More than one type of stretch activated channel contributes to the action potential duration in guinea pig

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Previously, we provided evidence of the differential involvement of stretch activated channels in the shaping of the action potential through the left ventricular wall of the rat heart. We postulated a role for these channels in the control of dispersion of repolarisation. In this study we aimed to establish if this phenomenon holds for a different species, the guinea pig and also to dissect the contributions of non-selective cation channels (SACs) and the family of stretch activated, 2 pore 4 transmembrane domain, potassium channels (TREK).

We used Langendorff perfused guinea pig heart preparations (N=6) and recorded monophasic action potentials (MAP) simultaneously from the epicardium and the endocardium of the left ventricular free wall under left ventricular end diastolic pressures of 0-5 mmHg (no stretch), 20-25 mmHg (moderate stretch) and 50-55 mmHg (elevated stretch). Hearts were perfused with Hepes buffered Tyrode's solution (pH 7.35-7.37) at 37°C bubbled with oxygen and paced at 4 Hz. This was repeated in the presence of the reported SAC channel blocker streptomycin (80μM). Action potential durations (APDs) at 20, 50 and 80% repolarisation were measured and analysed using general linear model ANOVA followed post hoc by Tukey's pairwise comparisons.

APDs were unchanged compared to control following both moderate and elevated stretch in both the epi- and endocardial layers when measured at 20 and 50% repolarisation. At APD_{80} there was a slight increase in duration although this was not statistically significant. Following blockade of SACs by streptomycin there was a decrease in APDs for 20, 50 and 80% of repolarisation which was significant for both levels of stretch at $APD_{80.}$

These results suggest that both SACs and the family of stretch activated, 2 pore 4 transmembrane domain, potassium channels which we interpret to be TREK contribute to the shaping of the action potential in the guinea pig. We further suggest that the guinea pig may be more susceptible to stretch than the rat as the decrease attributed to TREK was already maximal at 20-25mmHg (moderate stretch).