Mechanical stress enhances serotonin 2B receptor modulating brain natriuretic peptide through nuclear factor-kappaB in cardiomyocytes

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摘要

Abstract

OBJECTIVE: Serotonin via serotonin 2B receptors (SR2BR) regulates cardiac embryonic development and adult heart functions. However, the role of SR2BR in the failing heart due to pressure overload is not well understood. METHODS: Wistar rats of aortic banding and neonatal cardiomyocyte with mechanical stretch were used as cardiomyopathy models. RESULTS: After two weeks of aortic banding surgery, serum serotonin, mRNA and protein expression of SR2BR increased significantly. The selective SR2BR antagonist, SB215505 (SB), significantly reduced the increase in heart weight, decreased heart wall thickness, left ventricular mass and the expression of the brain natriuretic peptide (BNP) but did not attenuate the up-regulation of SR2BR protein expression in rats after aortic banding for three weeks. After following in vitro mechanical stretch of cardiomyocytes and incubation with serotonin 1 muM, the level of SR2BR and BNP protein increased time-dependently. When transfected by specific siRNA of SR2BR or pretreated with caffeic acid phenethyl ester in cardiomyocytes, the increase of nuclear factor-kappaB (NF-kappaB) translocation and BNP protein induced by serotonin incubation plus mechanical stretch were both reversed. CONCLUSIONS: SR2BR expression is involved in pressure-induced cardiomyopathy and its downstream signaling may involve NF-kappaB to modulate BNP expression in cardiomyocyte