# Effects of Adrenaline on Beat-to-Beat Variability of hiPSC-CMs with Hypertrophic Cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is one of the major causes of sudden cardiac death in young individuals, often triggered by adrenergic stress. Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) offer an *in vitro* platform for investigating patient-specific electrophysiology. Here, we studied how adrenaline affects beat-to-beat variability (B2BV) in spontaneously beating hiPSC-CMs with heart rate variability (HRV)–based metrics in cells carrying HCM-related mutations.

The dataset consists of different hiPSC-CM lines: two control lines, two lines with a MYBPC3-Gln1061X mutation (HCMM), and three lines with a TPM1-Asp175Asn mutation (HCMT). Previous studies have shown that hiPSC-CMs carrying HCMM or HCMT mutations exhibit, respectively, a higher incidence of arrhythmias. Interbeat intervals were extracted from patch-clamp recordings, preprocessed, and analyzed across baseline (BL), adrenaline (ADR), and washout (WO) phases. Rhythm dynamics were characterized using a range of HRV methods, with a focus on time-domain and nonlinear metrics.

Adrenaline induced mutation-dependent changes in rhythm variability. As shown in Fig. 1A-B, both mean RR and RMSSD were altered, with high adrenaline concentrations producing effects that persisted into the washout phase, suggesting incomplete recovery of spontaneous rhythm regulation. The $\Delta$-values showed a similar pattern (Fig. 1C-D), whereas measures such as DFA $\alpha 1$ showed no genotype-dependent differences. Overall, the findings demonstrate genotype-specific modulation of beat-to-beat variability under adrenergic stimulation, suggesting that HRV-based analysis of hiPSC-CMs may provide useful insights into arrhythmia-related cellular phenotypes in HCM.

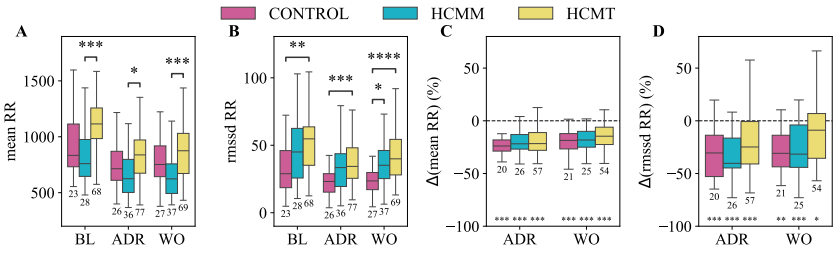


Figure 1. Mean RR (**A**), RMSSD RR (**B**) and corresponding $\Delta$values (**C-D**) across BL, ADR, and WO phases and genotype groups. Only statistically significant differences are shown ($p <= 5.0 * 10^{-2}$; Mann-Whitney with Bonferroni correction; Wilcoxon for within-group changes). Sample numbers appear below the bottom whiskers.