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# Heart rate variability in coronary artery disease patients with and without panic disorder

Kim L. Lavoie[a,b,c,*], Richard P. Fleet[a,b], Catherine Laurin[a,b], Andre Arsenault[b], Sydney B. Miller[c], Simon L. Bacon[a,d]

[a] *Research Center, Sacre-Coeur Hospital, 5400 Gouin West, Montreal, Quebec, Canada H4J 1C5*
[b] *Research Center, Dept. of Nuclear Medicine, Montreal Heart Institute, 5000 Belanger East, Montreal, Quebec, Canada H1T 1C8*
[c] *Department of Psychology, Concordia University, 7141 Sherbrooke St. West, Montreal, Quebec, Canada H4B 1R6*
[d] *Department of Psychiatry, Duke University Medical Center, Durham, NC 27710, USA*

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**Abstract**

Panic disorder (PD) and coronary artery disease (CAD) often co-occur, and CAD patients with comorbid PD suffer greater cardiovascular morbidity and mortality relative to CAD patients without PD. However, the mechanisms underlying these associations are still unknown. Reduced heart rate variability (HRV), a non-invasive measure of cardiac autonomic modulation, is an important predictor of adverse cardiac events. Interestingly, reduced HRV has been observed in patients with panic-like anxiety and PD, as well as in various CAD populations. However, the extent to which HRV is altered in patients with both PD and CAD is unknown. This study evaluated HRV in 42 CAD patients with ($n = 20$) and without ($n = 22$) PD. Patients underwent 48-h electrocardiographic monitoring. Power spectral analysis of HRV indicated that CAD patients with PD exhibited significantly lower LF/HF ratios, which may reflect lower sympathetic modulation, compared with non-PD patients. Additionally, total power in PD patients was made up of a significantly higher proportion of HF power and a significantly lower proportion of VLF power than in non-PD patients. No other significant differences in HRV indices were observed. Results suggest that contrary to what has been observed in the majority of PD-only and CAD-only populations; patients with both PD and CAD appear to exhibit lower sympathetic modulation during ordinary daily life conditions. Though preliminary, these findings suggest that changes in HRV may not be the mechanism underlying greater cardiovascular morbidity and mortality among CAD patients with PD.


*Keywords:* Sympathetic modulation; Parasympathetic modulation; Cardiovascular risk

## 1. Introduction

Symptoms of panic-like anxiety and panic disorder (PD) have been shown to be disproportionately prevalent among coronary artery disease (CAD) patients, where PD alone has been shown to affect approximately 10–50% of patients with established CAD (for review, see Fleet et al., 2000). There is also evidence to suggest that PD and panic-like anxiety is related to poorer CAD prognosis, including increased risk for post-myocardial infarction in-hospital complications (e.g., acute ischemia, re-infarction, sustained ventric-

* Corresponding author. Research Center, Hôpital du Sacré-Coeur de Montréal, 5400 Gouin West, Montreal, Quebec, Canada H4J 1C5. Tel.: +1-514-338-2222x3364; fax: +1-514-338-3213.
*E-mail address:* kimlavoie@crhsc.umontreal.ca (K.L. Lavoie).

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ular tachycardia and ventricular fibrillation) and mortality (Moser and Dracup, 1996; Coryell et al., 1982, 1986; Kawachi et al., 1994). However, the precise mechanisms underlying greater cardiovascular risk among CAD patients with PD remain unknown.

Basic heart rate (HR) and HR modulation are primarily determined by alterations in cardiac autonomic activity (Aubert and Ramaekers, 1999). Power spectral analysis (PSA) of beat-to-beat heart rate variability (HRV) has been increasingly employed to study autonomic regulation of cardiac functioning. PSA of HRV is said to offer both non-invasive and reliable measurement of cardiac autonomic tone via assessments of peripheral sympathetic and parasympathetic modulation (Friedman and Thayer, 1998; Stein et al., 1994). It is speculated that reductions in parasympathetic modulation leave the heart exposed to uninhibited stimulation by the sympathetic nervous system. This may in turn make the heart vulnerable to arrhythmia and sudden death, and may also accelerate the progression of CAD. To support this hypothesis is robust evidence of a link between reduced HRV in post-myocardial infarction (MI) patients and increased risk for adverse cardiovascular events, including ventricular arrhythmias and sudden death (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Bigger et al., 1992; Kleiger et al., 1987). Reduced HRV has also been shown to predict mortality 1 year following elective angiography in patients with no history of MI (Rich et al., 1988), as well as future cardiac events in patients initially free of CAD (Tsuji et al., 1996).

Interestingly, the results of several studies indicate that patients with certain psychiatric disorders exhibit abnormally low HRV compared with non-psychiatric controls. Several studies have provided evidence of reduced HRV in non-cardiac patients with depressive symptomatology (Horsten et al., 1999) and major depressive disorder (MDD) (Dalack and Roose, 1990; Yeragani, 2000), and among CAD patients with both depressive symptoms (Krittayaphong et al., 1997; Light et al., 1998; Sheffield et al., 1998) and MDD (Carney et al., 1995, 2001; Stein et al., 2000). Panic disorder has also been associated with reduced HRV. Studies have found evidence of reduced HRV, decreased cardiac vagal tone and elevated sympathetic activity in patients with both panic-like anxiety (Friedman and Thayer, 1998; George et al., 1989; Kawachi et al., 1995; Piccirillo et al., 1997; Yeragani et al., 1990, 1993) and actual PD (Cohen et al., 1999, 2000; Klein et al., 1995; Yeragani et al., 1991, 1993).

Traditional views of PD posit that it may be related to physiological changes resulting from sympathetic dysregulation (Cohen et al., 1999; Klein et al., 1995). It has been hypothesized that such autonomic instability is interpreted by the central nervous system (CNS) as a source of persistent novel stimuli, which leads the CNS to respond to these stimuli with fear (Costello, 1971). A related hypothesis is that somatic variability leads to a heightened perception of bodily sensations, which are then catastrophically misinterpreted (Anastasiades et al., 1990). Thus, the result of increased sympathetic activity and decreased parasympathetic activity is poor control of heart rate, which can confer risk for tachycardia.

We are aware of only one study to date that has investigated long-term (24-h) HRV in PD patients (McCraty et al., 2001), as most studies have focused on short-term resting recordings and/or recordings during laboratory challenges, such as postural change, cold pressor test, and various pharmacological challenges (e.g., sodium lactate infusion) (Yeragani et al., 1990, 1991, 1995; Yeragani et al., 1994; Klein et al., 1995). Though the majority of these studies have reported evidence of reduced HRV, specific findings with regard to individual HRV components reveal a series of inconsistencies. For example, some studies found evidence of reduced HF power in PD patients relative to controls under resting conditions in some investigations (e.g., Klein et al., 1995; Seier et al., 1997) but others did not (e.g., Yeragani et al., 1993; Rechlin, 1994). One study found reduced short-term LF power at rest in PD patients (Middleton et al., 1994), while similar studies found no differences in LF power between PD patients and controls (Yeragani et al., 1993; Rechlin, 1994). Finally, a study by Seier et al. (1997) found decreases in both HF and LF power among PD patients in response to lactate infusion, whereas others found decreases in only HF power (Yeragani et al., 1994). Thus, although the literature generally reveals a trend towards dysregulation of HRV in PD patients, the specific HRV components that may be driving the decreases, and in some cases increases, remain unclear.

Despite evidence of dysregulated HRV in PD patients, and evidence of reduced HRV in CAD