Re-Entry in a Model of Ischaemic Human Ventricular Tissue

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BACKGROUND: Ventricular fibrillation in the human heart generally induces global ischaemia, and so the aim of this study was to understand how ischaemia modulates the stability and period of re-entry in models of human ventricular tissue. METHODS: Tissue simulations used a monodomain model with a diffusion coefficient of 1.171 cm2/ms. Membrane excitability was described using the 2006 version of the TNNP model for human ventricular cells, with parameters set to give steep APD restitution and unstable re-entry. To simulate ischaemia, extracellular K+ concentration was increased from a normal value of 5.4 mM to 7.0 and 8.0 mM, maximum L type Ca2+ channel conductance decreased to 90% and 80% of its default level, and an ATP dependent K+ current was activated with intracellular ATP concentrations reduced from a normal value of 6.8 mM to 5.5 and 5.0 mM. Action potential duration (APD) and conduction velocity (CV) restitution were measured with an S1S2 protocol in thin 2D strips of simulated tissue, and the stability of re-entry was assessed in a square domain representing a 25 x 25 cm 2D sheet. RESULTS: Increasing extracellular K+ concentration to 8.0 mM reduced the minimum diastolic interval supporting S2 propagation from 380 to 340 ms, and reduced CV from 64 to 49 cm/s. Changes in maximal L type Ca2+ channel conductance and intracellular ATP led to modest changes in APD and CV. Combining these changes resulted in flatter APD and CV restitution curves in simulated ischaemic tissue. Re-entry was unstable in simulated normal tissue with a period varying between 300 and 230 ms, but stable in simulated ischaemic tissue with a period of around 400 ms. Simulated ischaemic tissue with extracellular K+ set to 8.0 mM converted unstable re-entry to re-entry, but simulated ischaemic tissue with extracellular K+ set to 7.0 mM did not. CONCLUSION: In these models, simulated ischaemia acted to flatten APD and CV restitution, reduced CV and increased the period of re-entry, but did not always result in the conversion of unstable re-entry to stable re-entry. The characteristics of fibrillation in normal and globally ischaemic ventricular tissue are likely to be different.