CARDIAC PHENOTYPING THE TASK-1 DEFICIENT MOUSE

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Background: TASK-1, a potassium background channel (K2P channel) is mainly expressed in the heart and the brain. Pharmacological inhibition of TASK-1 in isolated cardiomyocytes results in prolongation of the action potential duration and early afterdepolarizations pointing to a potential functional role in repolarization.

Methods: By cardiac phenotyping the TASK-1 deficient mouse (TASK-1 KO) we used techniques from molecular and cellular biology (RT-PCR, immunoblot), measured monophasic action potential duration (MAPs) in the Langendorff perfused heart and applied in vivo cardiac diagnostics (echocardiography, surface and telemetric ECG for 24 h and under defined physical stress (treadmill and swimming)). By transient ligation of the left anterior descending artery ischemia/reperfusion (I/R) was induced and the incidence of premature ventricular beats was studied.

Results: TASK-1 is the most predominantly expressed K2P channel in the heart compared with eight other K2P channels. TASK-1 KO mice have no structural or functional abnormalities in echocardiography compared with wild-type mice (WT). Arrhythmia did neither occur spontaneously nor during exercise (5 min swimming, treadmill with ramp protocol until physical exhaustion). I/R resulted in an increase in ventricular arrhythmia in WT and TASK-1 KO mice with no significant difference in number. However, MAPs are significantly prolonged in TASK-1 KO during spontaneous rhythm and when paced at different cycle lengths (e.g, APD90 at CL 125 ms: WT 38±6 ms vs. TASK-1 KO 46±5 ms, n=6, p<0.02). In accordance, the corrected QT time is significantly prolonged in surface ECGs in TASK-1 KO (QTc: WT 23±2 ms vs. TASK-1 KO 26±2 ms, n=7, p<0.05).

Conclusion: TASK-1 is the mainly expressed K2P channel in the heart. TASK-1 deficiency does not result in an increased incidence of arrhythmia during inactivity or physical exercise. I/R does not alter the increase in ventricular premature beats in TASK-1 KO compared to WT mice. However, deficiency of TASK-1 does affect repolarization as seen by prolonged MAP duration and QTc time.

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