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Role of Protein Kinase C in α_1-Adrenergic Regulation of a^i_{Na} in Single Guinea Pig Ventricular Myocytes

Su-Hyun Jo*, and Chin-Ok Lee
Department of Life Science, Pohang University of Science and Technology, Pohang 790-784, Republic of Korea.

Stimulation of α_1-adrenergic receptor (α_1-AR) by phenylephrine produced a decrease in intracellular Na^+ activity (a^i_{Na}) in multicellular preparations of cardiac tissues. The role of protein kinase C (PKC) in α_1-adrenergic regulation of a^i_{Na} was studied in single ventricular myocyte isolated from guinea pig hearts. a^i_{Na} and membrane potential were measured with Na^+ indicator, sodium-binding benzofuran isophthalate tetraacetoxy methyl ester (SBFI/AM) and microelectrodes respectively when ventricular myocyte was stimulated at 0.3 Hz. Stimulation of α_1-AR by phenylephrine (in the presence of β-AR antagonist, atenolol) decreased a^i_{Na}. Activation of PKC by 4β-phorbol 12-myristate 13-acetate (PMA) also decreased a^i_{Na} in concentration-dependent manner. Furthermore, the decrease in a^i_{Na} by PMA was inhibited by PKC inhibitor, staurosporin and the decrease by PMA was not mimicked by non-PKC-activating phorbol, 4α-phorbol 12-myristate 13-acetate (4α-PMA). The decrease in a^i_{Na} by phenylephrine was inhibited by pretreatment of PMA or staurosporin. The results indicate that the decrease in a^i_{Na} by α_1-AR stimulation is mediated by activation of PKC. The decrease in a^i_{Na} by PMA was not prevented by pretreatment of tetrodotoxin (TTX), and the decrease in a^i_{Na} by TTX was not inhibited by pretreatment of PMA. However, the decrease in a^i_{Na} by PMA was prevented by pretreatment of either strophanthidin or high $[K^+]_o$. PMA decreased a^i_{Na} in resting ventricular myocyte voltage-clamped at -80 mV. The results suggest that α_1-adrenergic -induced decrease in a^i_{Na} is caused by stimulation of Na^+-K^+ pump via PKC activation in guinea pig ventricular myocytes.