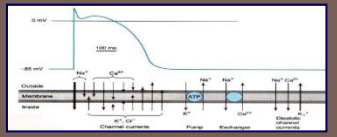
MECHANISTIC EXPLORATION OF MECHANISMS UNDERLYING AUTONOMIC-INDUCED ATRIAL REMODELING: A NEW STEP IN THE MOLECULAR CHANGES RELATED WITH ARRHYTHMOGENIC VULNERABILITY?

Mário M. Oliveira[1,2], Mafalda Carvalho[1], G. Postolache[1], V. Geraldes[1], J. Paulo Gomes[3], C. Tavares[1], Sérgio Laranjo[1,3], Isabel Rocha[1]

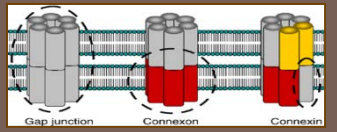
There is evidence suggesting an increase prevalence of atrial arrhythmias, particularly atrial fibrillation, in trained athletes. This appears to be strongly related with a combination of factors, including an important contribution of autonomic nervous system (ANS) changes. However, the basic mechanisms underlying autonomic-induced atrial arrhythmogenic remodeling still speculative.

Aim: to investigate the impact of increased ANS activity on atrial-remodeling by analyzing 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.

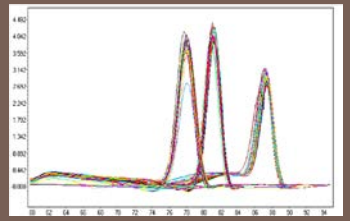


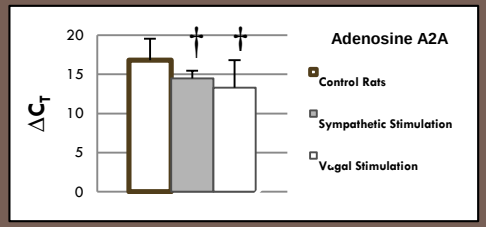
Methods:

- **4 groups of** anesthetized,artificially ventilated Wistar rats (aged 12 weeks, n=80) »»» 2 hours of continuous thoracic trunk S and right cervical PS stim
- after ANS stim, animals were sacrificed and separate samples of the left (LA) and right (RA) atria collected for mRNA Real Time PCR quantification for each condition
  - *gene expression levels for K+ (KCND2, KCND3, KCNA5, KCNJ3, KCNJ6), Na+ (SCN5A), Ca2+ (CACNA1), Cl- (CFTR), connexins (Cx40, Cx43) and adenosine (A1 , A2A) receptors*
- *a sham group (n=40) was used as control - matching number, age and sex -.*
- receptors mRNA quantification used the housekeeping gene 18SrRNA as internal control.



Results:





Melting peaks from the RT-PCR for both the target genes and the internal control 18S rRNA.

Compared with controls:

- S stim increased KCND2 and A2A expression in both atria and SCN5A expression in the LA.
- PS stim produced an increase of A2A expression in both atria and a decrease in LA KCNA5 and Cx43.
- Cx40, KCNJ6, CFTR and A1 mRNA levels did not change significantly.
- LA showed larger ion channel and connexin expression changes.

[1]Translational Research Unit, IMM-FML
[2]Cardiology Department, Hospital Sta Marta, CHLC
[3]National Institute of Health Dr Ricardo Jorge

(authors have nothing to declare)

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.