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Capsaicin Inhibits Phospholipase C-coupled Signaling via the Capacitative Ca^{2+} Entry in PC12 Cells

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The effects of capsaicin on phospholipase (PLC)-induced capacitative Ca^{2+} entry (CCE) were investigated in PC12 cells. Capsaicin inhibited one of PLC-linked signal, extracellular ATP-induced norepinephrine secretion with a concentration range, 10-100 μM. Capsaicin did not inhibit the peak portion of extracellular ATP-mediated $[Ca^{2+}]i$ rise, but it recovered more rapidly to the normal level of $[Ca^{2+}]i$ from the sustained $[Ca^{2+}]i$ level. Similar result could be obtained with bradykinin, another stimulant for PLC in PC12 cells. However, capsaicin did not inhibit bradykinin and ATP-induced inositol 1,4,5-trisphosphate ($InsP_3$) production. Capsaicin dramatically reduced the thapsigargin-induced sustained Ca^{2+} level in a concentration dependent manner. Thapsigargin-induced Ba^{2+} and Mn^{2+} influx also inhibited by capsaicin. Furthermore, capsaicin show overlapped inhibitory effect with SKF96365, the inhibitor of CCE, which suggests that capsaicin inhibit the CCE in PC12 cells. Capsaicin-induced inhibition of CCE was confirmed with the similar result on thapsigargin-induced CCE in Jurkat-T cell, which has been a model system for CCE. Resiniferatoxin, the potent agonist of vanilloid receptor also did not mimic the effect of capsaicin. The antagonists for vanilloid receptor, ruthenium red and capsazepine, did not show any inhibitory manner. In addition, capsazepine reduced the thapsigargin-induced sustained Ca^{2+} level in a concentration dependent manner. The inhibition manner did not mediated by the activation of protein kinase C, which is known as one of negative modulator for CCE, because phorbol 12-myristate 13-acetate (PMA) and capsaicin did not show overlapped effect and GF109203X did not reverse the inhibitory effect of capsaicin. The results suggest that capsaicin possibly modulate PLC-mediated Ca^{2+} mobilization or neurotransmitter secretion thorough the modulation of CCE.