CASE STUDY

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Cardiac Protection in a Novel Large Hibernator Model of Ischemia Induced Arrythmias

Introduction

Sudden Cardiac Death (SCD) is the leading cause of mortality worldwide, accounting for 25% of the 17 million deaths annually.[1] The most common cause of SCD are arrythmias, which lead to abnormal pumping of the heart and inadequate oxygenation to vital organs. Despite advancements in cardiac research over the past 30 years, high mortality rates and clinical treatment challenges still exist. As a result, novel animal models and techniques are required for improved understanding of cardiac protection during arrhythmic and SCD events.

The Background

Natural hibernators go through various physiological adaptations during times of hibernation in the cold seasons, including a decrease in basal metabolic rate and myocardial oxygen requirements. When exposed to hypothermic conditions, resistance to temperature induced arrythmias are observed. Researchers selected the woodchuck, the largest living true hibernator, as the animal model for investigating the susceptibility of ventricular arrythmias during myocardial ischemia at both hibernation (winter) and non-hibernation (summer) cycles.

The Study

Wild-caught woodchucks were obtained during the summer and winter months and individually housed in room temperature conditions for 2 - 4 weeks prior to terminal studies.

Subjects were prepared with telemetry transmitters (D70-PCTP, Data Sciences International, St. Paul, MN USA) and ECG leads. The coronary artery was ligated to induce ischemic ventricular arrythmias. Arrythmias were recorded and analyzed offline using a modified arrythmia scoring system. Monophasic action potentials (MAPs) were recorded simultaneously with telemetry using an epicardial contact electrode (Harvard Apparatus, Holliston, MA, USA) and a differential amplifier (Warner Instruments, Hamden, CT, USA). Treatment and control groups were formed each season. The treatment group receiving calmodulin-dependent protein kinase II (CaMKII) inhibitor, which has been shown to influence antiarrhythmic activity. In addition, catalase adenovirus or a control (green fluorescent) was injected 48 hours prior to surgery to allow time for protein overexpression. ECG telemetry data was collected continuously for 24 hours. Cellular analysis was conducted postmortem.

The Results

ECG telemetry recordings showed elevated ST-segments in all subjects, confirming cardiac ischemia induced by coronary artery occlusion (CAO). Arrythmia detection was found to be significantly higher during the non-hibernation months. These subjects experienced frequent premature ventricular contractions (PVCs) 7 hours after CAO, followed by ventricular tachycardia (VT) and fibrillation (Fig 1). Subjects in hibernation showed resistance to fatal ischemia-induced arrythmias, with lower incidences of PVCs and only one benign episode of VT.

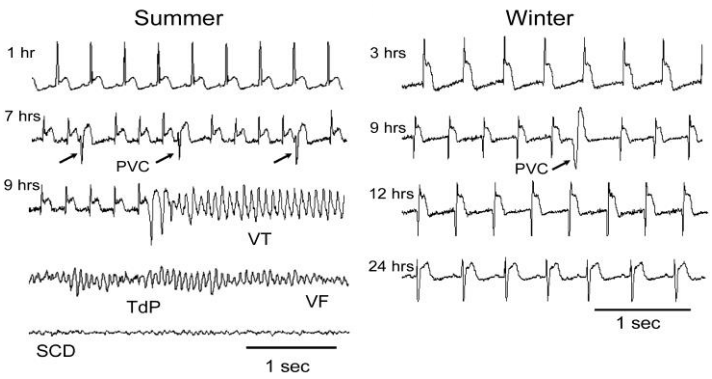

Figure 1: ECG recordings showing a decrease in ventricular arrythmias and SCD during hibernation

MAPs recorded simultaneously with ECG reported smooth depolarizing phases with a disappearing P wave following CAO, indicating that delayed afterdepolarizations are involved with triggering VT during non-hibernating periods (Fig. 2).

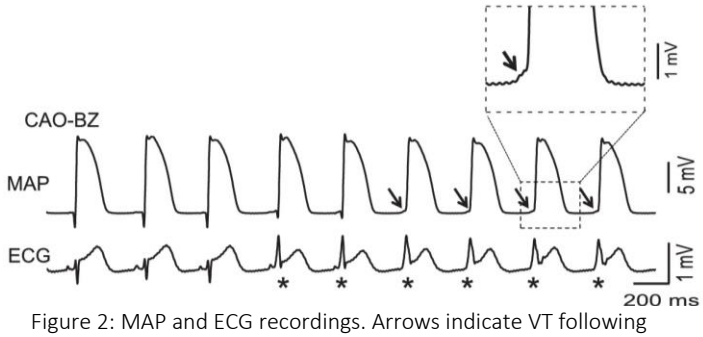

Figure 2: MAP and ECG recordings. Arrows indicate VT following delayed afterdepolarizations

After termination, samples from left ventricular myocytes revealed differences at the cellular level between seasons and the treatment/control groups. All winter subjects showed decreased oxidative stress exhibited through increased catalase activity and greater resistance to H_2O_2 induced afterdepolarizations. Overall, CaMKII activation was highest and the greatest number of arrythmias detected in the non-hibernation control group.

The Successes

Researchers utilized previous knowledge of adaptive mechanisms of the woodchuck heart when designing their study. Identifying ventricular arrythmias via continuous ECG telemetry, revealed for the first time that woodchucks display a much greater resistance to ischemia-induced arrythmias during periods of hibernation through overexpression of catalase or inhibition of CaMKII. With SCD remaining the leading cause of mortality worldwide, this study supports the use of woodchucks in providing valuable insight into arrythmia resistance and protective cardiac physiology for studying future strategies in protecting non-hibernating species from cardiac injury.

DSI

Data Sciences International (DSI) offers complete systems that sense, transmit, acquire, and report physiologic data. To create a more robust study design, scientists rely on DSI and Harvard Bioscience technology to study specific targets as well as obtain a holistic view; allowing them to look at side effects that are upstream or downstream of the main pathology.

The DSI team ensures that researchers are equipped and prepared from the first minute of their study to the last, because your research is everything.

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References:

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