Mechanistic exploration of mechanisms underlying autonomic-induced atrial remodeling: a new step in the molecular changes related with arrhythmogenic vulnerability?

Mário Martins Oliveira1, M.Carvalho2, G. Postolache2, V. Geraldes2, JP Gomes3, C. Tavares2, S. Laranjo2, I. Rocha2

(1) Hospital Santa Marta, Lisbon, Portugal (2) University of Lisbon, Faculty of Medicine, Lisbon, Portugal (3) National Institute of Health Dr. Ricardo Jorge (INSA), Lisbon, Portugal

There is evidence suggesting an increase prevalence of atrial arrhythmias, particularly atrial fibrillation, in trained athletes. This appears to be strongly related with a combination of factors, including an important contribution of autonomic nervous system (ANS) changes. However, the basic mechanisms underlying autonomic-induced atrial arrhythmogenic remodeling still speculative. **Aim:** to study the effects of sympathetic (S) and parasympathetic (PS) stimulation (stim) on mRNA expression of major ion channels, connexins and adenosine receptors in the rat atria. **Methods:** we studied gene expression levels for K+, Na+, Ca2+, and Cl- channels, connexins (Cx40, Cx43), and adenosine A1 and A2A receptors (A2A) after 2 hours (2h) of continuous S and PS stim (4 groups of anesthetized, artificially ventilated Wistar rats; n=80). A sham group (n=40) was used as control matching number, age and sex. The S group received thoracic S trunk stim and the PS group underwent right cervical vagus stim. Right (RA) and left (LA) atrial mRNA amounts for KCND2, KCND3, KCNA5, KCNJ3, KCNJ6, SCN5A, CACNA1, and CFTR, Cx40/Cx43 and A1 and A2A genes were quantified with a two-step real time PCR assay for each condition. Receptors mRNA quantification used the housekeeping gene 18SrRNA as internal control. T-student test was used (significance for $p<0.05$). **Results:** Compared with controls, S stim increased KCND2 and A2A expression in both atria and SCN5A expression in LA; PS stim produced an increase of A2A expression in both atria and a decrease in LA KCNA5 and in LA Cx43. Cx40, KCNJ6, CFTR and A1 mRNA levels did not change significantly. LA showed larger ion channel and connexin expression changes. **Conclusion:** ANS stim induces premature heterogeneous changes in connexin, ion channel and A2A receptors expression in rat atria, suggesting that interaction in S and PS activity may play a role in atrial arrhythmogenic remodeling.