Vulnerability to Re-entry Arising from LPC-induced Alternations of Cardiac Sodium Current Kinetics: A Simulation Study

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Introduction: Accumulation of Lysophosphatidylcholine (LPC) during myocardial ischemia (MI) causes the remodelling of sodium channel currents (INa: INaT & INaL). However, the pro-arrhythmic effect of the remodelled INa has not been elucidated yet. The aim of this study was to use biophysically detailed computer models to investigate the functional effects of the LPC-induced changes of INa on ventricular excitation wave conduction. Methods and Results: Computational models of INa were developed for applications to experimental data describing the actions of LPC on Na+ channel kinetics, such findings were then incorporated into biophysically detailed cellular and tissue computer model to exploit and characterize the actions of the LPC-induced changes in the sodium channels on arrhythmic substrate. The simulations showed that the remodelled INa prolonged ventricular action potential duration and effective refractory period, thereby prolonging electrocardiographic QT interval. It increased the transmural heterogeneity of repolarisation and the temporal vulnerability of tissue to initiate re-entry. It also reduced the excitability of ventricular tissue, resulted in decreased conduction velocity and reduced wavelength (WL) of excitation waves. Consequentially the critical minimal substrate size which is required to maintain re-entrant excitation was reduced. Conclusion: Collectively these simulation data demonstrate the increased susceptibility of ventricular tissue to arrhythmogenesis and provide insights toward the pro-arrhythmic effect of regulated INa by LPC in patients with ischemic conditions.