COUPLING OF CANNABINOID RECEPTORS TO INTRACELLULAR CALCIUM MOBILIZATION IN RAT INSULINOMA β-CELLS

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In RIN-m5F rat insulinoma β cells agonists at cannabinoid CB_1 receptors modulate insulin release. Here we investigated in these cells the effect on intracellular Ca^{2+} ($[Ca^{2+}]_i$) of activation of cannabinoid receptors. CB_1 agonist arachidonoyl-chloro-ethanolamide (ACEA), and the CB_2 agonist JWH133, elevated $[Ca^{2+}]_i$ in a way sensitive to the inhibitor of phosphoinositide-specific phospholipase C (PI-PLC), U73122, but not to pertussis toxin and forskolin, and independent from extracellular Ca^{2+}. PI-PLC-dependent Ca^{2+} mobilization by ACEA was entirely accounted for by activation of inositol-1,3,4-phosphate (IP_3) receptors on the endoplasmic reticulum (ER), whereas the effect of JWH133 was not sensitive to all tested inhibitors of IP_3 and ryanodine receptors. CB_1 receptors cross-talk with other agents that elevate $[Ca^{2+}]_i$ in RIN-m5F cells. ACEA, but not JWH133, significantly inhibited the effect of bombesin on $[Ca^{2+}]_i$. The endogenous CB_1 agonists, anandamide and *N*-arachidonoyldopamine, which also activate transient receptor potential vanilloid type 1 (TRPV1) receptors expressed in RIN-m5F cells, exhibited higher potency at elevating $[Ca^{2+}]_i$ in the presence of extracellular Ca^{2+}, in a way sensitive to CB_1 and TRPV1 antagonists. These results suggest that, in RIN-m5F cells, CB_1 receptors are coupled to PI-PLC-mediated mobilization of $[Ca^{2+}]_i$ and inhibit bombesin signalling, while facilitating TRPV1-induced effects on $[Ca^{2+}]_i$.