Comparing Cardiac Dynamics between Neonatal and Adult Rats

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INTRODUCTION

In the broad field of cardiology, pediatric research has lagged behind in establishing appropriate models to study the developing heart. Human cardiomyocytes exhibit a limited life span and immortalized cell lines lack physiologically relevant automaticity. Whole-heart pediatric animal models display unique characteristics related to action potential morphology, ion channel expression, and excitation-contraction coupling unseen in other 2D models. This study aimed to establish a research model by monitoring changes that occur in these parameters, as the transitions that take place as the animal develops from neonate to adult are relatively unknown.

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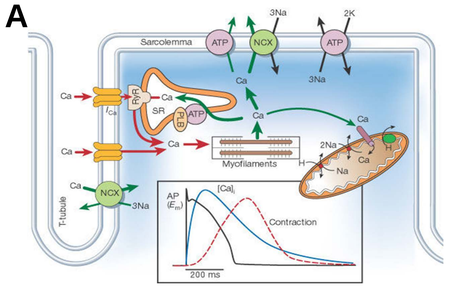

Fig. A Calcium induce Calcium release mechanism, excitation-contraction coupling in the cardiac cell.

METHODS

The hearts of rats, ranging in age from 2 days old up to adult, were excised, and the aorta was cannulated. We utilized the Langendorff method by inserting an aortic cannula and providing oxygenated Krebs-Henseleit buffer. Rat hearts were mechanical uncoupled using 5 µM of Blebbistatin to eliminate motion artifacts.

B

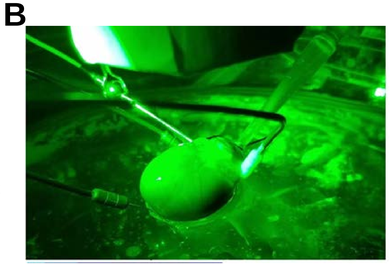

Fig. B Excised rat heart is continuously perfused and monitored during optical mapping

Additionally hearts were loaded with 62$_u$g RH237 and 50$_u$g of RHOD2 to optically map both action potentials and calcium transience respectively. With electrodes places on the epicardial surface, the hearts were subjected to a ventricular pacing protocol. Action potentials were recorded using an Andor iXon camera (> 500 fps).

RESULTS

C

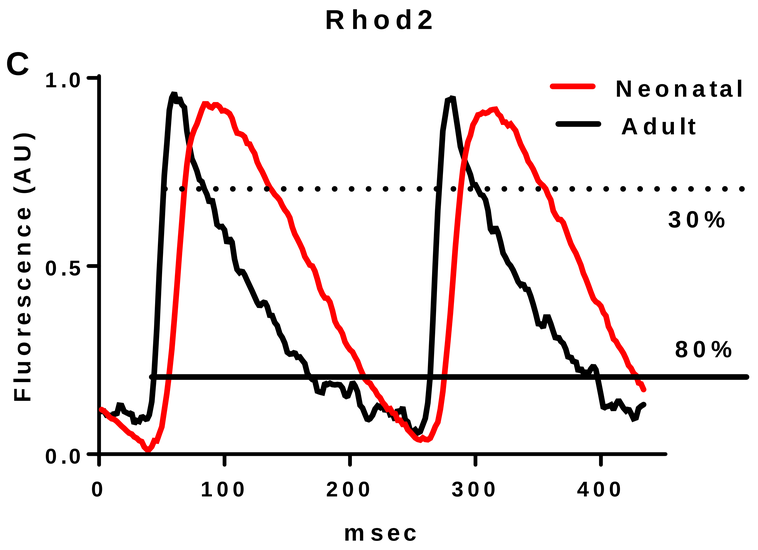

Fig. C Rhod2 staining displays calcium transients.

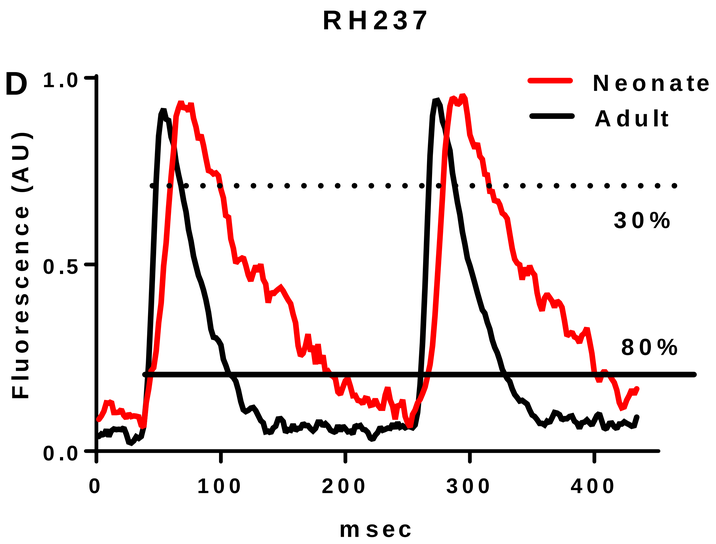

Fig. D RH237 staining displays voltage fluctuations.

ACKNOWLEDGMENTS

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RESULTS

Preliminary results showed that compared to adult cohorts, neonatal rats displayed a longer action potential duration (APD80: adult= 85.9ms, neonatal=95.5ms, p=0.026), likely associated with delayed I_{to} expression. Likewise, calcium handling was also slower in the neonatal hearts as shown by the calcium imaging (Cad80: Adults: 128.9ms, neonatal=138.8, p=.004). A comparison of heart weight to body weight showed that from day 5-11 of life, the heart weight increased at a rate faster than the body; this is a natural stage in cardiac development known as hypertrophy.

E

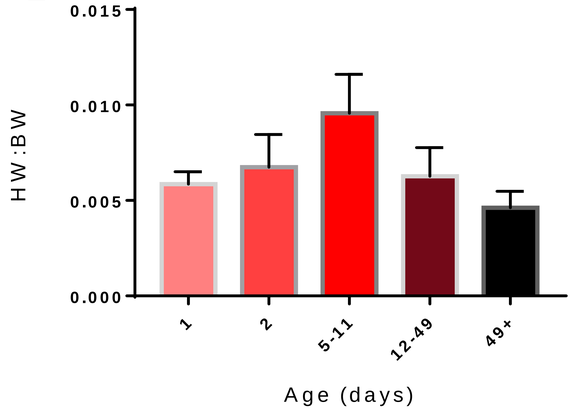
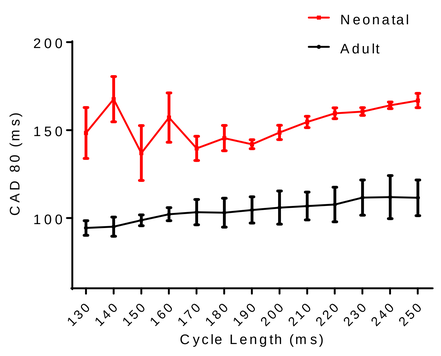


Fig. E Comparison of Heart weight to Body weight.
Fig. F Calcium restitution at 80%.
Fig. G Action potential restitution at 80%.

F



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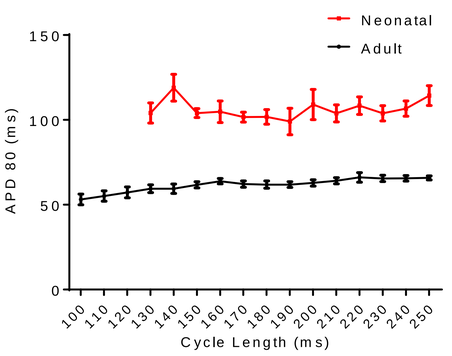

CONCLUSION

Calcium handling was slower in the neonatal hearts, most likely due to immature calcium handling and less robust calcium-induced calcium release. The developing excitation-contraction coupling machinery will be further probed using pharmacological tools to elucidate underlying mechanisms; and the newly developed pediatric model will be used for toxicological screening.