Abstract: P79

the effects of vagus nerve stimulation on ventricular electrophysiology and nitric oxide release in the rabbit ventricle

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Topic(s):
Basic Science - Cardiac Biology and Physiology: Ion Channels, Electrophysiology

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S21

Background

Autonomic imbalance is a known hallmark of heart failure (HF). Our group has previously shown that vagus nerve stimulation protects the heart against ventricular fibrillation (VF) via a nitric oxide (NO) pathway which could be relevant in HF. Clinical studies using vagus nerve stimulators in HF have produced ambiguous outcome results and it has been questioned whether an adequate level of stimulation was actually achieved which raises the question as to the optimal stimulation parameters needed to produce relevant functional effects

Purpose

To assess the effects of different voltages and frequencies of right VNS on cardiac electrophysiology and NO release in the rabbit ventricle.

Methods

Hearts from adult male NZW rabbits (n=20, 2.0–2.5Kg) were procured for dual-innervated Langendorff perfused preparations ex vivo. The right cervical vagus was stimulated at 2 ms with i) high voltage (80% HRmax) at 1, 2, and 3 Hz, and ii) low voltage (10% HRbase) at 5, 10, and 20 Hz. Effective refractory period (ERP) and monophasic action potential duration restitution (MAPDR) were measured using a single extra-stimulus protocol. Ventricular fibrillation threshold (VFT) was measured using a burst pacing protocol (30x30 ms) as the minimum current required to induce sustained VF. NO release in the left ventricle was investigated using a single bifurcated light guide system and DAF2-DA dye. Data presented as mean±SEM, p<0.05 considered significant.

Results

Right VNS (RVNS) at a voltage that gave 80% HRmax (6.71±0.67 V) reduced HR significantly at 1, 2 and 3 Hz (-13.64±2.26%, -18.29±2.42%, and -26.86±3.29% respectively). At voltages that resulted in a 10% HRbase (1.31±0.12 V), changes in HR were less - even at 5, 10 and 20 Hz (-5.39±1.60%, -6.29±1.70%, and -8.39±2.20% respectively). High levels of NO release were observed at 10 and 20 Hz of 10% HRbase stimulation, (81.93±29.32 and 230.60±54.70 mV). RVNS increased VFT during all stimulation protocols

Conclusion

High voltage VNS affects the level of HR reduction more but not the level of NO release in the rabbit ventricle. In contrast, high frequency VNS, even at very low voltages, alters NO release whilst causing relatively little changes in HR suggesting a potential mechanistic pathway for relevant clinical application.
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Figure 1. Percentage change of heart rate reduction (ΔHR), increased in F490 nitric oxide fluorescence signal, and changed in ventricular fibrillation threshold (VFT) with vagus nerve stimulations at 80%ΔHRmax and 10%ΔHRbaseline voltages. *P<0.05, **P<0.01, ****P<0.0001