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Presentation Abstract

Session:	Poster Session 2 Thursday, May 13, 2010, 9:00 AM -12:00 PM
Presentation:	PO2-91 - Sensitivity Of Atrial Fibrillation Related Biomarkers To Changes In Ionic Current Properties
Location:	Exhibit Hall
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Abstract:	Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia and significant efforts are devoted to identifying new anti-AF drugs. Clinical research has shown that persistent AF is mainly sustained by reentrant wavelets. However, ionic mechanisms underlying AF-related reentrant activity are still unclear. Our goal is to perform a systematic investigation to quantify the sensitivity of properties determining reentry stability to changes in atrial ion channel properties. Methods: A human atrial 2D tissue model was developed using the Maleckar action potential (AP) model. Stimulation protocols used in clinical studies were applied to quantify the sensitivity of parameters related to reentry stability (AP duration (APD), resting potential (Vrest), APD restitution slopes (APDRs), time for APD rate adaptation, refractory period (ERP) and conduction velocity (CV)) to changes in ionic current properties. Simulation results were validated using experimental data from the literature. Results: IK1 inhibition results in an anti-arrhythmic increase in APD and Vrest. Both overexpression of IK1 and block of INaK flattens APDRs, which could facilitate reentrant stability. Block of ICaL and INaK, as in heart failure, delays rate adaptation and favours afterdepolarizations, indicating a higher arrhythmic risk. INa block leads to anti-arrhythmic increase in ERP and decrease in CV. Conclusions: Sensitivity of parameters related to reentry stability to changes in ion channel properties

as provided here can be key in the development of new multi-channel action anti-AF drugs.

	G_{CaL}	G_{NaCa}	G_{K1}	G_{NaK}	G_{Kur}	G_{to}
APD_{90}	31%	3%	**141%**	36%	37%	16%
V_{rest}	6%	0%	**28%**	18%	4%	1%
τ_{fast}	**1598%**	124%	100%	6%	334%	72%
τ_{slow}	42%	19%	28%	**1005%**	43%	9%
S_{s1s2}	90%	32%	73%	**97%**	92%	25%
S_{dyn}	7%	3%	**1364%**	400%	120%	70%

Relative Sensitivity = 1
0.2 < Relative Sensitivity ≤ 1
0.04 < Relative Sensitivity ≤ 0.2
Relative Sensitivity < 0.04

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