Regional heterogeneity in cardiac electrophysiological effects from sympathetic nerve stimulation; evidence for cardiotoptic sympathetic innervation

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Topic(s):
Basic Science - Cardiac Diseases: Arrhythmias

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S34

Funding Acknowledgements:
BHF Program Grant

Background: Intrinsic electrical heterogeneity of the heart is well documented, and factors that cause an amplification of the heterogeneities, such as sympathetic stimulation, can be proarrhythmic. Stimulation of the left sympathetic neurones has been demonstrated previously to be arrhythmogenic, and removal of the left stellate ganglion has anti-arrhythmic effects. However, detailed studies into differential sympathetic innervations and effects on regional cardiac electrophysiology are lacking.

Purpose: This study will investigate the regional heterogeneities in ventricular electrophysiological parameters and the differential effects of the left and right sympathetic neurones.

Methods: Using the isolated innervated rabbit heart preparation, optical action potentials were obtained with the voltage sensitive dye di-4-ANEPPS over the anterior left ventricle using a Hamamatsu 16 × 16 element photodiode array. (n=12). The spinal cord was stimulated with both sympathetic chains intact (Bilateral sympathetic stimulation; SS), after removal of the left sympathetic chain (left denervation; LD) and after both chains were removed (left and right denervation; LRD). Heart rate, action potential duration (APD), action potential duration restitution (RT), dispersion of repolarisation (DOR) and effective refractory period (ERP) were measured. Data are Mean±SEM; compared using ANOVA or paired t-test.

Results: SS increased heart rate from 130.9±7.2 bpm to 216±3.9 bpm (P<0.0001, 74.5±10.5% increase). Spinal stimulation after LD still produced a large heart rate increase from 127.5±5.5 bpm to 170±7.1 bpm (P<0.0001, 39.2±8.2% ). After LRD, stimulation produced no change in heart rate. SS caused shortening of APD across the ventricle (mean APD: 148.2±1.2 ms) when compared to baseline (154.4±1.5 ms), with the greatest shortening observed at the base and freewall. After LD, stimulation caused much less shortening (154.7±1.2ms) from baseline (157.3±1.4ms). There was no change in APD during stimulation after LRD. The maximum slope of RT displayed the same trend as APD as the increase in slope values observed during SS was greatly reduced after LD and eliminated after LRD. DOR increased from 4.1±0.3 to 5.2±0.4 with SS (P>0.05), from 6.2±0.8 to 6.4±0.8 after LD (P=NS) and there was no change after LRD. ERP decreased from 171.7±2.4 ms to 157.8±2.2 ms with SS (P<0.0001, -8.1±1.3%) and there was less of a decrease from 171.1±2.2 ms to 169.4±1.9 ms after LD (P<0.0001, -2.3±1.0%). There was no change in ERP from baseline after LRD.

Conclusion: This study highlights preferential electrophysiological effects at the base of the ventricle from stimulating left sympathetic neurones, and improves the understanding of the mechanisms behind the dominant influence of the left sympathetic neurones on cardiac excitability and arrhythmic mechanisms. These results have implications in refining treatment modalities involving sympathetic innervation such as stellectomy.
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Figure 1. Regional changes in maximum slope of APD restitution during sympathetic stimulation and removal of sympathetic chains.