2 I cry over every little thing.
3 I feel like crying, but I can't.

_____ Subtotal Page 1

Continued on Back

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11. Agitation

0 I am no more restless or wound up than usual.

1 I feel more restless or wound up than usual.

2 I am so restless or agitated that it's hard to stay still.

3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

0 I have not lost interest in other people or activities.

1 I am less interested in other people or things than before.

2 I have lost most of my interest in other people or things.

3 It's hard to get interested in anything.

13. Indecisiveness

0 I make decisions about as well as ever.

1 I find it more difficult to make decisions than usual.

2 I have much greater difficulty in making decisions than I used to.

3 I have trouble making any decisions.

14. Worthlessness

0 I do not feel I am worthless.

1 I don't consider myself as worthwhile and useful as I used to.

2 I feel more worthless as compared to other people.

3 I feel utterly worthless.

15. Loss of Energy

0 I have as much energy as ever.

1 I have less energy than I used to have.

2 I don't have enough energy to do very much.

3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0 I have not experienced any change in my sleeping pattern.

1a I sleep somewhat more than usual.

1b I sleep somewhat less than usual.

2a I sleep a lot more than usual.

2b I sleep a lot less than usual.

3a I sleep most of the day.

3b I wake up 1–2 hours early and can't get back to sleep.

17. Irritability

0 I am no more irritable than usual.

1 I am more irritable than usual.

2 I am much more irritable than usual.

3 I am irritable all the time.

18. Changes in Appetite

0 I have not experienced any change in my appetite.

1a My appetite is somewhat less than usual.

1b My appetite is somewhat greater than usual.

2a My appetite is much less than before.

2b My appetite is much greater than usual.

3a I have no appetite at all.

3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.

1 I can't concentrate as well as usual.

2 It's hard to keep my mind on anything for very long.

3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.

1 I get more tired or fatigued more easily than usual.

2 I am too tired or fatigued to do a lot of the things I used to do.

3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

0 I have not noticed any recent change in my interest in sex.

1 I am less interested in sex than I used to be.

2 I am much less interested in sex now.

3 I have lost interest in sex completely.

2 3 4 5 6 7 8 9 10 11 12 A B C D E

_____ Subtotal Page 2

_____ Subtotal Page 1

Appendix D:

Cook-Medley Hostility Inventory (CMHO)

DIRECTIONS : Pensez à la façon dont chaque énoncé suivant s'applique à vos croyances et /ou comportements. Indiquez si l'énoncé est plutôt **vrai** ou **faux** selon vous, en encerclant la réponse. S.V.P., répondre à **tous** les énoncés.

1. Dans un nouvel emploi, j'essaie d'avoir des indices sur les personnes importantes à côtoyer.	V	F
2. Lorsque quelqu'un me fait du tort, je sens que je devrais me venger, si possible, uniquement par principe.	V	F
3. Je préfère ne pas aborder en premier les gens que je n'ai pas vus depuis longtemps.	V	F
4. J'ai souvent dû obéir à des gens qui n'en savaient pas autant que moi.	V	F
5. Je crois que nombre de gens exagèrent leurs malheurs pour s'attirer la sympathie et l'aide des autres.	V	F
6. Il faut apporter beaucoup d'arguments pour convaincre la plupart des gens de la vérité.	V	F
7. Je crois que la plupart des gens mentiraient pour réussir.	V	F
8. Quelqu'un m'en veut.	V	F
9. La plupart des membres de ma famille sympathisent avec moi.	V	F
10. La plupart des gens sont honnêtes surtout parce qu'ils ont peur de se faire prendre.	V	F
11. La plupart des gens vont employer des moyens quelque peu malhonnêtes pour obtenir un gain ou un avantage plutôt que de le perdre.	V	F
12. Lorsqu'une personne est gentille avec moi, je me demande souvent quels sont ses véritables motifs.	V	F
13. Quand je travaille sur quelque chose d'important, cela m'impatiente que les gens me demandent conseil ou m'interrompent.	V	F
14. Je crois avoir été souvent puni(e) sans raison.	V	F
15. Je suis contre le fait de donner de l'argent aux mendiants.	V	F
16. Certains membres de ma famille ont des habitudes qui m'agacent et m'ennuient profondément.	V	F
17. Ma façon de faire est souvent mal comprise par les autres.	V	F
18. Je peux être ami(e) avec des gens qui commettent des actions que je considère mauvaises.	V	F
19. Je ne blâme personne d'essayer de s'approprier tout ce qu'on peut en ce bas monde.	V	F
20. Les gens se soucient peu de ce qui vous arrive.	V	F
21. Il est plus sûr de ne se fier à personne.	V	F
22. Je ne blâme pas quelqu'un qui profite d'un autre qui se laisse faire.	V	F

23. J'ai souvent senti que des inconnus me regardaient de façon critique.	V	F
24. La plupart des gens se font des amis parce que ces amis leur seront probablement utiles.	V	F
25. Je suis sûr(e) qu'on parle de moi.	V	F
26. Je ne suis pas porté(e) à parler aux autres avant qu'ils ne l'aient fait d'abord.	V	F
27. Dans leur for intérieur, la plupart des gens détestent se déranger pour aider les autres.	V	F
28. J'ai tendance à être sur mes gardes avec les gens qui sont plus sympathiques que ce à quoi je m'attendais.	V	F
29. Les gens me déçoivent souvent.	V	F
30. J'ai souvent rencontré de supposés experts qui n'étaient pas meilleurs que moi.	V	F
31. Je me sens comme un(e) raté(e) lorsque j'apprends qu'une personne que je connais bien a du succès.	V	F
32. Je ne me fâche pas facilement.	V	F
33. En général, les gens exigent plus de respect de leurs propres droits qu'ils ne sont prêts à en accorder à ceux des autres.	V	F
34. Je suis très souvent exclu(e) des conversations et du bavardage de mon entourage.	V	F
35. Souvent les gens sont jaloux de mes bonnes idées parce qu'ils n'y ont pas pensé en premier.	V	F
36. J'ai quelques fois évité une personne parce que j'avais peur de dire ou faire des choses que j'aurais pu regretter par la suite.	V	F
37. J'éprouverais certainement du plaisir à battre un escroc à son propre jeu.	V	F
38. J'ai dû parfois être brutal(e) avec des gens grossiers ou importuns.	V	F
39. Je déteste certaines personnes au point de me sentir heureux(se) intérieurement lorsqu'elles sont punies pour ce qu'elles ont fait.	V	F
40. Je suis souvent porté(e) à fournir des efforts pour faire triompher mon point de vue contre mes adversaires.	V	F
41. L'homme qui s'est surtout occupé de moi durant mon enfance (père, beau-père) était très strict.	V	F
42. J'aime laisser les gens deviner ce que je vais faire.	V	F
43. Quand un homme se trouve avec une femme, il pense habituellement à des aspects reliés à sa sexualité.	V	F
44. Je ne tente pas de cacher à une personne la piètre opinion que j'ai d'elle ou la pitié qu'elle m'inspire.	V	F
45. Règle générale, je défends énergiquement mes opinions.	V	F

46. Je demande souvent l'avis des gens.	V	F
47. J'ai souvent travaillé pour des gens qui s'appropriaient le crédit du bon travail et attribuaient les erreurs à leurs subordonnés.	V	F
48. Les gens peuvent facilement me faire changer d'idée même si je croyais avoir une opinion bien arrêtée.	V	F
49. Parfois, je suis sûr(e) que les gens peuvent deviner ce que je pense.	V	F
50. Un grand nombre de gens sont coupables de mauvaise conduite sexuelle.	V	F

DIRECTIONS : Read each statement and decide whether it is true as applied to you or false as applied to you. If the statement is **TRUE** or MOSTLY TRUE, circle the (**T**). If it is **FALSE** or NOT USUALLY TRUE, circle the (**F**). Remember to give your own opinion of yourself. Please answer **every statement.**

1. When I take a new job, I like to be tipped off on who should be gotten next to.	**T**	**F**
2. When someone does me wrong, I feel I should pay him back if I can, just for the principle of the thing.	**T**	**F**
3. I prefer to pass by school friends or people I know but have not seen for a long time, unless they speak to me first.	**T**	**F**
4. I have often had to take orders from someone who did not know as much as I did.	**T**	**F**
5. I think a great many people exaggerate their misfortunes in order to gain the sympathy and help of others.	**T**	**F**
6. It takes a lot of argument to convince most people of the truth.	**T**	**F**
7. I think most people would lie to get ahead.	**T**	**F**
8. Someone has it in for me.	**T**	**F**
9. My relatives are nearly all in sympathy with me.	**T**	**F**
10. Most people are honest chiefly through fear of being caught.	**T**	**F**
11. Most people will use somewhat unfair means to gain profit or an advantage.	**T**	**F**
12. I commonly wonder what hidden reason another person may have for doing something nice for me.	**T**	**F**
13. It makes me impatient to have people ask my advice or otherwise interrupt me when I am working on something important.	**T**	**F**
14. I feel that I have often been punished without cause.	**T**	**F**
15. I am against giving money to beggars.	**T**	**F**
16. Some of my family have habits that bother me and annoy me very much.	**T**	**F**
17. My way of doing things is apt to be misunderstood by others.	**T**	**F**
18. I can be friendly with people who do things which I consider wrong.	**T**	**F**
19. I don't blame anyone for trying to grab everything he can get in this world.	**T**	**F**
20. No one cares much what happens to you.	**T**	**F**
21. It is safer to trust nobody.	**T**	**F**
22. I don't blame a person for taking advantage of someone who lays himself open to it.	**T**	**F**
23. I have often felt that strangers were looking at me critically.	**T**	**F**

24. Most people make friends because friends are likely to be useful to them.	**T**	**F**
25. I am sure I am being talked about.	**T**	**F**
26. I am not likely to speak to people until they speak to me.	**T**	**F**
27. Most people inwardly dislike putting themselves out to help other people.	**T**	**F**
28. I tend to be on my guard with people who are somewhat more friendly than I had expected.	**T**	**F**
29. People often disappoint me.	**T**	**F**
30. I have often met people who were supposed to be experts who were no better than I.	**T**	**F**
31. It makes me feel like a failure when I hear of the success of someone I know well.	**T**	**F**
32. I am not easily angered.	**T**	**F**
33. People generally demand more respect for their own rights than they are willing to give others.	**T**	**F**
34. I am quite often not « in » on the gossip and talk of the group I belong to.	**T**	**F**
35. I have often found people jealous of my good ideas, just because they had not thought of them first.	**T**	**F**
36. I have sometimes stayed away from another person because I feared doing or saying something that I might regret afterwards.	**T**	**F**
37. I would certainly enjoy beating a crook at his own game.	**T**	**F**
38. I have at times had to be rough with people who were rude or annoying.	**T**	**F**
39. There are certain people whom I dislike so much that I am inwardly pleased when they are caught for something they have done.	**T**	**F**
40. I am often inclined to go out of my way to win a point with someone who has opposed me.	**T**	**F**
41. The man who had most to do with me when I was a child (such as my father, stepfather, etc.) was very strict with me.	**T**	**F**
42. I like to keep people guessing about what I'm going to do next.	**T**	**F**
43. When a man is with a woman he is usually thinking about things related to her sexuality.	**T**	**F**
44. I do not try to cover up my poor opinion or pity of a person so that he won't know how I feel.	**T**	**F**
45. I strongly defend my opinions as a rule.	**T**	**F**
46. I frequently ask people for advice.	**T**	**F**
47. I have frequently worked under people who seem to have things arranged so that they get credit for good work but are able to pass off mistakes onto those under them.	**T**	**F**

48. People can pretty easily change me even though I thought that my mind was already made up on a subject.	**T**	**F**
49. Sometimes I am sure that other people can tell what I am thinking.	**T**	**F**
50. A large number of people are guilty of bad sexual conduct.	**T**	**F**

Appendix E:

State-Trait Anxiety Inventory (STAI)

QUESTIONNAIRE D'ÉVALUATION PERSONNELLE (IASTA)

Nom: _____ **Date:** _____

A) Vous trouverez ci-dessous un certain nombre d'énoncés que les gens ont déjà utilisés pour se décrire. Lisez chaque énoncé, puis en encerclant le chiffre approprié à droite de l'énoncé, indiquez comment vous vous sentez maintenant, c'est-à-dire à ce moment précis. Il n'y a pas de bonnes ou de mauvaises réponses. Ne vous attardez pas trop longtemps sur un énoncé ou l'autre mais donnez la réponse qui vous semble décrire le mieux les sentiments que vous éprouvez présentement.

		Pas du tout	Un peu	Modérément	Beaucoup
1.	Je me sens calme.	1	2	3	4
2.	Je me sens en sécurité.	1	2	3	4
3.	Je suis tendu(e).	1	2	3	4
4.	Je me sens surmené(e).	1	2	3	4
5.	Je me sens tranquille.	1	2	3	4
6.	Je me sens bouleversé(e).	1	2	3	4
7.	Je suis préoccupé(e) actuellement par des malheurs possibles.	1	2	3	4
8.	Je me sens comblé(e).	1	2	3	4
9.	Je me sens effrayé(e).	1	2	3	4
10.	Je me sens à l'aise.	1	2	3	4
11.	Je me sens sûr(e) de moi.	1	2	3	4
12.	Je me sens nerveux(se).	1	2	3	4
13.	Je suis affolé(e).	1	2	3	4
14.	Je me sens indécis(e).	1	2	3	4
15.	Je suis détendu(e).	1	2	3	4
16.	Je me sens satisfait(e).	1	2	3	4
17.	Je suis préoccupé(e).	1	2	3	4
18.	Je me sens tout mêlé(e).	1	2	3	4
19.	Je sens que j'ai les nerfs solides.	1	2	3	4
20.	Je me sens bien.	1	2	3	4

B) Vous trouverez ci-dessous un certain nombre d'énoncés qui ont déjà été utilisés par les gens pour se décrire. Lisez chaque énoncé, puis en encerclant le chiffre approprié à droite de l'énoncé, indiquez comment vous vous sentez en général. Il n'y a pas de bonnes ou de mauvaises réponses. Ne vous attardez pas trop longtemps sur un énoncé ou l'autre mais donnez la réponse qui vous semble décrire le mieux les sentiments que vous éprouvez en général.

		Presque jamais	Quelquefois	Souvent	Presque toujours
21.	Je me sens bien.	1	2	3	4
22.	Je me sens nerveux(se) et agité(e).	1	2	3	4
23.	Je me sens content(e) de moi-même.	1	2	3	4
24.	Je voudrais être aussi heureux(se) que les autres semblent l'être.	1	2	3	4
25.	J'ai l'impression d'être un(e) raté(e).	1	2	3	4
26.	Je me sens reposé(e).	1	2	3	4
27.	Je suis d'un grand calme.	1	2	3	4
28.	Je sens que les difficultés s'accumulent au point où je n'arrive pas à les surmonter.	1	2	3	4
29.	Je m'en fais trop pour des choses qui n'en valent pas vraiment la peine.	1	2	3	4
30.	Je suis heureux(se).	1	2	3	4
31.	J'ai des pensées troublantes.	1	2	3	4
32.	Je manque de confiance en moi.	1	2	3	4
33.	Je me sens en sécurité.	1	2	3	4
34.	Prendre des décisions m'est facile.	1	2	3	4
35.	Je sens que je ne suis pas à la hauteur de la situation.	1	2	3	4
36.	Je suis satisfait(e).	1	2	3	4
37.	Des idées sans importance me passent par la tête et me tracassent.	1	2	3	4
38.	Je prends les désappointements tellement à coeur que je n'arrive pas à les chasser de mon esprit.	1	2	3	4
39.	Je suis une personne qui a les nerfs solides.	1	2	3	4
40.	Je deviens tendu(e) ou bouleversé(e) quand je songe à mes préoccupations et à mes intérêts récents.	1	2	3	4

Développé par Charles D. Spielberger, en collaboration avec R.L. Gorsuch, R. Lushene, P.R. Vagg, et G.A. Jacobs. Traduit et adapté par Janel G. Gauthier en collaboration avec Stéphane Bouchard.

	almost never	some-times	often	almost always
1. I feel pleasant.	1	2	3	4
2. I feel nervous and restless.	1	2	3	4
3. I feel satisfied with myself.	1	2	3	4
4. I wish I could be as happy as others seem to be.	1	2	3	4
5. I feel like a failure.	1	2	3	4
6. I feel rested.	1	2	3	4
7. I am « calm, cool, and collected ».	1	2	3	4
8. I feel that difficulties are piling up so that I cannot overcome them.	1	2	3	4
9. I worry too much over something that really doesn't matter.	1	2	3	4
10. I am happy.	1	2	3	4
11. I have disturbing thoughts.	1	2	3	4
12. I lack self-confidence.	1	2	3	4
13. I feel secure.	1	2	3	4
14. I make decisions easily.	1	2	3	4
15. I feel inadequate.	1	2	3	4
16. I am content.	1	2	3	4
17. Some unimportant thought runs through my mind and bothers me.	1	2	3	4
18. I take disappointments so keenly that I can't put them out of my mind.	1	2	3	4
19. I am a steady person.	1	2	3	4
20. I get in a state of tension or turmoil as I think over my recent concerns and interests.	1	2	3	4

Appendix F:

State-Trait Anger Inventory (STAXI)

Questionnaire d'auto-analyse

DIRECTIONS : Voici une série d'énoncés que les gens utilisent fréquemment pour se décrire. Veuillez lire chaque énoncé et encercler le chiffre correspondant à la façon dont vous vous sentez habituellement. Il n'y a pas de bonne ou de mauvaise réponse. Ne vous attardez pas sur les énoncés et répondez en fonction de **votre façon habituelle de vous sentir**.

	presque jamais	quelque-fois	souvent	presque toujours
1. Je suis soupe-au-lait.	1	2	3	4
2. Je suis contrarié(e) lorsqu'on me corrige ou me punit.	1	2	3	4
3. Je suis une personne impétueuse.	1	2	3	4
4. J'ai un tempérament enflammé.	1	2	3	4
5. Je me sens en colère.	1	2	3	4
6. Je me sens irrité(e).	1	2	3	4
7. Je me fâche lorsque je suis ralenti(e) par les erreurs des autres.	1	2	3	4
8. Je suis contrarié(e) lorsque je n'obtiens pas de reconnaissance pour un travail bien fait.	1	2	3	4
9. Je m'emporte.	1	2	3	4
10. Lorsque je me mets en colère, je dis des choses désagréables.	1	2	3	4
11. Je suis irrité(e) par les gens qui croient toujours avoir raison.	1	2	3	4
12. Quand je suis frustré(e), j'ai le goût de frapper quelqu'un.	1	2	3	4
13. Je suis furieux(se) lorsque je fais un bon travail et n'en récolte qu'une évaluation médiocre.	1	2	3	4
14. Je me sens bouillir lorsque je suis sous pression.	1	2	3	4
15. Ça me rend furieux(se) lorsque je suis critiqué(e) devant les gens.	1	2	3	4

DIRECTIONS : A number of statements wich people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you generally feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer wich seems to describe how you **generally feel**.

	almost never	some-times	often	almost always
1. I am quick tempered.	1	2	3	4
2. I get annoyed when I am singled out for correction.	1	2	3	4
3. I am a hotheaded person	1	2	3	4
4. I have a fiery temper.	1	2	3	4
5. I feel angry.	1	2	3	4
6. I feel irritated.	1	2	3	4
7. I get angry when I'm slowed down by others' mistakes.	1	2	3	4
8. I feel annoyed when I am not given recognition for doing good work.	1	2	3	4
9. I fly off the handle.	1	2	3	4
10. When I get mad, I say nasty things.	1	2	3	4
11. People who think they are always right irritate me.	1	2	3	4
12. When I get frustrated, I feel like hitting someone.	1	2	3	4
13. I feel infuriated when I do a good job and get a poor evaluation.	1	2	3	4
14. It makes my blood boil when I am pressured.	1	2	3	4
15. It makes me furious when I am criticized in front of others.	1	2	3	4

Appendix G:

Anxiety Disorder Interview Schedule for DSM-IV (ADIS-IV)

Nom: _____ **Date:** _____

No. Dossier: _____ **Évaluateur:** _____

ADIS-IV Condensé

Trouble panique

1) Présence actuelle de poussées d'anxiété soudaine très intense - impression que quelque chose de grave va se produire? Attaque la plus récente?

2) Quelles situations?Inattentues et spontanées?

3) Combien de temps avant que l'anxiété devienne intense (moins de 10 min.)?

4) Combien de temps dure l'anxiété à son niveau plus élevé?

5) Symptômes ressentis: encercler symptômes pertinents et coter sévérité de 0 à 8

Symptômes	Sévérité
a) souffle court ou sensation d'étouffement b) étranglement c) palpitations d) douleur thoracique e) transpiration abondante f) étourdissement, vertige, perte d'équilibre g) nausée, maux de ventre h) dépersonnalisation / irréalité i) engourdissement, picotements j) bouffées de chaleur / frissons k) tremblements / tension musculaire l) peur de mourir m) peur de devenir fou / perdre le contrôle n) autres:	

- Ressentis à chaque attaque de panique ou non? Présence d'attaques à symptômes limités (mini-crises)? Spécifier symptômes des attaques limitées (moins de 4 symptômes).

6) Nombre d'attaques au cours du dernier mois / des 6 derniers mois?

7) Anticipation à propos d'autres paniques au cours du dernier mois? Sévérité actuelle de l'anticipation 0-8?

8) Événements anticipés à la suite d'une attaque de panique: crise cardiaque, étouffement, mourir, devenir fou, perdre le contrôle, s'évanouir, tomber, avoir l'air fou, devenir paralysé ou aveugle?

9) Changements dans le comportement résultant des crises (évitement, fuite, sensibilité interoceptive, comportements sécurisants, distraction, changement style de vie)? Coter détresse et interférence de 0 à 8.

10) Histoire de la première attaque de panique: quand, où, comment, avec qui, stresseurs à l'époque, substance psychoactive, comment a-t-elle réagi?

11) Quand est-ce devenu un problème?

12) Déclencheurs actuels des attaques de panique?

10) Actuellement, comment faites-vous face à vos attaques?

Impression clinique - présence du trouble? OUI NON

Agoraphobie:

1) Présence d'évitement de certaines situations par crainte de paniquer / de ressentir des malaises? Occasion la plus récente? Anticipation de ces situations? Symptômes redoutés?

2) Situations problématiques: encercler situations pertinentes et coter appréhension et évitement de 0 à 8 (coter seulement situations relatives à l'agoraphobie)

Situation	Appréhension	Évitement	Commentaires
a) conduire ou aller en automobile			
b) épicerie			
c) centre d'achat			
d) foule			
e) transports en commun			
f) avion			
g) médecin / dentiste			
h) coiffeur			
i) attendre en ligne			
j) marcher à l'extérieur			
k) ponts			
l) être à la maison seul			
m) s'éloigner de chez soi			
n) cinéma / théâtre			
o) restaurants			
p) église			
q) espaces clos et petits			
r) espaces vastes			
s) travail			
t) autres:			

3) Comportements sécurisants: besoin d'être accompagné? transporter objets? évitement des heures d'achalandage?

4) Conséquences sur le fonctionnement quotidien (travail, vie social, activités routinières)? Coter détresse et interférence de l'évitement de 0 à 8.

5) Date d'apparition de l'évitement agoraphobique?

Impression clinique - présence du trouble? OUI NON

Phobie sociale:

1) Dans les situations sociales où vous pouvez être observé ou évalué par les autres, vous sentez-vous anxieux(se)? Incident le plus récent?

- Etes -vous préoccupé par le fait de pouvoir faire ou dire des chose embarrassantes ou humiliantes devant les autres et d'être jugé négativement?

2) Situations problématiques: encercler situations pertinentes reliées à l'anxiété sociale et coter crainte et évitement de 0 à 8.

Situations	Crainte	Évitement	Commentaires
a) rencontres sociales b) réunions / cours c) parler formellement devant un groupe d) parler à des inconnus e) manger en public f) utiliser les toilettes publiques g) écrire en public h) rendez-vous galant i) parler à une personne en position d'autorité j) vous affirmer k) initier une conversation l) maintenir une conversation m) autres:			

3) Que craignez-vous dans ces situations?

4) Etes-vous anxieux presque à chaque fois que vous y faites face?

5) Anxiété apparait avant d'entrer? au moment d'entrer dans la situation? avec délai? innatendue?

6) Crainte d'y faire une attaque de panique? Présence d'attaques de panique actuelles ou antérieures? (Voir liste de symptômes de panique à la première page et relever symptômes pertinents et leur sévérité de 0 à 8.). Si oui, la phobie sociale était-elle présente avant l'apparition des attaques de panique?

7) Conséquences sur le fonctionnement quotidien (travail, routine, vie sociale)? Influence sur la vie professionnelle ou académique? Coter degré de détresse et d'interférence de 0 à 8.

8) Début du problème à un niveau sévère?

9) Facteurs ayant pu entraîner le problème?

Impression clinique - présence du trouble? OUI NON

Quel est le degré de difficulté posé par les activités suivantes ?

Pour chaque cote : a) Degré de difficulté subjectif
b) Degré d'évitement habituel

A)

1	2	3	4	5
Facile, aucun malaise	Un peu de malaise	Anxiété	Beaucoup de difficulté	Extrêmement difficile

B)

1	2	3	4	5
En général le fait	Le fait si circonstances favorables	Fait si mis en situation	Evite autant que possible	Evite toujours

	INTERPERSONNEL												IMPERSONNEL
	Couple		Intimité		Rel. sociale		Famille		Travail		Étrangère en fonction (ex.: caissière, taxi...)		Commentaire (spécifier)
	A	B	A	B	A	B	A	B	A	B	A	B	
CONVERSATION (participer, poser questions, raconter histoires, donner opinion)													
DEVOILEMENT (parler de soi, se confier, paler des problèmes)													
EXPRESSIONS NÉGATIVES (désaccord, critique)													
EXPRESSIONS POSITIVES (appréciation, affection, compliment)													
AFFIRMATION (refuser des demandes, faire des demandes)													
ATTITUDE AMICALE (être concerté pour les autres, faire des suggestions,offrir son aide													

Trouble d'anxiété généralisée

1) Présence d'inquiétude excessive au cours des derniers mois à propos de plusieurs événements ou aspects de la vie quotidienne? Occasion la plus récente

2) Qu'est-ce qui vous inquiète?

3) Sujets d'inquiétude: encercler situations pertinentes et coter à quel point l'inquiétude est fréquente, excessive et difficile à contrôler (incapable d'arrêter, aspect intrusif) de 0 à 8.

Sujet d'inquiétude	Fréquence	Excessif	Diff. contrôle	Commentaires
a) affaires mineures b) travail / études c) famille d) finances e) social / interpersonnel f) santé (soi) g) santé (proches) h) communauté / affaires mondiales i) autres:				

4) Fréquence de l'inquiétude au cours des 6 derniers mois (presque à tous les jours / % de la journée / nombre d'heures par jour)?

5) Est-ce que votre entourage trouve que vous vous inquiétez de façon excessive? Est-ce que quelqu'un vivant les mêmes situations que vous s'inquiéterait autant que vous?

6) Conséquences négatives redoutées?

7) Symptômes physiques: présence au cours des 6 derniers mois, coter sévérité de 0 à 8.

Symptômes ressentis	Sévérité	La plupart du temps (O / N)
a) agitation / se sentir sur les nerfs b) facilement fatigué c) difficulté à se concentrer d) irritabilité e) tension musculaire f) insomnie / sommeil difficile		

8) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

9) Début du problème à un niveau sévère?

10) Facteurs ayant pu entraîner le problème? stresseurs? Que se passait-il à l'époque?

11) Facteurs qui déclenchent l'inquiétude? Fréquence d'inquiétude spontanée (0 à 8)?

12) Comportements sécurisants: vérifications, mesures de prévention, chercher à être rassuré, distraction)? Fréquence des comportements les plus fréquents de 0 à 8.

Impression clinique - présence du trouble? OUI NON

Trouble obsessif-compulsif

1) Êtes-vous dérangé par des pensées/images/impulsions qui vous reviennent constamment à l'esprit, qui semblent insensées mais que vous ne pouvez pas empêcher (eg. penser de blesser quelqu'un)? Présent? Passé?

- Présence de comportements ou de pensées répétitives afin de soulager l'anxiété? Présent? Passé?

2) Cotation des obsessions et compulsions

Obsessions: encercler obsessions pertinentes et coter persistance / détresse et résistance de 0 à 8.

Types d'obsession	Persistance / Détresse	Résistance	Commentaires
a) doute b) contamination c) impulsions insensées d) impulsions agressives e) sexuel f) religieux / satanique g) blesser autrui h) images horribles i) pensées/images insensées (e.g., chiffres, lettres) j) autres:			

Compulsions: Encercler comportements pertinents et coter fréquence de 0 à 8.

Types de compulsion	Fréquence	Commentaires
a) compter b) vérifier c) laver d) accumuler e) répéter (physiquement, mentalement) f) séquence / ordre stéréotypé(e) g) autres:		

3) Pourcentage de la journée occupé par chaque obsession / par l'ensemble des obsessions (au moins 1 heure / jour)?

4) Pourcentage de croyance en chaque obsession au moment où elle occupe l'esprit? lorsqu'elle n'occupe pas l'esprit?

5) Facteurs déclenchants? Obsessions imposées de l'extérieur?

6) Signification accordée aux obsessions?

7) Pourcentage de la journée occupée par chaque compulsion / par l'ensemble des compulsions (au moins 1 heure/jour)?

8) Conscience de l'absurdité des compulsions / de leur caractère excessif? Présent? Passé?

9) Résistance aux compulsions: fréquence de la résistance? degré d'anxiété provoqué? conséquences redoutées?

10) Conséquences sur le fonctionnement quotidien? Coter détresse et interférence des obsessions et compulsions de 0 à 8.

11) Début du problème à un niveau sévère?

12) Facteurs ayant pu entraîner le problème? Stresseurs? Que se passait-il à l'époque?

Impression clinique - présence du trouble? OUI NON

Phobie spécifique

1) Présence de crainte ou d'évitement face à une des situations suivantes? Présent? Passé? Coter crainte et évitement de 0 à 8.

Situation anxiogène	Crainte	Evitement	Commentaires
a) animaux b) environnement naturel (hauteurs, tempêtes, eau) c) sang/injections/blessures-soi d) sang/inject./blessures-autrui e) avion f) espaces clos g) autres (interv. chirurg., dentiste, étouffement, vomiss., maladies):			

2) Conséquences redoutées dans chaque situation phobogène?

3) Anxiété ressentie à chaque exposition?

4) Anxiété au moment de l'exposition, retardée, anticipée?

5) Crainte de subir une attaque de panique? Présence d'attaques spontanées (voir trouble panique)? Situations où de telles crises se sont produites?

6) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

7) Début du problème à un niveau sévère?

8) Facteurs ayant pu entraîner le problème?

Impression clinique - présence du trouble? OUI NON

Trouble de stress post-traumatique / Trouble de stress aigu

1) Présence d'un événement traumatisant dans le présent ou dans le passé? Événement arrivé à soi? ... été témoin d'un tel événement? Préciser événement et date.

2) Réaction émotive au cours de l'événement (peur intense, impuissance, horreur)?

3) Présence de souvenirs / pensées intrusives / rêves / sentiment de détresse en se rappelant l'événement? Présent? Passé?

4) Combien de temps après l'événement les symptômes sont-ils apparus?

5) Cotation des symptômes de stress post-traumatique: encercler symptômes pertinents et coter fréquence et détresse / sévérité de 0 à 8.

Symptômes	Fréquence	Détresse/Sévérité	Commentaires
a) souvenirs envahissants b) rêves c) impression de revivre l'événement d) détresse lorsqu'exposé à des stimuli associés à l'événement e) réaction physique lorsqu'exposé à des stimuli f) évite d'y penser ou d'en parler g) évite activités / situations associées h) trous de mémoire i) perte d'intérêt j) détachement émotionnel k) restriction des émotions l) désespoir face à l'avenir m) insomnie n) irritabilité / colère o) concentration difficile p) hypervigilance q) réaction de sursaut exagéré r) agitation s) dépersonnalisation / irréalité t) autres:			

6) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

7) Souvenir de la date précise de l'événement? Début et fin lorsque stresseur chronique?

8) Début du problème à un niveau sévère?

Impression clinique - présence du trouble? OUI NON

Trouble dépressif majeur

1) Présence d'humeur dépressive, de tristesse, de perte d'intérêt pour les activités habituelles? Présent? Passé?

2) Fréquence de l'humeur dépressive et/ou de la perte d'intérêt au cours des 2 dernières semaines (presque tous les jours)?

3) Cotation des symptômes dépressifs: encercler symptômes pertinents et coter sévérité de 0 à 8.

Symptômes dépressifs	Sévérité	Presque tous les jours O / N
a) humeur triste / pleurs b) perte d'intérêt / de motivation c) perte ou gain d'appétit d) insomnie ou hypersomnie e) agitation ou ralentissement f) fatigue ou perte d'énergie g) sentiment d'être un vaurien h) culpabilité / blâmes i) difficulté à se concentrer j) difficulté à prendre décisions k) penser à la mort ou au suicide l) autres:		

4) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

5) Début du problème à un niveau sévère?

6) Facteurs ayant pu entraîner le problème? stresseurs? Que se passait-il à l'époque?

Impression clinique - présence du trouble? OUI NON

Trouble dysthymique

1) Présence d'humeur dépressive ou de tristesse au cours des 2 dernières années? Présent? Passé?

2) Pourcentage du temps où l'humeur est dépressive presque toute la journée?

3) Persistance: présence de périodes de 2 mois ou plus où l'humeur était normale? Quand?

4) Cotation des symptômes dépressifs: encercler les symptômes pertinents, coter sévérité de 0 à 8 et persistance.

Symptômes dépressifs	Sévérité	Persistance O / N
a) perte d'appétit ou hyperphagie b) insomnie ou hypersomnie c) baisse d'énergie ou fatigue d) faible estime de soi / sentiment d'échec e) difficulté concentration ou prise de décision f) désespoir / pessimisme g) autres:		

5) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

6) Début du problème à un niveau sévère?

7) Facteurs ayant pu entrainer le problème? Stresseurs? Que se passait-il à l'époque?

Impression clinique - présence du trouble? OUI NON

Manie / Cyclothymie

1) Présence d'épisodes d'humeur excessivement exaltée ou irritable? Période la plus récente? Durée

2) Cotation des symptômes de manie: encercler symptômes pertinents. coter sévérité de 0 à 8 et persistance.

Symptômes de manie	Sévérité	Presque tous les jours O / N
a) irritabilité b) humeur exaltée ou expansive c) estime de soi exagérée / idées de grandeur d) réduction du besoin de dormir e) fuite des idées / idées défilent rapidement f) distraction g) augmentation des activités h) activités agréables mais dommageables (e.g., achats, promiscuité sexuelle) i) volubilité j) idées délirantes / hallucinations k) autres:		

3) Durée du dernier épisode maniaque? Persistance au delà d'une semaine? Dates début et fin?

4) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

5) Début du problème à un niveau sévère?

6) Facteurs ayant pu entraîner le problème?

7) Proximité d'un épisode dépressif (avant / après)?

Impression clinique - présence du trouble? OUI NON

Hypochondrie

1) Présence de crainte ou conviction d'avoir une maladie grave? Préciser maladies redoutées? Présent? Passé? Épisode le plus récent?

2) Présence de symptômes réels associés à la maladie? Lesquels? Fréquence?

3) Consultations médicales? Fréquence? Résultats des examens?

4) Capacité de se rassurer si les examens sont négatifs? Durée du sentiment de rassurance? Réapparition de la crainte?

5) Pourcentage actuel de conviction d'avoir la maladie? Existence de preuves qui permettraient de rassurer la personne?

6) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

7) Début du problème à un niveau sévère? Présence au cours des 6 derniers mois?

8) Facteurs ayant pu entraîner le problème?

Impression clinique - présence du trouble? OUI NON

Trouble de somatisation

1) Présence de nombreux problèmes de santé différents au cours de la vie? Consultations médicales répétées? Interférence sur la vie quotidienne? Difficulté à déterminer l'origine de ces problèmes de santé?

2) Cotation des symptômes physiques: encercler symptômes pertinents. coter sévérité de 0 à 8, spécifier si apparition avant 30 ans et si le symptôme est non organique ou excessif.

Symptômes physiques	Sévérité	Avant 30 ans O / N	Non organique - excessif O / N
a) Douleurs (au moins 4)			
maux de tête			
douleurs abdominales			
maux de dos			
douleurs articulaires			
douleurs aux extrémités			
douleurs thoraciques			
douleurs rectales			
douleurs durant relations sexuelles			
douleurs durant menstruations			
douleurs urinaires			
b) Gastro-intestinaux (au moins 2)			
nausées			
diarrhée			
ballonnements			
vomissements			
intolérances à des aliments			
c) Pseudoneurologiques (au moins 1)			
cécité			
vision double			
surdité			
perte de sensations tactiles			
hallucinations			
aphonie			
trouble de coordination / équilibre			
paralysie ou faiblesse musculaire			
difficulté à avaler			
difficultés respiratoires			
rétention urinaire			
crises ou convulsions			
amnésie			
perte de conscience			
d) Symptômes sexuels (au moins 1)			
indifférence sexuelle			
troubles érectiles ou de l'éjaculation			
cycles menstruels irréguliers			
saignement menstruel excessif			
vomissements durant grossesse			

3) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

4) Début du problème à un niveau sévère?

5) Facteurs ayant pu entraîner le problème?

Impression clinique - présence du trouble? OUI NON

Trouble mixte anxiété-dépression

N.B. Ne pas faire passer aux personnes recevant actuellement ou ayant déjà reçu un diagnostic de trouble anxieux ou de l'humeur.

1) Ces temps-ci, la personne se sent-elle abattue ou déprimée, ou bien anxieuse ou tendue? Passé? Indiquer épisode le plus récent.

2) Pourcentage du temps occupé par ces sentiments au cours du dernier mois (majorité des jours)?

3) Cotation des symptômes: encercler symptômes pertinents et coter sévérité de 0 à 8.

Symptômes	Sévérité 0 à 8
a) difficultés de concentration ou impression d'avoir la tête vide b) insomnie ou sommeil interrompu, agité ou peu reposant c) fatigue ou faible niveau d'énergie d) irritabilité e) inquiétude à propos de sujets quotidiens f) tendance à pleurer facilement g) hypervigilance h) tendance à craindre le pire i) désespoir face à l'avenir j) faible estime de soi - sentiment d'être un vaurien	

4) Conséquences sur le fonctionnement quotidien? Voter interférence et détresse de 0 à 8.

5) Début du problème à un niveau sévère?

6) Facteurs ayant pu entraîner le problème? Stresseurs? Que se passait-il à l'époque?

Impression clinique - présence du trouble? OUI NON

Abus d'alcool / Dépendance à l'alcool

1) Consommation d'alcool habituelle?: préciser types et quantités. Passé? Épisode le plus récent?

2) Problèmes associés à l'abus / la dépendance à l'alcool: encercler problèmes pertinents et coter fréquence / sévérité de 0 à 8.

Problèmes associés à l'abus / la dépendance à l'alcool	Fréquence / Sévérité
a) rendement réduit ou absentéisme au travail (aux études) b) problèmes légaux c) disputes avec la famille ou amis à propos de l'alcool d) consommation d'alcool dans des conditions dangereuses e) consommation pour diminuer anxiété ou humeur dépressive f) besoin de boire davantage pour obtenir effet recherché g) diminution des effets de la même quantité d'alcool h) symptômes de sevrage i) besoin de prendre une autre substance pour diminuer effet de sevrage j) consommation excédant ce que la personne aimerait k) difficulté à diminuer ou contrôler consommation l) accorder beaucoup de temps à l'alcool m) abandon ou diminution des activités de loisir et sociales n) poursuite de la consommation en dépit des problèmes médicaux ou émotionnels qu'elle occasionne	

3) Conséquences sur le fonctionnement quotidien? coter interférence et détresse de 0 à 8.

4) Début du problème à un niveau sévère?

5) Facteurs ayant pu entraîner le problème? Stresseurs? Que se passait-il à l'époque?

Impression clinique - présence du trouble? OUI NON

Abus de substances psychoactives / Dépendance à des substances psychoactives

1) Consommation de caféine habituelle?: préciser type et quantités. Problèmes médicaux associés?

2) Consommation de substances illicites? Présent? Passé? Préciser type et quantités.

3) Consommation excessive de médicaments d'ordonnance ou en vente libre? Préciser type et quantités.

4) Problèmes associés à l'utilisation d'une substance psychoactive: encercler problèmes pertinents et coter fréquence / sévérité de 0 à 8.

Problèmes associés à l'utilisation d'une substance psychoactive	Fréquence / Sévérité
a) rendement réduit ou absentéisme au travail (aux études) b) problèmes légaux c) disputes avec la famille ou amis à propos de la consommation d) consommation dans des conditions dangereuses e) consommation pour diminuer anxiété ou humeur dépressive f) besoin de consommer davantage pour obtenir effet recherché g) diminution des effets de la même quantité de la substance h) symptômes de sevrage i) besoin de prendre une autre substance pour diminuer effet de sevrage j) consommation excédant ce que la personne aimerait k) difficulté à diminuer ou contrôler consommation l) accorder beaucoup de temps à consommer ou à se procurer la substance m) abandon ou diminution des activités de loisir et sociales n) poursuite de la consommation en dépit des problèmes médicaux ou émotionnels qu'elle occasionne	

5) Conséquences sur le fonctionnement quotidien? Coter interférence et détresse de 0 à 8.

6) Début du problème à un niveau sévère?

7) Facteurs ayant pu entraîner le problème? Stresseurs? Que se passait-il à l'époque?

Impression clinique - présence du trouble? OUI NON

Psychose non organique / Symptômes de conversion

1) Présence d'un déficit dans le fonctionnement physique (paralysie, convulsions, douleurs intenses)? Présent? Passé? Préciser nature.

2) Présence d'expériences étranges et inhabituelles:
   a) entendre ou voir des choses que les autres ne perçoivent pas
   b) entendre des voix ou des conversations alors qu'il n'y a personne
   c) avoir des visions que les autres n'ont pas
   d) avoir la sensation que quelque chose d'étrange se passe autour de soi
   e) penser que les gens font des choses pour vous mettre à l'épreuve, vous blesser
   f) devoir être sur vos gardes face aux autres

Antécédents familiaux de troubles psychologiques

Présence de maladie mentale dans la famille: préciser trouble, lien de parenté, date du problème et traitement reçu

Antécédents médicaux et de traitement

1) Antécédents d'hospitalisation pour anxiété, dépression, abus de substance ou autre problème émotionnel?: préciser trouble, date, hôpital, résultats / traitement reçu

2) Antécédents de traitement à l'externe ou d'évaluation pour des problèmes émotionnels ou personnels?: préciser trouble, date, hôpital, résultats / traitement reçu

3) Prise actuelle/antérieure de médicaments contre l'anxiété, la dépression ou autre problème émotionnel?: préciser type et quantités, problèmes reliés à la consommation de ces médicaments, au sevrage, etc.

4) Taille: Poids:

5) Médecin traitant et clinique habituelle:

6) Traitements actuels pour une condition physique particulière:

7) Date du dernier examen médical:

8) Résultats du dernier examen médical:

9) Hospitalisations antérieures pour problèmes physiques:

10) Présence des maladies suivantes:

Conditions physiques	Oui / Non	Date	Commentaires
a) diabète b) problèmes cardiaques c) hypertension/hypotension d) épilepsie e) cancer f) maladie de la thyroïde g) autre problème hormonal h) asthme i) autre problème respiratoire j) migraines / céphalées k) accident cérébrovasculaire l) troubles gastro-intestinaux m) maladies du sang n) VIH/SIDA o) allergies:			

11) Présence des conditions physiques précédentes dans la famille?

12) Fumez-vous?

13) Examens médicaux au cours des 5 dernières années?

Quel est le problème principal pour lequel vous désirez de l'aide?

Y'a-t-il un sujet que nous n'avons pas abordé ou dont nous n'avons pas suffisamment parlé?

État mental:

Comportement pendant l'entrevue:

Notes:

Résumé narratif: description par le clinicien des symptômes qui ont motivé la consultation, les antécédents, les facteurs de maintien, l'impression diagnostique, etc.

Cotation de la sévérité et diagnostics selon le DSM-IV:

0	1	2	3	4	5	6	7	8
Aucune		Légèrement dérangeant/ handicapant		Passablement dérangeant/ handicapant		Très dérangeant/ handicapant		Extrêmement dérangeant/ handicapant

Axe I: Principal: Sévérité:

Secondaires: Sévérité:

Axe II:

Axe III:

Axe IV: Aigu: Persistant:

Facteurs de stress:

Axe V: Actuel: Dernière année:

Niveau de certitude diagnostique (0 - 100):

Si moins de 70, commenter:

Appendix H:

Sample Diary page

CARNET

D'AUTO-OBSERVATION

PARTICIPANT : NOM _____ N° _____

DATE : _____ JOUR **1** ☐ JOUR **2** ☐

Heure à laquelle le ***Holter*** *a débuté* _____

Heure à laquelle le ***Holter*** *a terminé* _____

Heure à laquelle vous vous êtes réveillé(e) aujourd'hui _____

Date / heure du changement de piles et de cassette _____

Avez-vous bien dormi ? 0 1 2 3 4

PAS DU TOUT — EXTRÊMEMENT

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

Merci !

CARNET

D'AUTO-OBSERVATION

PARTICIPANT : NOM _____ N° _____

DATE : _____ JOUR **1** ☐ JOUR **2** ☐

Heure à laquelle le ***Holter*** *a débuté* _____

Heure à laquelle le ***Holter*** *a terminé* _____

Heure à laquelle vous vous êtes réveillé(e) aujourd'hui _____

Date / heure du changement de piles et de cassette _____

Avez-vous bien dormi ? 0 1 2 3 4

PAS DU TOUT — EXTRÊMEMENT

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

Merci !

SIGNAL ☐ HEURE : ___:___ A.M. ☐ P.M. ☐ POSITION : ASSIS ☐ DEBOUT ☐ ÉTENDU ☐

LIEU : MAISON ☐ TRAVAIL ☐ AUTRE : _____ AVEC QUI ? : _____

Depuis la dernière entrée, avez-vous consommé ...

TABAC : oui ☐ non ☐ ___cigarettes / CAFÉINE : oui ☐ non ☐ ___tasses / ALCOOL : oui ☐ non ☐ ___verres

Pour les questions à numéros, encerclez le numéro qui vous semble le plus approprié entre **0** ***(pas du tout)*** *et* **4** ***(extrêmement)***

ACTIVITÉS :

- vais me coucher ☐
- dors ☐
- me repose ☐
- me lave / m'habille ☐
- urine / selle ☐
- conduit / passager ☐
- magasine ☐
- mange / bois ☐
- travaux ménagers ☐
- marche ☐
- monte / descend ☐
- attends ☐
- fais l'amour ☐
- parle / écoute ☐
- lis ☐
- travail de bureau ☐
- écoute TV / radio ☐
- pense / concentre ☐
- chicane / conflit ☐
- exercice ☐
- AUTRE : _____

NIVEAU D'EFFORT DÉPENSÉ :

- physique 0 1 2 3 4
- mental 0 1 2 3 4

HUMEUR : *En ce moment, je suis ...*

- paniqué(e) 0 1 2 3 4
- frustré(e) 0 1 2 3 4
- tendu(e) 0 1 2 3 4
- triste 0 1 2 3 4
- heureux(se) 0 1 2 3 4
- stressé(e) 0 1 2 3 4
- AUTRE : _____ 0 1 2 3 4
- fatigué(e) 0 1 2 3 4
- en colère 0 1 2 3 4
- en contrôle 0 1 2 3 4
- anxieux 0 1 2 3 4
- inquiet(e) 0 1 2 3 4
- irrité(e) 0 1 2 3 4
- peur 0 1 2 3 4

SYMPTÔMES : *en ce moment, j'ai les symptômes suivants :*

- transpiration 0 1 2 3 4
- douleur dans la poitrine 0 1 2 3 4
- difficulté à respirer 0 1 2 3 4
- étourdissements 0 1 2 3 4
- tremblements 0 1 2 3 4
- engourdissements 0 1 2 3 4
- palpitations 0 1 2 3 4
- frissons 0 1 2 3 4
- bouffées de chaleur 0 1 2 3 4
- tension musculaire 0 1 2 3 4
- faiblesses 0 1 2 3 4
- nausées 0 1 2 3 4
- souffle court 0 1 2 3 4
- serrement dans la poitrine 0 1 2 3 4
- peur de mourir 0 1 2 3 4
- maux de tête 0 1 2 3 4

ISCHÉMIE : *Croyez-vous souffrir d'un épisode d'**ischémie** en ce moment ?* **OUI** ☐ **NON** ☐

Si **OUI**, *pourquoi, selon vous ?* _____

Avez-vous ...

- *... pris de la nitro ?* **OUI** ☐ **NON** ☐
- *... continué votre activité sans rien changer ?* **OUI** ☐ **NON** ☐
- *... réduit la cadence de votre effort ?* **OUI** ☐ **NON** ☐
- *... cessé temporairement toute activité physique ?* **OUI** ☐ **NON** ☐

AUTRE : _____

SELF-MONITORING

DIARY

SUBJECT : NAME _____ N° _____

DATE : _____ DAY **1** ☐ DAY **2** ☐

*Time **Holter** recording began* _____

*Time **Holter** recording ended* _____

Time you woke up today _____

Date / time you need to change battery and cassette _____

How restful was your sleep ? 0 1 2 3 4

0 NOT AT ALL — 4 VERY MUCH

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

Thank you !

SELF-MONITORING

DIARY

SUBJECT : NAME _____ N° _____

DATE : _____ DAY **1** ☐ DAY **2** ☐

*Time **Holter** recording began* _____

*Time **Holter** recording ended* _____

Time you woke up today _____

Date / time you need to change battery and cassette _____

How restful was your sleep ? 0 1 2 3 4

0 NOT AT ALL — 4 VERY MUCH

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

Thank you !

PAGER ☐ TIME : ___:___ A.M. ☐ P.M. ☐ POSITION : SITTING ☐ STANDING ☐ LYING ☐

LOCATION : HOME ☐ WORK ☐ OTHER : _____ WITH WHO ? : _____

Since the last entry. have you consumed ...

TABACCO : yes ☐ no ☐ ___ cigarettes / CAFEINE : yes ☐ no ☐ ___ cups / ALCOHOL : yes ☐ no ☐ ___ servings

For the questions with numbered scales, circle the most appropriate number between **0** *(**not at all**) and* **4** *(**very much**)*

ACTIVITIES :

- going to sleep ☐
- sleeping ☐
- resting ☐
- washing / dressing ☐
- urinating / BM ☐
- driving / passenger ☐
- shopping ☐
- eating / drinking ☐
- household chores ☐
- walking ☐
- climbing / descending ☐
- waiting ☐
- sexual activity ☐
- talking / listening ☐
- reading ☐
- office work ☐
- listening to TV / radio ☐
- thinking / concentrating ☐
- argument / conflict ☐
- exercise ☐
- OTHER : _____

AMOUNT OF EFFORT EXPANDED :

- physical 0 1 2 3 4
- mental 0 1 2 3 4

MOOD : *At this moment, I feel ...*

- panicky 0 1 2 3 4
- frustrated 0 1 2 3 4
- tense 0 1 2 3 4
- sad 0 1 2 3 4
- happy 0 1 2 3 4
- stressed 0 1 2 3 4
- tired 0 1 2 3 4
- angry 0 1 2 3 4
- in control 0 1 2 3 4
- anxious 0 1 2 3 4
- worried 0 1 2 3 4
- irritated 0 1 2 3 4
- scared 0 1 2 3 4
- OTHER : _____ 0 1 2 3 4

SYMPTOMS : *at this moment, I am experiencing the following symptoms :*

• sweating	0	1	2	3	4	• hot flushes	0	1	2	3	4
• chest pain / discomfort	0	1	2	3	4	• muscle tension	0	1	2	3	4
• difficulty breathing	0	1	2	3	4	• weakness	0	1	2	3	4
• dizzy / lightheaded	0	1	2	3	4	• nausea	0	1	2	3	4
• shaky	0	1	2	3	4	• shortness of breath	0	1	2	3	4
• tingling sensations	0	1	2	3	4	• tightness in the chest	0	1	2	3	4
• heart palpitations	0	1	2	3	4	• fear of dying / heart attack	0	1	2	3	4
• chills	0	1	2	3	4	• headache	0	1	2	3	4

ISCHEMIA : *Do you think you are having an episode of ischemia at this moment ?* YES ☐ NO ☐

If **YES**, *what do you think provoked this episode ?* _____

Did you ...

- *... take nitroglycerine ?* YES ☐ NO ☐
- *... continue your activities without intervening ?* YES ☐ NO ☐
- *... reduce the intensity of physical exertion ?* YES ☐ NO ☐
- *... stop all physical activity temporarily ?* YES ☐ NO ☐

OTHER : _____

Appendix I:

Consent Form

PROJET DE RECHERCHE
ICM 99-075

Recherche en Psychologie sur l'Ischemie et le Stress
(REPIS)

Investigateur principal et collaborateurs

Richard Fleet, Ph.D., Andre Arsenault, M.D.,
Denis Burelle, M.D., and Sydney B. Miller, Ph.D.

INFORMATION

DESCRIPTION GÉNÉRALE

Vous avez ete refere en medecine nucleaire pour un test a l'effort dans le but d'evaluer l'origine et la severite de vos symptomes sur le plan cardiaque. Dans le cadre de cette evaluation, nous vous proposons de participer a une etude dont le but est d'evaluer si vos symptomes peuvent etre relies au stress mental ou emotionnel que vous vivez au quotidien. L'impact du stress mental-emotionnel sur le cœur et sur la sante cardiaque est bien documente en cardiologie. La presente etude vise a etablir l'existence d'un lien entre le stress mental ou emotionnel du quotidien, les symptomes cardiaques (douleurs thoraciques, palpitations, sensation d'etouffement) et l'ischemie, qui est un trouble de circulation cardiaque souvent associee a la douleur thoracique ou l'angine.

DÉROULEMENT DE L'ÉTUDE

Si vous acceptez de participer a cette etude, nous vous demanderons de passer une entrevue concernant votre histoire medicale et vos experiences de stress mental ou emotionnel, ainsi que de completer quelques petits questionnaires. Le tout ne devait pas prendre plus de 20 minutes de votre temps. Si vous rencontrez les premiers criteres d'admissibilite de notre etude, une assistante de recherche vous contactera par telephone pour vous demandez de vous soumettre a une courte evaluation psychologique additionnelle. Par la suite, si vous repondez a tous les criteres d'eligibilite, nous vous donnerons un rendez-vous avec la coordonnatrice de la recherche pour qu'elle vous pose un monitor cardiaque « d'Holter » que vous devez garder pendant 48 heures consecutives. A l'aide d'electrodes placees sur votre peau, ce moniteur enregistrera vos

battements cardiaques de facon a ce que vous puissez poursuivre vos activites quotidiennes. Durant cette periode de 48 heures, nous vous demanderons de completer un journal d'auto-observation de vos activites, symptomes, et emotions. Nous vous demanderons egalement de porter un tele-avertisseur, qui sonnera a chaque fois que vous devrez remplir une page dans le journal. Le moniteur cardiaque nous permettra d'evaluer l'incidence, la frequence, et la duree des episodes ischemiques et le journal, la relation entre les episodes ischemiques et le stress mental-emotionnel. Cettre procedure se fera sous la supervision de l'equipe medicale et de recherche.

RISQUES ET INCONVÉNIENTS

Phase Entrevue : Cette phase ne comporte aucun risque connu. Elle requiert environ 20 minutes, ce qui peut representer, pour certaines personnes, un inconvenient.

Phase Ambulatoire : Si vous etes eligible pour la phase ambulatoire, vous porterez un moniteur cardiaque pendant 48 heures consecutives, qui implique la mise en place de 5 petites electrodes (la grosseur d'un 1$) sur votre peau pour enregistrer votre pouls cardiaque. Les electrodes ne font qu'adherer a votre peau, vous ne sentirez rien. Le port du moniteur avec electrodes pour une duree de 48 heures peut etre percu pour certaines personnes comme un inconvenient.

Tout au long de cette phase de 48 heures, vous serez amene a remplir plusieurs fois votre journal format de poche (environ 2-3 fois par heure durant les heures d'eveil seulement). Le tele-avertisseur que vous porterez durant cette periode vous indiquera les moments pour remplir le journal (durant les heures d'eveil seulement), ce qui, encore une fois, peut representer pour certaines personnes un inconvenient.

FEMMES ENCEINTES

Si vous etes enceinte ou pensez l'etre, vous ne serez pas eligible pour participer a la phase ambulatoire de l'etude.

AVANTAGES

Il est possible que vous ne retiriez pas d'avantage personnel a participer a cette etude. Toutefois, en y participant, vous nous aiderez a ameliorer les connaissances actuelles sur les conditions qui placent l'individu avec le stress mental a risque d'evenements cardiaques. Advenant que, suite a notre evaluation et a votre participation a cette etude, nous decouvrons que vous avez des symptomes de stress mental (v.g., anxiete, panique, depression, irritabilite, etc.) et que ces symptomes influencent votre sante cardiaque, il pourra etre avantageux pour vous d'en etre informe et de recevoir un traitement.

PARTICIPATION VOLONTAIRE

Vous êtes libre de participer à cette étude ou de vous en retirer en tout temps sur simple avis verbal. Si vous décidez de ne pas y participer ou de vous en retirer, vous recevrez les soins médicaux usuels pour le traitement de votre condition. Quelle que soit votre décision, celle-ci n'influencera en rien la qualité des soins que vous êtes en droit de recevoir.

Vous serez informé de toute nouvelle découverte importante faite au cours de l'étude et susceptible d'influencer votre décision de maintenir ou non votre participation à l'étude.

Si vous avez des questions supplémentaires ou des problèmes reliés à l'étude, vous devriez contacter le Docteur Richard Fleet au (514) 376-3330, poste 3111 ou Madame Kim Lavoie ou Catherine Laurin au (514) 376-3330, poste 3214.

Pour tout renseignement concernant vos droits à titre de participant à une recherche, vous pouvez contacter pendant les heures d'ouverture le Docteur Raymond Martineau, Président du Comité d'éthique de la recherche, qui peut être rejoint par l'intermédiaire du Secrétariat du Centre de recherche au numéro de téléphone suivant: (514) 376-3330, poste 3533.

CONFIDENTIALITÉ

Toute information relative à ce projet et qui vous concerne (histoire médicale, examen physique, résultats de laboratoire) sera gardée confidentielle et seulement les personnes autorisées y auront accès. Dans certains cas, des représentants du commanditaire, de la Direction des produits thérapeutiques (DPT) de Santé Canada ou du "United States Food and Drug Administration" (FDA), pourraient demander à voir votre dossier médical pour vérifier les données de cette étude. Il est également possible que des représentants du Comité d'éthique de la recherche consultent vos dossiers médicaux.

Toutes les données médicales vous concernant seront conservées dans des fichiers informatisés et seront analysées avec les données des autres participants, mais ni votre nom ni toute autre forme d'identification ne figurera dans ces fichiers. Les résultats de cette étude pourront être publiés, mais votre identité ne sera pas dévoilée.

COMPENSATION

Dans l'éventualité où vous seriez victime d'une complication reliée au projet de recherche, vous n 'aurai pas à défrayer les coûts des soins et des services de santé que vous pourriez requérir et qui ne sont pas couverts par les régimes d'assurance-hospitalisation et d'assurance-maladie du Québec.

Toutefois, Smithkline Beecham Pharma ne s'engage pas à vous indemniser pour les pertes pécuniaires que vous pourriez encourir du fait notamment de votre incapacité à reprendre votre travail.

Quoi qu'il en soit, vous conserverez le droit de faire valoir, le cas échéant, tous vos recours légaux advenant un accident qui vous causerait préjudice.

CONSENTEMENT ÉCLAIRÉ
ICM 99-075

Recherche en Psychologie sur l'Ischemie et le Stress
(REPIS)

Investigateur principal et collaborateurs

Richard Fleet, Ph.D., Andre Arsenault, M.D.,
Denis Burelle, M.D., and Sydney B. Miller, Ph.D.

J'ai eu l'occasion de poser toutes les questions voulues au sujet de cette étude et on y a répondu à ma satisfaction.

Je comprends que je demeure libre de me retirer de cette étude en tout temps sans que cela n'affecte en aucune façon les soins dont je pourrais bénéficier dans l'avenir.

J'ai lu et je comprends le contenu de ce formulaire de consentement.

Je, soussigné(e), accepte de participer au présent projet de recherche.

_____	_____	_____
Signature du patient	Date	Heure
_____	_____	_____
Signature de l'un des chercheurs	Date	Heure

Je certifie que j'ai expliqué les buts du projet à _____
et il(elle) a signé le consentement en ma présence.

_____	_____	_____
Signature	Date	Heure

99-075

N.B. L'original de ce formulaire doit être inséré au dossier du patient, une copie versée au dossier de la recherche et une copie remise au patient.

RESEARCH PROJECT
ICM 99-075

Recherche En Psychologie sur l'Ischemie et le Stress
(REPIS)

Principal investigator and collaborators

Richard Fleet, Ph.D., Andre Arsenault, M.D.,
Denis Burelle, M.D., and Sydney B. Miller, Ph.D.

INFORMATION

GENERAL DESCRIPTION

You have been referred for a nuclear medicine exercise stress test for the evaluation of the origin and severity of your cardiac symptoms. In conjunction with this test, we would like to invite you to participate in a study whose main objective is to evaluate the extent to which your symptoms could be related to the mental or emotional stress you may experience in your daily life. The impact of mental/emotional stress on the heart and cardiac health is well documented in cardiology research. The present study's main goals are to evaluate whether there is link between the mental or emotional stress you experience during your daily life, cardiac symptoms (ie., chest pain, palpitations, shortness of breath) and ultimately ischemia, which is a condition of reduced circulation to the heart which is frequently associated with chest pain or angina.

STUDY PROCEDURE

If you accept to participate in this study, you will be asked to undergo a brief interview regarding your medical history and your experiences with mental/emotional stress, and to complete a series of brief questionnaires. The total duration of the interview and questionnaires should not exceed 20 minutes. If you meet initial eligibility criteria for the study, you will be contacted by telephone by a research assistant for an additional psychological evaluation. If you meet all eligibility criteria, you will be offered an appointment with the research co-ordinator to be instrumented with a a portable heart rate monitor for a period of 48 consecutive hours. This monitor will record heart rate responses noninvasively (through the placement of electrodes on the skin) while you go about your routine daily activities. During this 48 hour period, you will be required to carry and complete a self-monitoring diary of your activities, symptoms, and emotions. You will

also be required to carry a small digital beeper which will beep every time you are to make a diary entry. The portable heart rate monitor will permit us to evaluate the incidence, frequency, and duration of ischemic episodes, and the diary will permit us to evaluate the extent to which ischemic episodes are related to mental/emotional stress. The entire procedure for this study will be conducted under the supervision of a medical research team.

RISKS AND INCONVENIENCES

Interview Phase: There are no known risks associated with the interview and questionnaire phase of this study. It does require approximately 20 minutes of your time, which some may find inconvenient.

Ambulatory Phase: If you are eligible and consent to participate in the ambulatory monitoring phase, you will be required to wear a portable heart rate monitor which requires the placement of 5 small (looney-sized) electrodes on the skin for the recording of your heart rate. The electrodes only adhere to the skin, and will not be felt otherwise. Because you must wear this monitor for the entire 48 hours (without removing the electrodes), some may find this inconvenient at times.

Throughout the 48 hour monitoring phase, you will also be asked to make several entries in a pocket-sized diary (approximately 2-3 times per hour during waking hours only). A beeper which you will carry with you at all times will signal you whenever you are to make an entry. Again, some may find this inconvenient at times.

PREGNANT WOMEN

If you are or think you might be pregnant, you will be ineligible to participate in the 48 hour ECG monitoring phase of the study.

BENEFITS

It is possible that you will gain no personal benefits from participating in this study. However, through your participation, you will help us gain a greater understanding of the conditions under which mental stress places individuals at risk for cardiac events. In the event that as a result of your participation we discover that you suffer from symptoms of mental stress (e.g., anxiety, panic, depression, irritability etc.), and that these symptoms may be influencing your cardiac health, it would certainly be beneficial to be informed and receive appropriate treatment.

VOLUNTARY PARTICIPATION

You are free to participate in this study or withdraw from it at any time on verbal notice. If you decide not to participate or to withdraw, you will receive the standard medical care required by

your condition. Whatever your decision, it will not affect the quality of medical care to which you are entitled.

You will be informed of any new findings acquired during the course of the study which may influence your decision to maintain your participation in this study.

If you have any problems or questions regarding this study, you should contact Doctor Richard Fleet at (514) 376-3330, extension 3214 or Ms. Kim Lavoie (research coordinator) and/or Catherine Laurin (research assistant) at (514) 376-3330, extension 3214.

For information concerning your rights as a research participant, you should contact during working hours Doctor Raymond Martineau, Chairman of the Research Ethics Board, who can be reached through the Research Center Office at (514) 376-3330, extension 3533.

CONFIDENTIALITY

Any information related to this project that concerns you (medical history, physical examination, laboratory results) will be kept confidential and only authorized personnel will have access. In some cases, representatives of the sponsor, the Directorate of Therapeutic Products (DTP) of Health Canada, or the United States Food and Drug Administration (FDA), may ask to consult your medical charts to verify the data of this study. Representatives of the Research Ethics Board may also review your medical charts.

All medical data that concerns you will be kept in computer files and will be analyzed with data from other participants, but, neither your name nor any other identification will appear in these files. Results of this study may be published, but your identity will not be revealed.

COMPENSATION

In the event that you experience complications resulting from the study, you will not have to pay for the health services which are not covered by the Quebec Health Insurance Plan.
However, Smithkline Beecham Pharma, which is supporting this project, will not undertake to compensate you for any loss of wages that could occur because of an incapacity to work.
In the case of an accident which would cause you any injury, you still have the right to legal action.

CONSENT FORM
ICM 99-075

Recherche en Psychologie sur l'Ischemie et le Stress
(REPIS)

Principal investigator and collaborators

Richard Fleet, Ph.D., Andre Arsenault, M.D.,
Denis Burelle, M.D., and Sydney B. Miller, Ph.D..

I have asked all the questions I wanted on this research project and have received appropriate answers.

I understand that I remain free of withdrawing from the study at any time and this will not prejudice or change my future care.

I have read and understood the content of this form.

I, undersigned, accept to participate in this project.

_____	_____	_____
Patient's signature	Date	Hour
_____	_____	_____
Investigator's signature	Date	Hour

I certify that I have explained the purposes of this project to _____ and he(she) signed the consent form in my presence.

_____	_____	_____
Signature	Date	Hour

Approved by the Research Ethics Committee of the Montreal Heart Institute.

Appendix J:

Patient Diary Instructions

PROJET REPIS

INSTRUCTIONS AUX PATIENTS

Nom: _____ No dossier: _____

Date: _____ No patient: _____

I. <u>À RETENIR</u>:

1. Utilisez le premier journal pour le premier jour (_____)
   et le deuxième journal pour le deuxième jour (_____).
2. Vos 48 heures d'enregistrement finissent _____ à _____.
3. Assurez-vous de rapporter les deux jounaux (jours 1 et 2), le moniteur, le pagette, les cassettes, la montre, et tout autre materiel à votre dernière session le _____ à _____.

SI VOUS AVEZ DES QUESTIONS N'HÉSITEZ PAS À NOUS CONTACTER EN TOUT TEMPS:

<u>Kim Lavoie, M.A.</u>
Psychologue et Coordinatrice de l'étude

(514) 376-3330
poste 3214

<u>Catherine Laurin, B.A.</u>
Psychotechnicienne et Assistante de recherche

II. OBJECTIF DE L'ÉTUDE:

L'impact du stress mental-émotionnel sur le cœur et sur la santé cardiaque est bien documenté en cardiologie. La présente étude vise à établir l'existence d'un lien entre le stress mental ou émotionnel du quotidien, les symptômes cardiaques (v.g., douleurs throraciques, palpitations, sensation d'étouffement, transpiration...) et l'ischémie, qui est un trouble de circulation cardiaque souvent associé à la douleur thoracique ou l'angine.

Le port d'un moniteur d'Holter de 48 heures nous permettra d'évaluer l'effet des activités physiques et mentales (ainsi que vos états émotionnels) sur vous et votre cœur. Le moniteur enregistre continuellement l'activité de votre cœur pour une période de 48 heures pendant que vous notez vos activités, émotions, et symptômes physiques dans un petit journal.

Dans cette étude, nous voulons savoir comment vos différentes activités physiques et mentales ainsi que vos états émotionnels se traduisent dans l'activité de votre cœur et de votre électrocardiogramme (ECG). Un journal **COMPLET ET DÉTAILLÉ** est nécessaire pour déterminer le rôle précis que joue vos activités et émotions sur l'activité de votre coeur.

VOTRE PARTICIPATION EST IMPORTANTE!
MERCI POUR VOTRE COLLABORATION!

À la fin de l'étude, nous devrions pouvoir identifier les activités que vous avez faites ainsi que les émotions et les symptômes ressentis lors de celles-ci. Vos inscriptions dans le journal doivent donc être précises (v.g., heure exacte!). En cas d'incertitude pour certaines entrées, prenez des notes sur les pages du journal. Pour les données manquantes ou incomplêtes, nous ferons un retour lors de votre dernière session.

III. COMMENT REMPLIR LE JOURNAL:

- Veuillez svp remplir la page couverture de chaque journal (un par jour), particulièrement l'heure à laquelle vous vous êtes levé et la qualité de votre sommeil.
- Remplissez une feuille chaque fois que:

  (1) **Le PAGETTE SONNERA** (approx. 10-15 par par jour). (Si vous avez rempli une page suite à un "signal" de pagette, svp cochez la boîte en haut de la page!)
  (2) **Vos ACTIVITÉS changent** (v.g., mange=>marche).
  (3) **Vos HUMEURS changent** (v.g., heureux=>triste).
  (4) **Vos SYMPTÔMES changent** (v.g., pas de symtôme=> douleur thoracique).

- Pour chaque catégorie vous pouvez encercler plusieurs réponses (vous n'êtes pas obligé de faire un seul choix parmi chaque catégorie)!

HEURE: ____:____AM/PM

- Pour chaque entrée du journal, écrivez l'heure exacte. Si nous vous donnons une montre, svp portez cette montre en tout temps et utilisez l'heure incrite sur celle-ci.

POSITION:

ASSIS ___ DEBOUT ___ ÉTENDU ___

- Pour chaque entrée du journal, indiquez la position dans laquelle vous vous trouvez.

NIVEAU D'EFFORT DÉPENSÉ:

- Pour chaque entrée du journal, encerclez le chiffre (0 1 2 3 4) qui correspond le mieux à votre niveau d'effort mental et physique dépensé depuis votre dernière entrée dans le journal.

HUMEUR:

- Pour chaque entrée du journal, encerclez le chiffre (0 1 2 3 4) qui correspond le mieux à la façon dont vous vous sentez sur chaque descripteur d'humeur.

SYMPTÔMES:

- Pour chaque entrée du journal, encerclez le chiffre (0 1 2 3 4) qui correspond le mieux à l'intensité de chaque symptôme ressenti.

ISCHÉMIE:

- Pour chaque entrée dans le journal, indiquez si vous croyer souffrir d'un épisode d'ischémie (angine/douleur thoracique).

- Si vous avez répondu OUI, indiquez la raison pour laquelle vous croyez souffrir d'un épisode d'ischémie.

- Si vous avez répondu OUI, indiquez ce que vous avez fait suite à votre épisode d'ischémie:

- ...pris la nitro? OUI ___ NON ___
- ...continué votre activité sans rien changer? OUI ___ NON ___
- ...réduit la cadence de votre effort? OUI ___ NON ___
- ...cessé temporairement toute activité physique? OUI ___ NON ___

AUTRE: _____

IV. COMMENT VOUS OCCUPER DU MONITEUR D'HOLTER:

- Une fois les électrodes mises en place, elles ne doivent pas être pertubées pour les 48 heures à venir. Les électrodes seront enlevées par une des assistantes de recherche lorsque cette période sera finie.

- Le moniteur d'Holter et les électrodes ne doivent pas être trempés: vous ne pouvez pas prendre un bain ou une douche pendant la période d'enregistrement. Vous pouvez, par contre, vous laver à l'éponge en vous assurant de ne pas mouiller ou déplacer les électrodes ou la machinerie.

V. PAGETTE

- Le pagette peut être éteint pendant la nuit, MAIS DOIT ÊTRE RÉACTIVÉ ET PORTÉ LE LENDEMAIN MATIN!

- Le pagette doit être gardé au sec.

DÉFINITIONS DES ACTIVITES:

VAIS ME COUCHER: s'étendre avec l'intention de dormir (nuit ou petite sieste)

DORS: dormir

ME REPOSE: prendre une pause intentionnelle (physique ou mentale) pour rompre la routine habituelle

ME LAVE/HABILLE: faire sa toilette à l'éponge/débarbouillette et se brosser les dents, se raser, etc.

URINE/SELLE: encerclez un ou l'autre selon le cas

CONDUIT/ PASSAGER: Encerclez un ou l'autre selon le cas (voiture, autobus, métro, taxi, bateau, etc.).

MAGASINE: faire l'épicerie, se promener dans les magasins, acheter des vêtements, etc.

MANGE/BOIS: encerclez un ou l'aure selon le cas. N'oubliez pas que les breuvages caféinés ou alcoolisés doivent être inscrits en haut de chaque page!

TRAVAUX MÉNAGERS: laver la vaisselle, épousseter, cuisiner, faire le lit. Si un effort supplémentaire est utilisé pour certaines activités (v.g., frotter le plancher à la main sur les genoux), assurez-vous de bien le noter dans la section "niveau d'effort physique dépensé" à la droite de la page.

MARCHE: marcher pour une distance, un temps ou un effort prolongé (dans un but précis ou pour le plaisir).

MONTE/DECEND: ESCALIERS- peut se produire en combinaison avec d'autres activités. SVP n'évitez pas de prendre les escaliers afin de ne pas avoir à remplir une autre feuille de journal!!! C'est une activité très importante à enregistrer et à évaluer!!!

ATTENDS: rendez-vous chez le médecin, appel, etc.

FAIT L'AMOUR: caresser, embrasser, se masturber, avoir une relation sexuelle.

PARLE/ÉCOUTE: encerclez les deux lorsque vous êtes impliqué dans une conversation (en personne ou au téléphone); écoute réfère plutôt à un cours, un serment, etc.

LIS: journal, revue, livre, etc.

TRAVAIL DE BUREAU: travailler à la maison ou à l'extérieur (payer les factures, écrire une lettre, travailler sur un document, travailler sur l'ordinateur/ internet, etc.).

T.V./RADIO: encerclez un ou l'autre (ou les deux), selon le cas (télévision, film au cinéma ou à la maison, théatre, radio, stéréo, etc). Notez le type de programme/film/ théatre/musique etc. écouté.

PENSE/ ME CONCENTRE: planifier quelque chose ou rêver.

CHICANE/CONFLIT: argumenter ou être en désaccord, que ce soit exprimé ou non (physique ou verbal).

EXERCICE:	faire un effort physique intentionnel (à la maison, au gym, prendre une marche plus vigoureuse, etc.).
AUTRE:	Si vous n'êtes pas sûr de la catégorie de votre activité, écrivez-le ici. Nous en reparlerons lors de votre dernière session.

PROJET REPIS

PATIENT INSTRUCTIONS

Name : _____ No. Dossier : _____

Date : _____ No. Patient : _____

I. REMEMBER :

1. Use Journal No.1 on the first day of monitoring (_____)

   and Journal No.2 on the second day of monitoring (_____).

2. Your 48-hour monitoring period ends _____ at _____.

3. Remember to bring both journals (for days 1 and 2), the monitor, the pager,

   and all other research materials to your final appointment on

   _____ at _____.

IF YOU HAVE ANY QUESTIONS AT ANY TIME DURING THE STUDY, PLEASE DO NOT HESTITATE TO CONTACT US :

Kim Lavoie, M.A.
Psychologist and Study Coordinator
(514) 376-3330, ext. 3214

Catherine Laurin, B.A.
Psychotechnician and Research Assistant

II. OBJECTIVES OF THE STUDY :

The impact of mental and/or emotional stress on the heart and cardiac health is well documented in cardiology research. The purpose of the present study is to evaluate whether there is a link between the mental and/or emotional stress you experience during your daily life, your cardiac symptoms (e.g., chest pain, palpitations, shortness of breath, sweating, etc.) and myocardial ischemia, which is a condition of reduced blood flow to the heart and is often associated with chest pain or angina.

Wearing an ambulatory electrocardiographic (ECG) Holter monitor permits us to evaluate the effects of your physical and mental activities (as well as your emotional states) on your heart. The monitor will continuously monitor the activity of your heart while you go about your daily activities (for a period of 48 hours), during which time you will be taking note of your activities, emotions, and physical symptoms in a small diary. Therefore, a COMPLETE AND DETAILED DIARY is necessary in order for us to determine the precise role your activities and emotions play on your heart!

YOUR PARTICIPATION IS IMPORTANT !
THANK-YOU FOR YOUR COOPERATION !

At the end of the study, we should be able to determine what activities you did during the 48 hour monitoring period, how you felt and if you had any significant emotional experiences, what physical symptoms you experienced, and at what times. Your diary entries must therefore be complete and precise (i.e., you must indicate the exact time of each entry !). If you are uncertain of what to write for any part of an entry, please make a few short notes about what you were unsure of in the white spaces around the diary pages. In the event that there is any missing or incomplete information on one or more of your diary entries, we will review the entries together during your last appointment.

III. HOW TO COMPLETE THE DIARY :

- Please complete the cover pages of each diary (one for each day), indicating the time in which you woke up each morning and the quality of your sleep.

- Please complete a diary page each time one the following occurs :
  (1) **The PAGER BEEPS** (probably 10-15 times per day).
  (If you've completed a diary entry as a result of being « beeped », please check off the box at the top right hand corner of the page!)
  (2) **Your ACTIVITY(IES) change** (e.g., eating=>going for a walk).
  (3) **Your EMOTION(s) change** (e.g., feeling happy=>feeling sad).
  (4) **Your SYMPTOMS change** (e.g, no symptoms=>chest pain).

- Remember that for each category above, you may report doing more than one **activity**, feeling more than one **emotion**, and having more than one **symptom**! (You are not required to make only one choice from each category!)

TIME : ___ :___ AM/PM

- For each diary entry, indicate the exact time. If we provide you with a watch, please wear this watch for the duration of the study and use the time indicated on this watch for each entry.

POSITION :

SITTING ___ STANDING ___ LYING ___

- For each diary entry, indicate the position in which you find yourself.

LOCATION :

HOME ___ WORK ___ OTHER _____

- For each diary entry, indicate where you are.

WITH WHO? : _____

- For each diary entry, indicate the person or people you are currently with (e.g., husband/wife; daughter/son; boss; friend; neighbor etc.)

ALCOHOL/TOBACCO/CAFFEINE :

Since the last entry, have you consumed…

TOBACCO :	**yes ___ no ___**	**___ cigarettes/cigars**
CAFFEINE :	**yes ___ no ___**	**___ cups**
ALCOHOL :	**yes ___ no ___**	**___ servings**

- For each entry, indicate the amount of tobacco, caffeine (coffee, tea, cola, chocolate) and alcohol you have consumed since your last diary entry.

ACTIVITIES :

- For each diary entry, indicate what activity (ies) you doing.
- Consult the « Definitions of Activities » for a detailed description of each activity found in the list.

AMOUNT OF EFFORT EXPENDED :

- For each diary entry, circle the number (0 1 2 3 4) which best corresponds to the amount of physical and mental effort you have expended since the last diary entry.
- Note that for each scale, « 0 »= not all all and « 4 »= very much).

MOOD :

- For each diary entry, circle the number (0 1 2 3 4) which best corresponds to how you are feeling on each mood descripter presented on the list.
- Note that for each scale, « 0 »= not all all and « 4 »= very much).

SYMPTOMS :

- For each diary entry, circle the number (0 1 2 3 4) which best corresponds to the degree in which you feel each symptom presented on the list.
- Note that for each scale, « 0 »= not all all and « 4 »= very much).

ISCHEMIA :

- For each diary entry, indicate whether or not you think you may be experiencing an episode of ischemia (chest pain or angina).
- If you answered YES, indicate what you think may have provoked the ischemic episode in the space provided.
- If you answered YES, indicate what action(s) you took in reaction to experiencing an ischemic episode :
  - ...take nitroglycerine? YES ___ NO ___
  - ...continue your activities without intervening? YES ___ NO ___
  - ...reduce the intensity of your physical exertion? YES ___ NO ___
  - ...stop all physical activity temporarily? YES ___ NO ___

  OTHER : _____

IV. HOW TO OPERATE THE HOLTER MONITOR :

- Once the electrodes have been placed on the skin, they should not be removed or disturbed for the 48 hour monitoring period. The electrodes will be removed by one of the research assistants during your final appointment.

- The Holter monitor and the electrodes must stay dry at all times : you cannot take a bath or a shower during the 48 hour monitoring period ! You may, however, take « sponge baths » while ensuring the electrodes and monitor stay dry.

V. PAGER

- The pager may be turned off at night while you are sleeping, BUT MUST BE TURNED BACK ON AND WORN THE NEXT MORNING !

- The pager must be kept dry at all times.

DEFINITIONS OF DIFFERENT ACTIVITES :

GOING TO SLEEP : resting or lying down with the intention of going to sleep (for the night or a short nap).

SLEEPING : sleeping.

RESTING : intentionally taking a « mental » or « physical » break from the regular routine (i.e., from doing work, housework, etc.).

WASHING/ DRESSING : washing oneself (facecloth or sponge bath), brushing your teeth, shaving, getting dressed, etc.

URINATING/BM : circle one or both according to the situation.

DRIVING/ PASSENGER : car or public transport (bus, metro, taxi, boat, etc.). Circle one according to the situation.

SHOPPING : groceries, clothing, household products, window shopping, etc.

EATING/ DRINKING : Circle one or both according to the situation. Note that consumption of alcoholic and cafeinated beverages must be detailed at the top of each diary page !

HOUSEHOLD CHORES : washing dishes, vacuuming, cooking, making the bed, etc. If a supplementary effort is required for an activity (e.g., scrubbing the floors on your hands and knees or shoveling snow), make sure to note the AMOUNT OF EFFORT (PHYSICAL) EXPENDED on the top right side of the diary page !

WALKING : walking for a significant period (to go somewhere or for pleasure).

CLIMBING/ DESCENDING : STAIRS – may be combined with other activities (i.e., household chores, walking). Please do not avoid taking the stairs in order to avoid having to complete a diary entry ! This activity is VERY IMPORTANT to monitor and evaluate !

WAITING : doctor`s office, for an appointment, on hold (telephone), etc.

SEXUAL ACTIVITY : kissing, masturbating, mutual sexual touching, intercourse, etc.

TALKING/ LISTENING : circle both if you are in the middle of a conversation (in person or on the telephone) ; listening only applies to sitting in a class, listening to a sermon or lecture etc.

READING : a book, magazine, newspaper, etc.

OFFICE WORK : work at home, office, library, etc. Includes paying bills, writing letters and documents, typing, computer work (intenet), etc.

T.V/RADIO : circle one or both according to the situation. Includes television, movies at home or the cinema, theatre, radio, stereo, etc.). Note the type of T.V. program or film (i.e., drama, horror, comedy, suspense, documentary, action, news) and/or type of music (i.e., classical, rock, popular, country…).

THINKING/ CONCENTRATING : thinking, planning, or dreaming.

ARGUMENT/ CONFLICT : any argument or conflict (may be expressed physically or verbally or not at all, i.e., « kept inside »).

EXERCISE : any intentional phyisical effort (at home, in a gym, playground, court, vigorous walking etc.) for the purpose of getting or staying fit.

OTHER : if you are not sure of the category of your activity, write here. We will discuss it during your last appointment.

LIEU:

MAISON ___ TRAVAIL ___ AUTRE: _____

- Pour chaque entrée du journal, indiquez le lieu où vous vous trouvez.

AVEC QUI? : _____

- Indiquez la personne(s) avec qui vous vous trouvez (v.g., époux/épouse; fille/fils; patron; ami(s); voisin(s), etc.).

ALCOOL/CAFÉINE/TABAC:

Depuis la dernière entrée, avez-vous consommé…

TABAC:	**oui ___**	**non ___**	**___ cigarettes/cigares**
CAFÉINE:	**oui ___**	**non ___**	**___ tasses**
ALCOOL:	**oui ___**	**non ___**	**___ verres**

- Pour chaque entrée du journal, indiquez la quantité de tabac, caféine (café, thé, cola, chocolat) et alcool que vous avez consommé depuis votre dernière entrée dans le journal.

ACTIVITÉ(S):

- Pour chaque entrée du journal, indiquez l'activité(s) que vous faites.

- Voir "Définitions des activités" pour une description détaillée de chaque activité de la liste.