Electromechanical characterisation and computer simulation of a noradrenaline induced ventricular arrhythmia.

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Aims: To characterise the electromechanical aspects of an arrhythmia caused by a subepicardial infusion of noradrenaline (NA) into the ventricle of the anaesthetised pig and to reconstruct this arrhythmia using a 2D cellular network computational model. **Methods and Results:** *In-vivo Experiments:* NA (10 μM in saline; 150 μl/min) caused the QRS complex of the ECG to invert within a single beat. This was accompanied by a ventricular tachycardia ($\sim$ 20 bpm), a drop in left ventricular (LV) pressure ($\sim$ 20 mmHg), while LV ejection fraction halved. Location of earliest ventricular epicardial activation consistently shifted to the randomly chosen infusion site (27 observations) and preceded right atrial activation. Moreover, total ventricular epicardial activation time increased from 20 ± 4ms (control, $\pm$SD) to 50 ± 9ms ($p < 0.01$, 14 pigs). All changes fully reversed after the infusion was stopped. Electrical pacing at the needle site mimicked the electromechanical changes observed during infusion. *Arrhythmia Simulation:* Wave propagation was modelled using a 2D sheet of 256 by 256 resistively coupled ventricular cells. One edge of the sheet was stimulated at 1Hz to act as the normal pacemaker. To mimic in-vivo conditions, the central region was subjected to a five-fold increase in the conductance of the L-type and SR uptake calcium currents. The central zone gradually became the dominant pacemaker, thereafter capturing the activation sequence. **Conclusion:** Localised infusion of NA caused ventricular automaticity and computational reconstruction of this arrhythmia implicates intracellular calcium overload.