RELAXIN SUPPRESSES ATRIAL FIBRILLATION IN 24 MONTH OLD RATS BY REVERSING ATRIAL FIBROSIS AND UPREGULATING SODIUM CHANNELS

Poster Contributions
Poster Hall B1
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Session Title: What Constitutes Anti Arrhythmic Therapy for Atrial Fibrillation?
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Authors: Brian Henry, Ashish Parikh, Divyang Patel, Jamie Haney, Charles McTiernan, David Schwartzman, Sanjeev Shroff, Guy Salama, University of Pittsburgh, Pittsburgh, PA, USA

Background: Atrial fibrillation (AF) contributes significantly to morbidity and mortality in elderly patients and AF has been strongly correlated with the development of atrial fibrosis. Therefore, the antifibrotic hormone relaxin (RLX) was studied as a novel therapy for AF and age related fibrosis.

Methods: 24 month old rats (“aged rats”) were treated for 2 weeks with vehicle or RLX using implantable minipumps. Hearts were tested for AF vulnerability and optically mapped to analyze action potential durations, intracellular Ca²⁺-transients and restitution kinetics. Atrial tissue was also analyzed by real time PCR, immunofluorescence microscopy and patch clamping.

Results: Aged rats had significant atrial fibrosis and were highly susceptible to inducible AF. In contrast, aged RLX treated rats had reversal of atrial fibrosis and did not have inducible AF. Atrial optical mapping data demonstrated that RLX treatment suppressed AF by improving atrial conduction velocity and restitution kinetics. RLX decreased the presence of atrial collagen deposition and the expression of the profibrotic mRNA transcripts for transforming growth factor-β, matrix metalloproteinase-2 and collagen I/III. Independent of antifibrotic actions, RLX treatment increased Na⁺ current density (INa) by the upregulation of voltage dependent Na⁺ channels.

Conclusion: RLX treatment suppressed AF in aged rat hearts by increasing conduction velocity via a combination of reversal of atrial fibrosis and by increasing INa. This study provides compelling evidence that RLX may provide a novel therapy to manage AF in humans by reversing fibrosis and by modulating cardiac ionic currents.