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Meeting abstract

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Connexin 43 expression is impaired in beginning heart failure in spontaneously hypertensive rats

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Introduction

Arrhythmia is a severe problem in many pathological conditions of the heart such as cardiomyopathy and heart failure. As gap junctions provide the basis for a regular rhythmic beating and regular electrical propagation, connexins forming gap junctions in the heart have been very attractive targets for scientific research in the past.

While in hypertrophy Cx43 is up-regulated, in heart failure Cx43 has been shown to be decreased. We therefore wanted to elucidate whether spontaneously hypertensive rats showing signs of impaired ventricular function have altered Cx43 levels and if so, which pathways are involved in these changes.

Results

Hearts of 6 months old Wistar Kyoto Rats (WKY) and spontaneously hypertensive rats (SHR) showing signs of hypertrophy and impaired ventricular function, i.e. reduced cardiac output (SHR: 72 ± 3,5 ml/min; WKY 81 ± 4,3 ml/min) and impaired diastolic relaxation, where analyzed by western blot. SHR rats showed a marked decrease in Cx43 levels (80,9 ± 4,5%) compared to WKY rats. To elucidate the further signal transduction cascade we investigated phosphorylation of extracellular regulated kinase (ERK1/2) and glycogen synthase kinase 3-beta (GSK3-beta). Examination of MAPK pathways showed enhanced phosphorylation of ERK1 (116,8 ± 1,6%) and ERK2 (139,9 ± 12,6%) while the phosphorylation status of GSK3-beta was markedly decreased (64,4 ± 7,4%). An enhanced phosphorylation of phospholambane (PL) was detected, indicating an impaired Ca2+-handling in the failing heart.

Conclusion

Downregulation of Cx43 in failing hearts from SHR rats seems to be related to lower phosphorylation status of GSK3-beta together with phosphorylation of ERK1 (low degree) and ERK2 (modest degree).

The above findings are in contrast to the status of hypertrophy in which GSK3-beta is phosphorylated (= inactive form) and Cx43 is up-regulated.