Regional conduction slowing can explain inferolateral J waves and their attenuation by sodium channel blockers

Mark Potse, Veronique Meijborg, Charly Belterman, Jacques de Bakker, Chantal Conrath, Ruben Coronel

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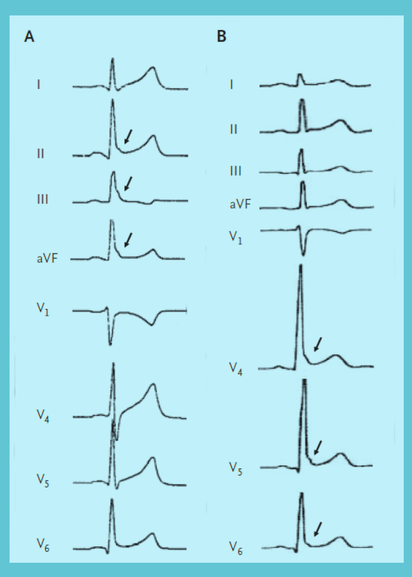
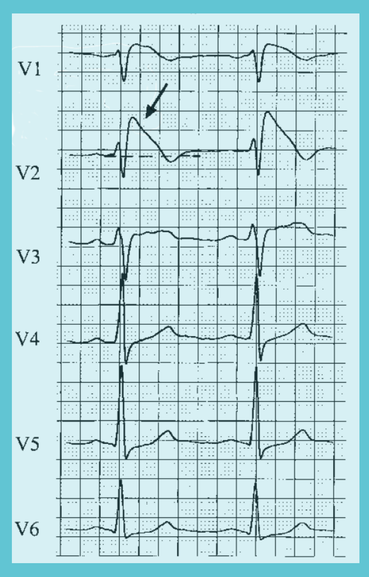
INTRODUCTION

J waves in the ECG are usually harmless, but when they occur in inferolateral leads they are associated with an increased risk of ventricular fibrillation. Similar waves occur in Brugada syndrome (BS) but then in right precordial leads. But when sodium-channel blockers are administered, J waves in BS increase while inferolateral J waves decrease (Roten et al. 2012). Our purpose was to **test different hypotheses to explain inferolateral J waves and the effect of sodium block.**



Inferolateral J waves
(Haïssaguerre et al. NEJM 358:2016, 2008)

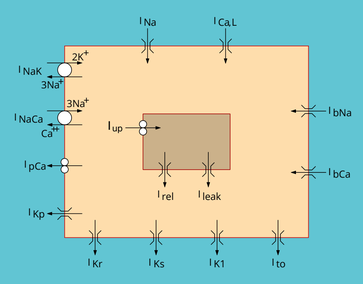


Brugada type 1
(Wilde et al. Circulation 106:2514, 2002)

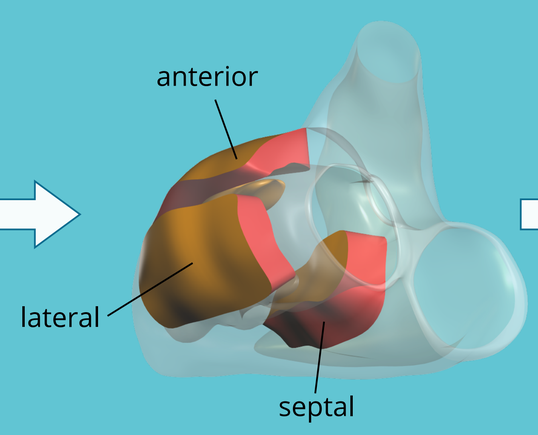
SIMULATION STUDIES

The effects of reduced Na current, reduced coupling, and increased transient outward current were evaluated with computer simulations using a detailed model of the human heart and torso.

Propagating action potentials were simulated with a monodomain reaction-diffusion model. At 1-ms intervals the simulated transmembrane currents were inserted in a torso model and a static bidomain problem was solved to obtain the ECG.



Ion channel dynamics were simulated using the model by Ten Tusscher et al. (2004)

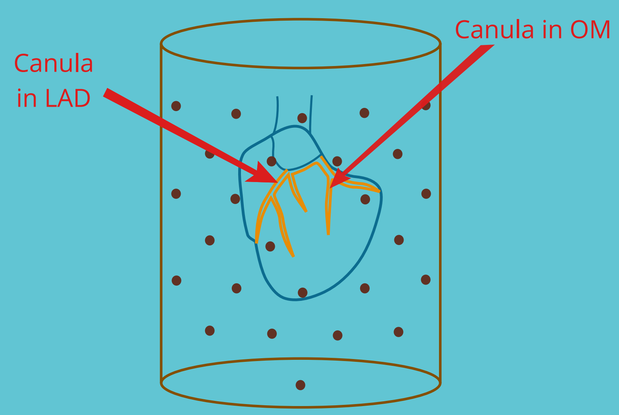


Model properties were locally modified in 3 zones

The ECG was computed in an inhomogeneous torso model

EXPERIMENTAL STUDIES

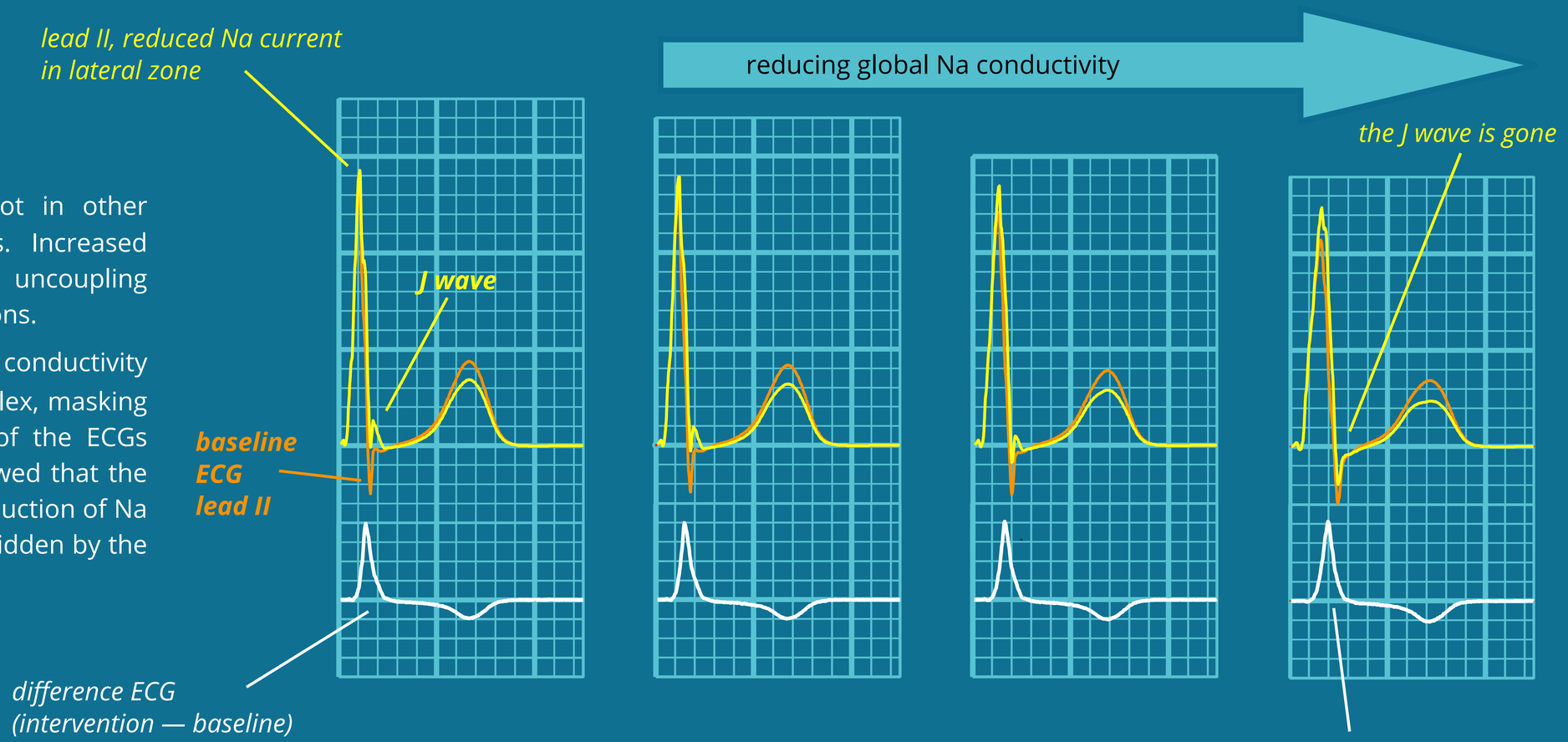
Key findings were backed up with experiments in explanted pig hearts. To obtain pseudo-ECGs the hearts were placed in a container, filled with perfusion fluid, with electrodes attached to the surface. Local interventions were made by selectively infusing medication in the obtuse marginal (OM) or left anterior descending (LAD) coronary artery.



RESULTS

Reduced Na current in lateral but not in other regions induced inferolateral J waves. Increased transient outward current and cellular uncoupling caused only subthreshold J-point elevations.

Global reduction of Na-channel conductivity deformed and prolonged the QRS complex, masking the inferolateral J waves. Subtraction of the ECGs with and without local intervention showed that the ECG change associated with the local reduction of Na current was not reduced, but was only hidden by the expanding QRS complex.



CONCLUSION

Regionally reduced Na current can explain inferolateral J waves. The normally late activation of the lateral region is crucial for the development of J waves and may explain the special importance of the inferolateral leads. The proposed mechanism also explains attenuation of J waves by Na-channel blockers.

LITERATURE

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Simulations ran on the IBM BlueGene/Q system Turing.

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