Shortening of Action Potential Duration with Increased Work in Contracting Rabbit Hearts

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Hypothesis
- In excised, contracting, crystallloid perfused hearts, the greater workload in LV working hearts will result in:
  - Shorter APDs during normal sinus rhythm (NSR) & pacing
  - Faster APD shortening during deoxygenation
- The KATP channel blocker, glibenclamide, will attenuate APD shortening during deoxygenation.

Background
- Hypoxic or ischemic tissue that results from coronary blockage in CHD does not receive oxygen or fuels to maintain normal cardiac function.
- KATP channels open when [ADP]/[ATP] increases, increasing the outward K+ current and shortening APD.
- Understanding the link between the metabolic and electrical states of the heart provides crucial knowledge in prevention of heart disease.
- Ratiometric optical mapping of fully loaded hearts is a novel method to study electrical activity while replicating in vivo energy consumption.

Methods
- Rabbit hearts perfused with oxygenated KH solution were cannulated in two preparations, alternatively:
  - 1. unloaded Langendorff, 2. fully-loaded left working heart (LWH)
- Epicardial APs were measured using optical mapping of Di-4-ANEPPS, a voltage sensitive fluorescent dye.
- Aortic pressure, left atrial preload, epicardial electrograms, LA flow rate, coronary flow rate, and media O2 saturation in and out of the heart were measured.
- Hearts were gradually deoxygenated by switching from 95%O2/5%CO2 gas in KH to N2 gas in KH.
- A range of workloads were studied by pacing at the following cycle lengths (CIs): 330, 220, and 170ms.
- APDs were calculated at 100% repolarization by using the time points of the maximum 1st and 2nd derivatives.

Experimental Setup

Excitation ratiometry with motion correction:
- 450nm (royal blue) and 505nm (cyan) LEDs excite epicardium
- Excitation illumination rapidly cycled between the 2 colors
- Emission light filtered before images are collected by CCD camera
- Blue light results in upright APs, cyan light results in inverted APs. Ratiometry (blue/cyan) assists in removing motion artifact.

Motion Correction Algorithm
- Optical Mapping of LW and Bi-V Working Rabbit Hearts
- Dual-excitation light
- 635±28nm emission filter
- RV LV
- Pacing electrode
- CCD

Results

A. APD during Deoxygenation: Effect of Glibenclamide

B. Oxygen Consumption

C. APD during Pacing

AP Propagation

Propagation of AP across epicardial surface during pacing. The depolarization (blue), plateau phase (yellow), and repolarization (red) propagating across the epicardium are clearly demonstrated.

Conclusion
- Optical mapping with motion tracking and ratiometry provides electrophysiological assessments during high workloads.
- KATP channels are activated more readily in LWH vs. LANG.
- KATP channel opening is attenuated in Langendorff perfused hearts.
- Conducting excised heart studies that more closely mimic physiologic workload is vital.

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References