

Signaling mechanisms mediating the positive inotropic response to apelin in the intact rat heart

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Background: Apelin is emerging as an important regulator of the cardiovascular system. We previously demonstrated that apelin is one of the most potent endogenous stimulators of myocardial contractility; however, the signal transduction pathways mediating this effect are still obscure. Here we studied the role of protein kinase C (PKC) and extracellular signal-regulated kinase 1/2 (ERK1/2) in the positive inotropic effect of apelin.

Methods and Results: In isolated perfused rat hearts, infusion of apelin (2 nmol/L for 20 min) induced a slowly developing and sustained increase in cardiac contractility. The improvement of cardiac function was accompanied by the

activation of PKC and ERK1/2. Apelin induced a transient increase in the translocation of PKC[epsilon], but not PKC[alpha], from the cytosol to the particulate fraction, and a sustained increase in the phosphorylation of ERK1/2 in the left ventricle. Pharmacological inhibition of ERK1/2 activation significantly attenuated the inotropic response to apelin. Although inhibition of PKC reduced the inotropic effect of apelin, it did not prevent the activation of ERK1/2.

Conclusions: Stimulation of apelin receptors enhances myocardial contractility via parallel and independent activation of PKC[epsilon] and ERK1/2 in the intact adult rat heart. Selective activation of PKC[epsilon] and ERK1/2 signaling may represent a novel means to support cardiac function in diseased conditions.

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