ratio: 29.21±3.64 in WT vs. 50.28±8.3 in PMCA1 tg, $n=7$ each, $p<0.05$).

These results suggest that PMCA1 may be involved in excitation–contraction coupling specifically after β-adrenergic stimulation. In conclusion, both PMCA1 and 4 have relevant although different physiological functions in the heart.

Keywords: Calcium; B-Adrenergic receptors; Nitric oxide

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Status of β-adrenoceptor signal transduction in heart failure due to volume overload in female rats

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Many studies have shown that pre-menopausal females are protected from the development of heart failure due to different etiologies. In fact, it has been shown that female rats have a 10-fold lower mortality rate from volume overload-induced heart failure than males. However, the exact mechanism(s) responsible for the female cardioprotection is not clear. In this study, we examined the status of the β-adrenergic system in volume overloaded hearts induced by arteriovenous (AV) shunt in female Sprague–Dawley rats by the needle technique. A gender difference was observed showing preserved hemodynamic and echocardiographic function in females 16 weeks post-AV shunt. This is in contrast to a significantly depressed cardiac function and clinical signs of overt heart failure in their male counterparts. Although males showed depressed gene expression for adenylyl cyclase V and VI, females maintained the expression at control values. β1- and β2-adrenoceptor gene expression were depressed in male failing hearts; whereas females showed an increase in expression of both β-adrenoceptors. These data indicate that upregulation of β-adrenoceptor mechanisms is associated with maintenance of cardiac function in volume overloaded female hearts.

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Keywords: Gender differences; Heart failure; β-Adrenoceptors

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The mechanism of B-stimulation increases Ca^{2+} release in cardiomyocytes

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β-Adrenergic augmentation of Ca^{2+} release in cardiac myocytes has been linked to the phosphorylation-dependent dissociation of FKBP12.6 regulatory proteins from RYR2. If the disengagement of FKBP12.6 proteins from the RYR2 complex plays a significant role in the regulation of Ca^{2+} release, β-adrenergic stimulation would be expected to be less robust in hearts lacking FKBP12.6. We used FKBP12.6 null mice to directly test the extent to which the dissociation of FKBP12.6 proteins mediates Ca^{2+} release of isoproterenol (ISO) by measuring Ca^{2+} sparks from FKBP12.6 null and age, sex, and genetically matched mice. ISO (1 μM) increased Ca^{2+} spark frequency and altered the kinetics of the Ca^{2+} sparks in both wildtype and FKBP12.6 knockout mouse cardiac myocytes equally; whereas, dialysis of cyclic ADP-ribose (cADPR) through patch pipettes the frequency and kinetics of Ca^{2+} sparks changed only in wildtype cardiac myocytes; furthermore, in the presence of phospholamban antibody, 2D12, ISO failed to alter Ca^{2+} spark property; finally, left ventricular papillary muscles from wildtype and FKBP12.6$^{-/-}$ female mice were stimulated at 4 Hz to assess cardiac contractility before and during β-adrenergic stimulation with ISO, the increase of magnitude (45% versus 43%) and rate of stress development (47% versus 47%) to an equivalent degree in WT and KO mice. These data demonstrate that β-adrenergic stimulation of Ca^{2+} spark alteration does not require dissociation of FKBP12.6 proteins, and that cADPR mechanism likely predominates in the Ca^{2+} spark property alteration in cardiac myocytes.

Keywords: β-Adrenergic receptor; Cardiomyocytes; Calcium

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Rosuvastatin reduces myocardial β-adrenoceptor-density and -high affinity state without functional consequences

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In atorvastatin-treated neonatal rat cardiomyocytes the responsiveness of β-adrenoceptors (βAR) is impaired due to a reduced isoprenylation of the Gγ-subunit of the heterotrimeric G-protein and a reduction in the cellular level of the Gαs-subunit We investigated whether the myocardial βAR-signalling and function is altered in vivo with therapeutic doses of rosuvastatin (ROSU). Six female Labrador dogs were treated for 14 days with ROSU (3–10 mg/kg/BW; p.o.), four untreated dogs served as controls (ctr). Heart rate (HR) and left ventricular systolic and end-diastolic pressure (LVSP and LVEDP), plasma cholesterol levels (pCH), βAR-density and affinity constants of isoprenaline (ISO) in the presence and absence of 100 μM GTP were determined. 14 days after ROSU-treatment, pCH were significantly reduced (ctr 137±8 vs. ROSU 110±6 mg/dl; $p=0.025$). HR (ctr 111±6 vs. ROSU 114±5 bpm), LVSP (ctr 96±3 vs. ROSU 99±6mm Hg) and LVEDP (ctr 10±1 vs. ROSU 15±2 mm Hg) were not different. However, βAR-density was significantly