

## Heart rate variability in Long QT syndrome in children - beware the genotype!

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### Introduction:

The congenital Long QT Syndrome (LQTS) is an inherited life-threatening disease caused by mutations in genes encoding cardiac ion channels. In several LQTS genotypes, arrhythmia is associated with sudden increased sympathetic activity. The fact that an increase in sympathetic activity often triggers a cardiac event and that beta-adrenergic blocking and left cardiac denervation are effective treatments, makes it evident that the sympathetic nervous system is involved in this disease. The sympathetic-parasympathetic interaction can be studied by analysis of heart rate variability (HRV). The aim of this study was to evaluate HRV and the influence of medication in children/adolescents with long QT syndrome.

### Methods:

Twenty-four hour ambulatory electrocardiographic recordings from year 2000 to 2013 in 80 children with LQTS were retrospectively reviewed. HRV power spectrum analysis was performed to determine the total power (P<sub>tot</sub>, 0.003-0.50 Hz) and the power in the low-frequency (LF: 0.04-0.15 Hz) and high-frequency (HF: 0.15-0.50 Hz) regions as well as the PLF/PHF ratio. The control group consisted of 39 healthy children. Data are presented as mean±SE of log-transformed values.

### Results:

The LQTS patients off beta-blocker therapy (n=28) presented with statistically significantly lower P<sub>tot</sub> (3.54±0.05, P=0.02) than controls (3.66±0.04). However, when analyzing subgroups of genotypes, no significant differences were found between LQT1/LQT2 patients and controls. In contrast, LQT3 patients showed a lower P<sub>tot</sub> (3.06±0.09, P<0.001) but a higher LF/HF ratio (0.47±0.08, P<0.001) than controls (0.08±0.05). Double-mutations (Jervell and Lange Nielsen syndrome, JLNS) also differed from controls: JLNS patients had a lower LF/HF ratio (-0.37±0.01, P<0.001) and a lower LF than controls (2.80±0.11 vs. 3.10±0.04, P=0.01). In 18 patients that were examined both off and on beta-blocker therapy, treatment with beta-blockers resulted in a significantly reduction of the LF/HF ratio with 16% (0.07 in log-transformed units, P=0.01).

### Conclusions:

This study indicates that impact on HRV in LQTS patients seems to be genotype dependent. Furthermore, beta-blockade reduces LF/HF in LQTS patients, indicating a reduced sympathetic activity acting as a protection against arrhythmias. HRV analysis in Holter recording might become a useful tool for risk assessment and treatment strategy in LQTS patients.