Modeling the chronotropic effect of isoprenaline on bio-pacemaker

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Aims: Comparing with traditional electrical pacemaker, one of the superiorities of biological pacemaker (bio-pacemaker) was that it can facilitate chronotropic responses of autonomic nervous regulation. However, how the bio-pacemaker response to autonomic nervous regulation was still not clear. Autonomic nervous regulated intrinsic sinoatrial node (SAN) by two neurotransmitters: isoprenaline and acetylcholine. Here we simulate the chronotropic effect of isoprenaline (ISO) on the pacemaking ability of bio-pacemaker.

Methods: We modified our previous pacemaker cell model of electrical activity by incorporating equations for the known dose-dependent actions of ISO on various ionic channel currents (I_{CaL}, I_{Kr}, and I_{Ks}), kinetics of I_{Kr} and I_f in intrinsic SAN. To investigate the ionic basis of the effects of ISO, we simulated the chronotropic effect of a range of ISO concentrations on individual ionic channel or a subset of them.

Results: Results showed that an increase in I_{Kr} and I_{Ks} caused by ISO made maximum diastolic potential more negative, which motivated the activation level of I_{Na}, thus accelerated pacemaking rate. ISO can accelerate the action of I_f, so that promote pacemaking activity. But the increased I_{CaL} have a negative effect on pacemaking cycle length.

Conclusion: ISO have great effect on the pacemaking rate in our model. And the autonomic nervous regulation of bio-pacemaker may differ from intrinsic SAN. This study may provide a new sight into the underlying risk of bio-pacemaker therapy.