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INTRODUCTION

- The estimated lifetime prevalence of post-traumatic stress disorder (PTSD) is 10-30% and of great concern for military medicine¹⁻³.
- More than 50% of individuals remain refractory to treatment⁴.
- Trauma may manifest in altered behavioral patterns and physiological responses when exposed to the context in which the trauma occurred.
- Recall of the trauma (re-experiencing/ intrusive thoughts) can incubate overtime.
- This process of fear incubation and its physiological impact are often overlooked in preclinical models.

Objectives

1. Characterized a rat model of incubation of fear.
2. Assess the impact of trauma on the electrocardiogram (ECG) waveform to determine cardiovascular profiles of trauma.

METHODS

Animals: Male Sprague-Dawley Rats

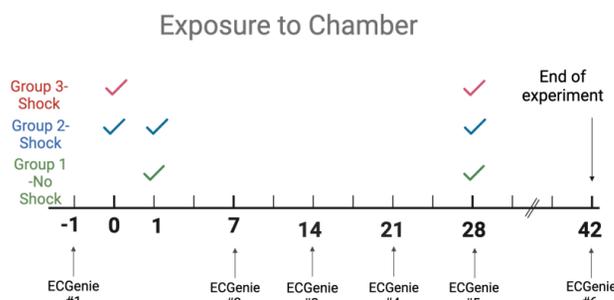
Group 1: Control - no shock

Group 2: Shock - Recall day 1

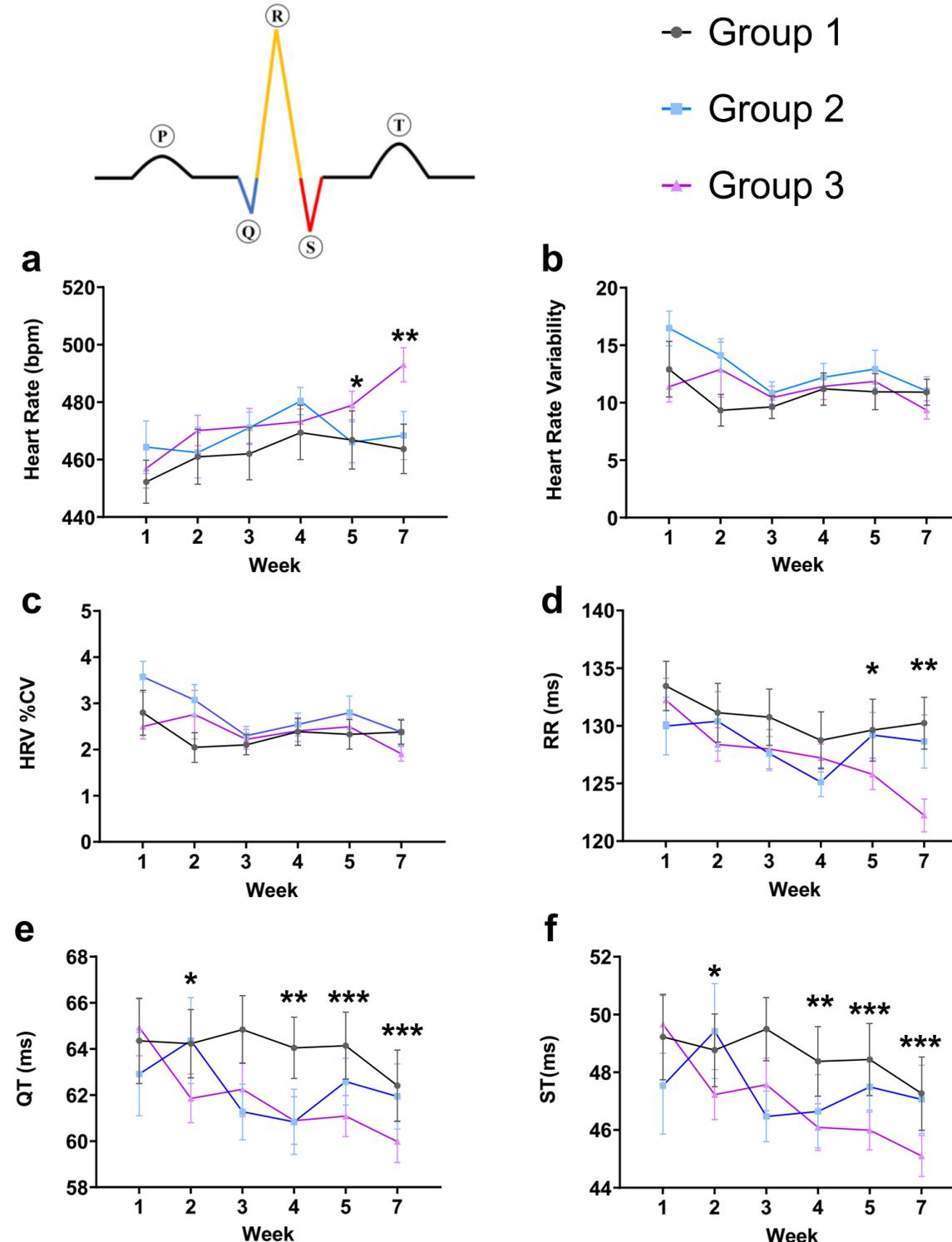
Group 3: Shock - Recall day 28

Incubation of fear: Rats were administered a single 1.5 mA shock (2 s duration), occurring approximately 120 s into their 180 s session. Contextual fear memory recall was assessed in sound attenuating chambers (Coulbourn, Inc), and measured as percentage of time freezing, during a 180 s test session on day 1 (group 2), or day 28 (group 3) post conditioning.

Electrocardiograms (ECG): Tracked weekly using the ECGenie Clinic and analyzed using the EzCG Signal Analysis Software (Mouse Specifics Inc.)

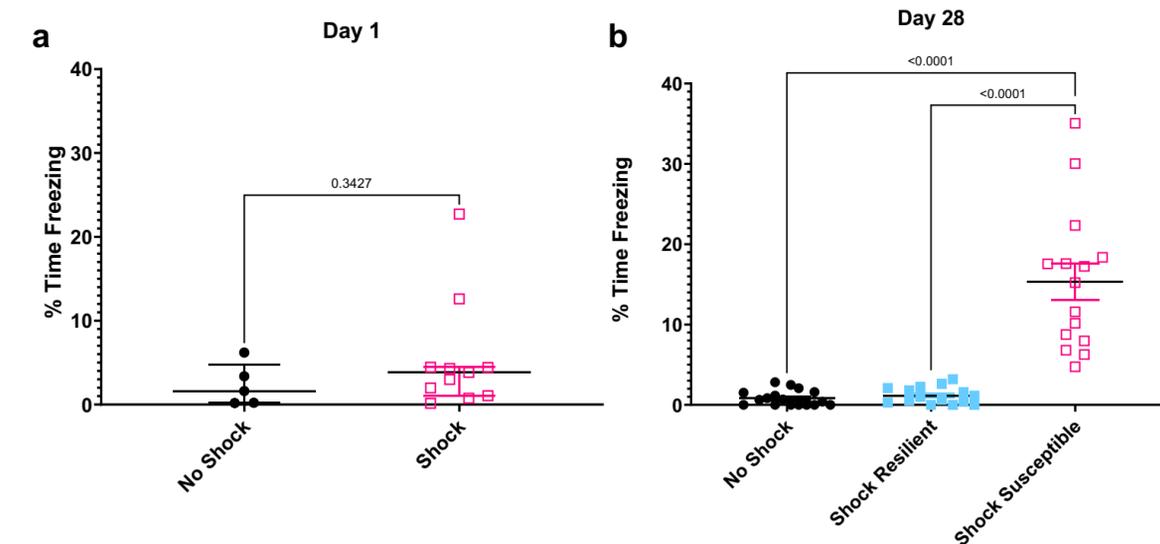


RESULTS



Persistent alterations in ECG waveform in rats with incubation of fear

There was a main effect of shock on a) Heart Rate b) heart rate variability, c) CV% of HRV d) R-wave interval, e) Q-T interval (QT) and f) ST segment. Dunnett's multiple comparisons for within group assessments determined significant differences for several measures relative to their baseline profiles on week 1. The symbols *, ** and *** represent $p = 0.05$, $p = 0.01$, and $p = 0.001$ respectively between Group 1 and Group 3.



Incubation of fear apparent at 28 days post shock

On day 1 post conditioning (Group 2), no difference in freezing behavior was evident ($p=0.3427$). When retested at day 7 and day 28 (data not shown), Group 2 (Day 1 recall) did not exhibit incubation of fear. In contrast, on day 28 post conditioning (Group 3), animals exhibited greater than control levels of freezing behavior ($F(2,44)= 20.15$, $p<0.0001$). Based on a criteria of mean ± 2 SD as a cut off, 15/30 animals were deemed shock susceptible.

DISCUSSION

- Incubation of fear was observed on day 28 post shock, with 50% of animals showing the trauma associated phenotype.
- A clear physiological impact of shock on ECG profiles was evident in the later weeks following stress exposure.
- The persistent physiological differences during fear incubation in rats may be similar to the lasting impact induced by trauma in humans.

Conclusions

1. The incubation of fear model is feasible and will be characterized further.
2. The persistent ECG alterations post shock are reliable. Normalization of ECG profiles by this non-invasive method, will be an additional screening tool for novel therapeutics

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Conflict of Interest: None

Disclaimer: The content and conclusions do not necessarily represent the official position or policy of the Uniformed Services University of the Health Sciences, the Department of Defense, or the U.S. Government.

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