Regulation of connexin 43 gene expression by cyclical mechanical stretch in neonatal rat cardiomyocytes

王宗倫

Wang TL;Tseng YZ;Chang H;;

摘要

Abstract

Myocardial cells respond to changes in the mechanical forces imposed on them with changes in myocardial tension in the short term and with structural remodeling in the long term. Since these responses involve intercellular communication, we have investigated regulation of the gap junction proteins, connexin 43 (Cx43), connexin 40 (Cx40) and connexin 37 (Cx37), by cyclical mechanical stretch. Results were compared with parallel experiments on c-*fos* and GAPDH. Twenty percent stretch of cultured rat cardiomyocytes caused a 3-fold increase in Cx43 mRNA levels by 2 h. c-*fos* mRNA levels increased after 30 min of stretch, whereas Cx40, Cx37, and GADPH mRNA did not change. Protein levels of Cx43 increased by 4 h and remained elevated for 16 h. New protein synthesis was not a requirement for the stretch-induced rise in Cx43 expression, since mRNA levels were unaffected by treatment with cycloheximide. In addition, mechanical stretch induced alkalization of cardiomyocytes that was antagonized by inhibiting Na-H exchanger (NHE). Gap junction potential (Gj) was concomitantly elevated. Chemical closure of Cx channels by insulin was followed by inhibition of NHE. In conclusion, cyclical mechanical stretch caused increased expression of the gap junction protein Cx43 in cardiomyocytes and also the Gj. The augmentation of Cx43 mRNA expression and its functional status were associated with activation of NHE.