SPATIOTEMPORAL MODULATION OF ACTION POTENTIAL DURATION IN INTACT HEARTS BY SUB-THRESHOLDS OPTOGENETICS STIMULATION

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Cardiac optogenetics is an emerging research field combining photo-sensitive ion channels such as channelrhodopsin-2 (ChR2) expressed in cardiomyocytes with targeted illumination to enable precise spatio-temporal modulation of cardiac electrical function. During the last years, optical pacing, resynchronization and defibrillation have been demonstrated and, more recently, the development of innovative optical platforms has proven the possibility of monitoring and manipulating action potential propagation pathways in whole mouse hearts in real time. However, current implementations of cardiac optogenetics were limited to a purely binary control (activation or inhibition) of muscle contraction. In this study, we explore sub-threshold illumination of ChR2-expressing mouse hearts to further expand the manipulation capabilities of optogenetics to include fine-tuning of action potential characteristics.

We first characterized the electrical response during a sub-threshold illumination in isolated cells expressing ChR2 using patch clamp experiments. Then, using an optical mapping system operating in the near infrared regime in combination with a stimulator generating customisable patterns of blue light, we characterized action potential properties in whole-heart Langendorff preparations. We found that the depolarization current occurring during continuous sub-threshold illumination causes a slight reduction of action potential amplitude as well as a decrease in conduction velocity. Moreover, we achieved a prolongation of action potential duration of up 50% in a fully reversible manner. The capability of our optical system to stimulate the epicardial surface of mouse hearts with an arbitrary illumination pattern was therefore exploited to produce a spatial heterogeneity in action potential duration across the ventricle. We have tested different spatial geometries in terms of action potential propagation and their propensity to induce cardiac arrhythmias.

We believe that this novel approach of using sub-threshold stimulation for the manipulation of cardiac activity will be useful in examining the arrhythmogenic mechanics underlying cardiac diseases characterise by an increased QT-interval dispersion.