



Stressful Work Involvement and Inherited Long QT-Syndrome

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Research Article

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ABSTRACT

Aims: The long QT syndrome (LQTS) is an inherited cardiac disorder which predisposes the mutation carrier to ventricular arrhythmias that can lead to sudden death. The objective of the study was to study whether stressful work involvement (i.e. worrying about work and job dissatisfaction) is related to arrhythmic risk in LQTS.

Study design: Cross-sectional study.

Place and Duration of Study: The study took place in Finland in 2006 for the LQTS mutation carriers and 2007 for the general Finnish population.

Methodology: The study subjects included 164 symptomatic and 229 asymptomatic LQTS mutation carriers from the Finnish LQTS registry and 1368 comparison subjects randomly derived from the population-based sample, Young Finns Study (YFS). Stressful work involvement was measured with questions derived from the Framingham type A scale.

Results: Upon assessment of the stressful work involvement, symptomatic LQTS

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mutation carriers scored higher than asymptomatic LQTS mutation carriers (1.51 vs. 1.40, $p=0.003$, $\eta^2=0.022$) and the general Finnish population (1.51 vs. 1.39, $p<0.001$, $\eta^2=0.012$), while asymptomatic LQTS mutation carriers did not differ from the general Finnish population in the corresponding scores (1.40 vs. 1.39, $p=0.374$, $\eta^2<0.001$).

Conclusion: The results confirm the suggestion that perceived stress, in terms of stressful work involvement, may increase the likelihood of arrhythmic events in LQTS mutation carriers. Thus, individual stress proneness may be a risk factor for LQT symptoms, which should be taken into account in counseling LQTS patients. There is previous evidence that stress proneness can be modified by behavioral therapy.

Keywords: Stress; stressful work involvement; arrhythmias; Long QT-Syndrome (LQTS).

1. INTRODUCTION

Long QT syndrome (LQTS) is an inherited cardiac disorder that predisposes its carriers to potentially fatal arrhythmias. LQTS manifests as a prolonged QT-interval on the electrocardiogram and as a tendency to develop ventricular arrhythmias which can lead to sudden death. Three of its most common subtypes are LQTS1, LQTS2 and LQTS3, two of which are caused by mutations in potassium channel genes *KCNQ1* and *KCNH2*, and the third by mutations of the sodium channel gene *SCN5A*, respectively (Schwartz et al., 1975). In addition, there are several more uncommon subtypes of LQTS (Morita et al., 2008; Hedley et al., 2009).

There is evidence that environmental factors may trigger arrhythmic events in LQTS (Schwartz et al., 2001). In addition, we have previously shown that LQTS mutation carriers show increased scores of temperamental harm avoidance (Määttänen et al., 2011) which is temperament trait reflecting stress-related high physiological reactivity as well as tendencies to experience negative emotions and to show avoidant behavior when faced with stress (Heponiemi et al., 2003; Puttonen et al., 2005).

We have also shown that the frequency of stressful life events is related to arrhythmic events in LQTS (Hintsä et al., 2010). Together these previous results imply that both symptomatic and asymptomatic LQTS mutation carriers may have a tendency towards physiological and emotional stress proneness while environmental loading plays a role whether arrhythmic events occur or not.

Thus, it has been suggested that both individual stress proneness and environmental stress might increase the risk of cardiac events in LQTS. The available data prompted us to study whether stressful work involvement is typical for subjects with LQTS. Accordingly, we examined whether symptomatic and asymptomatic LQTS mutation carriers show differences in their stressful involvement with work. In addition, we studied whether symptomatic and asymptomatic LQTS mutation carriers differ in stressful work involvement from the general population.

2. MATERIALS AND METHODS

Study subjects were from two large samples: the Finnish LQTS mutation carriers and the Young Finns Study (YFS).

2.1 LQTS Mutation Carriers

LQTS mutation carriers were recruited from the Finnish LQTS registry. The registry includes all established LQTS mutation carriers identified upon nationwide molecular genetic studies at the Helsinki University Central Hospital since 1993.

When this study was carried out, the Finnish LQTS registry included 1400 mutation carriers and 1700 unaffected relatives. To be included to the registry, the LQTS patients had to fulfill the following criteria: a molecular diagnosis of LQTS, age between 16 and 65, and residence in Finland.

The mutations in the genes *KCNQ1*, *KCNQ2* and *SCN5A* in this population have been described in detail elsewhere (Fodstad et al., 2004; Laitinen et al., 2000; Paavonen et al., 2001) (Swan et al., 1998). LQTS mutation carriers who fulfilled the criteria, received a psychological study questionnaire to their homes (Hintsala et al., 2009). The response rate was 79 %, and the reasons for attrition were unknown.

There were 393 LQTS mutation carriers who were included in the present study (164 symptomatic and 229 asymptomatic). Exclusion criteria were the following: missing information on sex, age, stressful work involvement and current employment or not being currently employed. Among symptomatic LQTS mutation carriers there were 97 excluded (76 not currently employed and 13 missing information on work status). Among the asymptomatic LQTS mutation carriers there were 106 excluded subjects (88 not currently working and 12 missing information on employment status).

Excluded symptomatic LQTS mutation carriers scored lower in work involvement (1.33 vs. 1.54; $p < 0.001$), and did not differ in sex (percent female: 80.4% vs. 69.5 %, $p = 0.054$) and age (44.08 vs. 41.69, $p = 0.166$) from the included ones.

Excluded asymptomatic LQTS mutation carriers did not differ from the included in stressful work involvement (1.46 vs. 1.40, $p = 0.191$), and in addition did not differ in sex (percent female: 60.4 % vs. 55.0 %, $p = 0.358$) or age (40.0 vs. 40.1, $p = 0.537$) from the included ones.

2.2 General Population

The sample representing Finnish population consisted of participants from the Young Finns Study (YFS), which is a prospective, population-based follow-up study on cardiovascular risk factors in the Finnish population ($n = 3596$). The study design has previously been described elsewhere in detail (Åkerblom et al., 1991; Raitakari et al., 2008). There were no suspected or diagnosed LQTS mutation carriers in this data, based on the medical examination of each participant in 2001 (O.T. Raitakari, personal communication, 31st August, 2009).

There were 1368 YFS participants in the present study. The exclusion criteria were the same as in LQTS mutation carriers, i.e. the subjects who had missing information on any of the study variables were excluded. In addition subjects who were not currently employed were

excluded. Among the general population, there were 2284 excluded (264 not currently employed and 1589 missing information on their current employment status). Excluded subjects did not differ from the included ones in stressful work involvement (1.41 vs. 1.39, $p=0.173$), but they were more often males (53.3% vs. 42.2 % $p<0.001$) and younger than the included ones (31.2 vs. 31.8, $p=0.001$).

2.3 Measures

Data on the occurrence of arrhythmic events (i.e. symptoms) in the LQTS group were collected with a questionnaire when an individual was entered into the LQTS registry. The data was updated in the year 2006 when the current survey was carried out. A sudden loss of consciousness due to a potentially arrhythmic reason, a documented LQTS-type ventricular arrhythmia and/or cardiac arrest were defined as symptoms in LQTS mutation carriers. A vasovagal fainting was not regarded as syncope. All of the participants filled the same questionnaire at the time of recruitment to the study.

Stressful work involvement was assessed in 2006 in LQTS mutation carriers and in 2001 in the YFS subjects with three items from the Framingham Type A Scale (FTAS) (Haynes et al., 1980). Stressful work involvement refers here to stressful loading caused by worrying about and being dissatisfied with one's work. The questions were as follows: "Feeling at the end of average day at work: a) Work stayed with you so you were thinking about it after working hours. b) Work often stretched you to the very limits of your energy and capacity. And c) Often felt uncertain, uncomfortable, or dissatisfied with how well you were doing at work." The response was given in yes/no (0 or 1) format to each question and sum of these answers was the total score of stressful work involvement (0-3). Reliability (Cronbach α) of the work involvement scale was 0.60 in the LQTS mutation carriers and 0.52 in the YFS population.

2.4 Statistical Analyses

All the comparisons in stressful work involvement were conducted with the analysis of covariance. Sex was the fixed factor and age was a covariate in each of the analyses, and thus all the analyses were adjusted for sex and age. In addition, depending on the analysis at hand, group (general population sample or LQTS mutation carriers sample) and symptom status (arrhythmic or not) were fixed factors.

First we compared means of stressful work involvement in symptomatic with asymptomatic LQTS mutation carriers. Then we compared both symptomatic and asymptomatic LQTS mutation carriers separately to the general Finnish population. The data was analyzed with PASW 18.0.2. software.

3. RESULTS AND DISCUSSION

3.1 RESULTS

Descriptives of the sample are presented in Table 1.

Symptomatic LQTS mutation carriers scored higher than asymptomatic LQTS mutation carriers ($F=8.818$, 1.51 vs. 1.40, $p=0.003$, $\eta^2=0.022$) and the general Finnish population ($F=18.187$, 1.51 vs. 1.39, $p<0.001$, $\eta^2=0.012$) in stressful work involvement (Figure 1). On

the other hand, asymptomatic LQTS mutation carriers did not differ from the general Finnish population in stressful work involvement ($F=0.790$, 1.40 vs. 1.39 , $p=0.374$, $\eta^2<0.001$). When added to the model, LQTS subtype did not explain stressful work involvement.

Table 1: Descriptives of the sample

	LQTS mutation carriers (n=393)		General population (n=1368)
	Symptomatic (n=164)	Asymptomatic (n=229)	
Age	41.7 (± 11.9)	41.0 (± 11.8)	31.8 (± 5.0)
Sex	114 (69.5 %)	126 (55.0 %)	791 (57.8%)
Stressful Work Involvement	1.51 (± 0.34)	1.40 (± 0.34)	1.39 (± 0.33)

**Note: Mean values and standard deviations presented, and for sex, the number and percentage of females.*

3.2 DISCUSSION

The results suggest that stressful work involvement is related to symptomatic status in LQTS. Symptomatic LQTS mutation carriers had a higher stressful work involvement than asymptomatic LQTS mutation carriers, who in turn, did not differ from the general Finnish population. Thus, a high work involvement, i.e. worrying about work and job dissatisfaction, may be linked to the increased risk of arrhythmic events. The results may imply that individual stress proneness might be a potential risk factor of arrhythmias in LQTS.

The present results are consistent with our previous finding suggesting that all LQTS mutation carriers may be more stress-prone than the general population, at least in terms of a stress related temperament (Määttä et al., 2011), and that chronic stress and stressful life events may increase the risk for arrhythmic events in LQTS (Hintsanen et al., 2010). Our results imply that stressful work involvement, that is feeling burdening worries about work and being dissatisfied with it, is also related to symptomatic status of LQTS.

Our series of studies is correlative in nature. In addition it cannot suggest any causality. It is possible that knowledge about the syndrome may cause a higher likelihood to perceive challenges as stress. Thus, experimental settings would be needed to identify the stress-related physiological mechanisms that may differentiate symptomatic and asymptomatic LQTS mutation carriers. Previous evidence suggests that increased sympathetic activity and stress-hormones may partly explain associations of stress with cardiac disease (McEwen and Stellar, 1993; Räikkönen et al., 1996; Hintsanen et al., 2005; Kivimäki et al., 2007).

To assess stressful work involvement, we used a scale derived from the Framingham type A questionnaire. The general validity of this scale is not known, which is a limitation of the study. Furthermore, although the measure assesses individual stressful work involvement, it is unable to distinguish the reasons for these perceptions, i.e. whether they are solely related to individual stress proneness or to actual stressors in the job. Although age was controlled for in all of the analyses, it is useful to note that the LQTS mutation carriers were 10 years older on average than the participants from the general Finnish population.

Special strength of the study is the availability of the very comprehensive, population based data bases in both Finnish population and a large sample of DNA-documented LQTS patients of Finland.

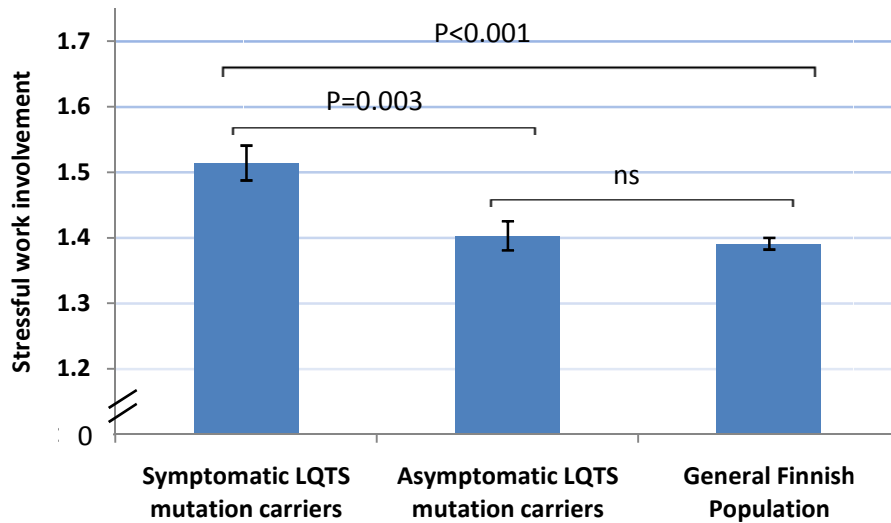


Figure 1: Mean values of stressful work involvement
 Error bars: standard errors of means.
 ns=non-significant

4. CONCLUSION

The findings of this study support the importance of stress in the manifestation of arrhythmic events in LQTS. The results suggest that perceived stress, in this case stressful work involvement, might increase the likelihood of symptoms in LQTS mutation carriers, and might suggest that one's individual stress proneness is a risk factor of LQT events. It must be noted that this study did not study the working conditions, but the perceived stress experience related to work in general. These findings may have direct clinical implications since there is evidence that one's proneness can be modified by behavioural therapy (Nunes, Frank et al., 1987).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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