comply to sinusoidal stimuli rather than the isogenic, conforming to rectangular monophasic stimuli. Furthermore, MELAS hiPSCs and native pathological cardiomyocytes show protein reduction of different subunits of OXPHOS (SDHB, ATPB and COX IV), compared to control line. The mutated cells increase the basal ROS production, higher in non-stimulated than in stimulated samples (1.3-fold vs 1.2-fold, normalized for control). Interestingly, this difference increases after 24 h from the stimulation (1.8-fold vs 1.3-fold). This study represents a systematic characterization of MELAS hiPSCs-cardiomyocytes and a unique insight in the pure cardiac side of such complex syndrome. Our kinematic insights not only deepen our understanding of the charges on the heart but investigate the prospect of cardiac memory via extracellular stimuli that could benefit the afflicted tissue. Ultimately, this research defines critical physiological and kinematic parameters for this intricate syndrome, opening new avenues for future studies.

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NOD-1 activation increases the spontaneous activity and the I(f) current of murine sinoatrial node cells

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Background

NOD1 is an intracellular innate immune receptor that recognizes infectious and non-infectious factors and plays a crucial role in inflammation. Recent studies indicate that in ventricular myocytes the activation of NOD1 causes cardiac dysfunction and pro-arrhythmogenic events. However, it is unclear whether the selective activation of NOD-1 can regulate the sinus rhythm.

Aim

The aim of this study is to investigate whether NOD1 activation affects the electrical activity of murine sinoatrial (SAN) cells.

Methods

Patch-clamp experiments in whole-cell configuration were performed in single SAN cells isolated from 2 to 3 month-old mice. Prior to cell isolation, SAN tissues were exposed for 48 h to: 1) vehicle, 2) C12-iE-DAP (NOD-1 activator; 20 μg/mL), 3) iE-Lys (negative control for NOD1 activation; 20 μg/mL).

Results

C12-iE-DAP increments the spontaneous action potential rate (+26%) by inducing an enhancement in the slope of the diastolic depolarization rate. This effect might be due to the observed increase of the If -current (~65% at full activation). In addition, C12-iE-DAP positively shifts the If activation curve by ~5 mV. Interestingly, preliminary data show that C12-iE-DAP also causes a reduction of the β-adrenergic modulation of cell chronotropism.

Conclusion

These findings suggest that NOD1-induced alteration of SAN electrical activity may contribute to the clinically observed changes in heart rate during inflammatory disease.

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Towards a digital twin for aorta: An in-silico image-based approach coupling numerical simulations and CT-gated images to assess patients specific aortic hemodynamics

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The digital twin (DT) has a crucial role in the personalized medicine since it represents a virtual replica of patient specific districts. Numerical simulations are an effective tool to build a reliable in silico DT of thoracic aorta (TA) since the capability to replicate the artery morphology and hemodynamics. Nevertheless, the simulation strategies commonly used present some limitations in the generation of a patient specific DT. The aim of this work is to develop a new procedure to obtain an automated and accurate TA digital twin integrating CFD simulations and CT-gated images. TA and left ventricle (LV) 3D models were reconstructed by segmenting ECG-gated CT images for ten phases of cardiac cycle by using a U-net deep neural network and a threshold algorithm respectively. A developed mesh morphing technique was adopted to follow the aortic changes during the hearth beat by using a spline interpolation on the mesh nodes position between each phase of cardiac cycle. Then the motion was included in the CFD simulation setup together with patient- specific boundary conditions. The aortic flow rate computed by deriving the volume of LV 3D models was assigned at the inlet and pressure conditions at the outlets. The implemented method was able to cope with the TA variation with high accuracy and maintaining high mesh quality. The results revealed differences in velocity distributions and wall shear stress-based indicators between the standard CFD and new approach. The latter also showed a time lag between the flow rate waveform at the descending TA and the inlet profile of about 0.05 s for the simulated subjects. The implemented procedure allows to obtain robust patient specific TA model overcoming the main limitations affecting cardiovascular DT by developing an accurate and realistic in-silico model, keeping computational costs reasonably low and adopting a less complex setup.

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