

QT interval duration in apparently healthy men is associated with depression-related personality trait neuroticism

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Abstract

Objective: High levels of neuroticism and low self-esteem are markers for vulnerability to depression, a condition associated with a higher risk of arrhythmias. The question as to whether these depression-related personality domains are related to cardiac repolarization (duration of QT interval) in apparently healthy men has been addressed in this study. **Methods:** Participants were 658 clinically healthy males who underwent a health screening programme. QT interval duration was determined in the resting 12-lead electrocardiogram using an automated analysis program. Neuroticism was assessed by the short-scale Eysenck Personality Questionnaire and self-esteem by the Rosenberg self-esteem scale. **Results:** Heart-rate corrected QT interval {QTc, formula of Bazett

[Bazett HC. An analysis of time relations of electrocardiograms. *Heart* 1920;7:353–370]} progressively increased across quartiles of neuroticism ratings. By contrast, no differences in QTc were observed across different degrees of self-esteem. A multivariate regression analysis showed that neuroticism was a statistically significant, independent predictor of QTc duration. **Conclusion:** After adjustment for potential confounders, neuroticism scores independently predicted QT interval duration in apparently healthy men. These findings highlight the possibility that higher arrhythmic risk could be present not only in patients with clinical depression but also in depression-prone, otherwise healthy individuals.

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Introduction

Ventricular repolarization is a complex electrical phenomenon, and as direct repolarization measurements obtained from epicardial monophasic action potential and body surface mapping have been found to be correlated with the QT interval on surface electrocardiograms (ECGs), simple measurements of the QT interval have been regarded as essential in monitoring cardiac repolarization [1,2].

During the past years, a bulk of published data has clearly shown that a prolonged QT interval is a risk marker

for cardiovascular morbidity and mortality in numerous different populations, including initially healthy subjects [3–5], subjects referred for Holter monitoring [6], as well as clinical cohorts of patients with diabetes mellitus [7,8] and cardiovascular disease [9,10]. Among the pathophysiological mechanisms advocated to account for this relationship, cardiac autonomic imbalance with decreased parasympathetic and increased sympathetic modulations has emerged as one of the most intriguing pathways [11].

Working from the assumption that an altered autonomic function may also be a feature of different psychiatric disorders, some authors have recently demonstrated significant alterations of the QT interval in clinical cohorts of psychiatric patients, including subjects with social phobia [12], panic disorder [13], and major depression [14]. The

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latter findings are of particular importance, because it is well-known that depressed patients show an increased risk for a number of cardiovascular complications, including ischemic heart disease [15], serious ventricular arrhythmias [16], and sudden cardiac death [17]. It has been therefore proposed that dysregulation of ventricular repolarization may be one of the mechanisms linking depressive mood states and cardiac risk [13,14,16,18]. At this time, however, no studies have assessed whether a relation exists between QT interval duration and personality-related vulnerability to depression. Nonetheless, this issue could be of interest in view of the strict interrelationships between the onset of major depressive episodes and personality traits in the domains of high neuroticism and low self-esteem [19].

Neuroticism is a dimensional measure of an individual's tendency to experience negative emotions that are manifested at one extreme as anxiety, low mood, and hostility and at the other as emotional stability [20]. Reflecting a tendency toward states of negative affect, it, together with extraversion and psychoticism, constituted the three key dimensions of personality, according to Eysenck and Eysenck [20], and has been included in nearly all theories of personality. Neuroticism is also known to possess good psychometric properties of item and construct validity, stability, and cross-cultural validation [21].

Differently from neuroticism, self-esteem has been given a number of different definitions, each emphasising different aspects [22]. The most significant division remains between the view that self-esteem is a generalised feeling about the self and the view that it is the sum of a set of judgments about one's value, worthiness, and competence in various domains [23]. In any case, different independent studies have clearly indicated that low self-esteem could be a marker for developing clinically relevant depressive episodes [24,25].

In the present report, we hypothesized that depression-related personality traits of neuroticism and self-esteem could be associated with QT interval duration as a possible pathway in the genesis of higher cardiovascular risk observed in depressive mood states. We addressed this issue by studying the relationships of neuroticism and self-esteem scores with QT interval in an Italian cohort of apparently healthy men undergoing a cardiovascular screening programme. We also reasoned that if these personality domains are independently related to QT interval duration, then effects should persist after statistical control for demographical, clinical, and biochemical characteristics of the study participants.

Methods

Study subjects

Participants were recruited from a general health survey (CardioTest Lecco) aiming to investigate the role of various genetic, biochemical, and psychological risk factors in the development of cardiovascular diseases and to initiate

appropriate primary prevention interventions in subjects at risk. All participating individuals were Caucasians of Italian descent, and the population was homogeneous with regard to ethnic background.

For the current investigation, the study cohort was composed of 658 clinically healthy males (age range 34–66 years, mean age=47.7, S.D.=6.9) with no past or present history of any psychiatric disease as well as of medical conditions that could alter electrocardiographic parameters. Specifically, to be eligible for the present study, none of subjects were permitted to suffer from (1) any known cardiac or pulmonary disease; (2) hypertension (blood pressure >140/90 mmHg or taking antihypertensive medication); (3) diabetes mellitus/impaired fasting glucose (fasting blood glucose >6.1 mmol/l or taking hypoglycemic drugs); (4) angina pectoris; (5) atrial fibrillation, bundle-branch block, frequent supraventricular or ventricular premature beats (>10 beats/min), delta waves, paced rhythm, or any arrhythmia; (6) renal, hepatic, or thyroid diseases (as assessed by self-reports and laboratory analyses); and (7) serum electrolyte imbalances. None of the subjects reported taking medication known to affect QT interval duration (i.e., beta-blockers, digitalis, anti-dysrhythmic, or antidepressant medication). Additionally, none of the participants had ever taken medications for psychiatric conditions.

Marital status, smoking status, and alcohol use of the study subjects were determined by questionnaire. We measured weight and height and calculated body mass index (BMI) as weight in kilograms divided by the square of the height in meters. Physical activity was determined using the multiple-choice question, "Which of the following statements best describes how physically active you have been during the last month, that is, done activities such as 15–20 min of brisk walking, swimming, general conditioning, or recreational sports?" Participants who answered fairly, quite, very, or extremely active (vs. not at all or little active) were considered physically active.

Systolic (SBP) and diastolic blood pressure (DBP) values were determined in the sitting position from the right arm using a sphygmomanometer after a 10-min rest period, with the mean of three determinations being recorded; diastolic pressure was measured at the fifth Korotkoff sound. We assayed total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, and fasting plasma glucose using commercially available kits.

The investigation conformed to the principles outlined in the Declaration of Helsinki, and the study protocol was approved by our local ethics committee. All participants provided their written, informed consent before entering the programme.

Measurements of QT interval

In order to reduce emotional stress and to avoid the possible influence of circadian patterns, all ECG recordings

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