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Increased QT variability in patients with panic disorder and depression

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Abstract

This study investigated beat-to-beat QT variability in patients with panic disorder and depression, and normal control subjects using an automated algorithm to compute QT intervals. An increase in QT variability appears to be associated with symptomatic patients with dilated cardiomyopathy and also with an increased risk for sudden death. QT_{vm} (QT variability normalized for mean QT interval) and QT_{vi} (a log ratio of QT variance normalized for mean QT over heart rate variability normalized for mean heart rate) were significantly higher in patients with panic disorder and depression in supine as well as standing postures ($P = 0.002$ and 0.0001 for QT_{vm} and QT_{vi}, respectively). In another analysis, QT_{vi} was significantly higher in patients with panic disorder compared to control subjects in supine as well as standing postures during spontaneous breathing as well as 12, 15 and 20 per minute breathing ($P = 0.005$). These findings are important especially in view of the recent reports of increased risk for cardiovascular mortality and sudden death in patients with anxiety and depression and the utility of QT_{vi} as a noninvasive measure of temporal repolarization lability.

Keywords: QT variability; Heart rate variability; Panic disorder; Depression; Normal controls; Autonomic; Cardiovascular mortality; Respiration

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1. Introduction

The QT interval on the surface electrocardiogram (ECG) reflects time for repolarization of the ventricular myocardium and prolongation of QT interval is an important predictor of ventricular arrhythmias (Jervell and Lange-Nelson, 1957; Schwartz and Wolf, 1978). Recent literature has implicated abnormal repolarization in the genesis of life-threatening arrhythmias (Nguyen et al., 1986; Binah and Rosen, 1992; Tomaselli et al., 1994). In another recent report, Berger and coworkers have described a novel and robust algorithm to calculate beat-to-beat fluctuations in QT interval automatically, comparing patients with dilated cardiomyopathy to normal control subjects (Berger et al., 1997). They have found that beat-to-beat QT variability is abnormally large in symptomatic patients with dilated cardiomyopathy.

QT interval variability is closely related to heart rate (HR) variability (Berger et al., 1997) and thus can be influenced by autonomic mechanisms. We have recently found that a change from supine to standing posture and intravenous infusions of isoproterenol result in highly significant increases in QT_{vi}, a normalized index of QT variability (Yeragani et al., 1999a,b). HR variability is influenced by several mechanisms including sympathetic and parasympathetic systems (Akselrod et al., 1981; Pomeranz et al., 1985; Malliani et al., 1991). A decrease in heart rate (HR) variability is associated with significant cardiac morbidity and sudden death in patients with heart disease as well as normal control subjects (Molgaard et al., 1991; Bigger et al., 1992). Thus, a decrease in HR variability in combination with increased QT variability may significantly increase the risk for cardiovascular mortality.

Patients with panic disorder experience panic attacks, which are associated with several autonomic symptoms, including chest pain, heart pounding, tachycardia, and shortness of breath, that suggest autonomic dysfunction. Recent studies suggest an association between anxiety and increased risk for sudden death and cardiovascular mortality (Coryell et al., 1986; Weissman et al., 1990; Kawachi et al., 1994a,b). Our previous studies showed decreased heart rate (HR) and heart period (HP) variability in patients with panic disorder compared to normal control subjects, suggesting a decreased cardiac vagal function in these patients (Yeragani et al., 1993, 1998). Patients with panic disorder also had an exaggerated response to pharmacological challenge with yohimbine, compared to normal control subjects (Yeragani et al., 1992), suggesting a relatively higher sympathetic function. Compared to control subjects, patients with panic disorder had an exaggerated vagal withdrawal and higher relative sympathetic activity during lactate and isoproterenol infusions (Yeragani et al., 1994, 1995). A recent report by Kawachi et al. (1995) also suggests that higher levels of phobic anxiety are associated with low heart rate variability. Thayer et al. (1996) have recently reported that patients with generalized anxiety disorder have decreased HF power, a finding suggesting decreased vagal function in patients with anxiety. Thus, several lines of evidence suggest that patients with anxiety states have decreased cardiac vagal function (Friedman and Thayer, 1998).

Several lines of evidence also suggest a strong association between depression and coronary heart disease, and increased cardiovascular mortality (Carney et al., 1997; Musselman et al., 1998). There is also evidence suggesting reduced heart rate variability in association with depression as well as in patients with depression and coronary artery disease (Carney et al., 1995; Thayer et al., 1998). Carney et al. (1993) have also described a higher prevalence of ventricular tachycardia in patients with coronary artery disease and depression compared to those with coronary artery disease without depression. Thus the investigation of beat-to-beat QT variability may yield important information about the risk of cardiovascular mortality in patients with anxiety and depression.

In this study, we investigated beat-to-beat QT variability in patients with panic disorder and depression and in normal control subjects using laboratory records of supine and standing ECG. Based on our previous findings and findings from the previous literature on depression, we hypothesized that patients with panic disorder as