Linoleic acid induces an increase in intracellular calcium concentration and a membrane hyperpolarization of primary cultured rat pancreatic β-cells

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Free fatty acids (FFAs) stimulate insulin secretion through activation of their receptor, GPR40. It is known that activation of GPR40 leads to an increase in intracellular free Ca^{2+} concentration ($[Ca^{2+}]_i$), which contributes to the secretion of insulin. Electrophysiological activities of β-cells are crucial in determining levels of $[Ca^{2+}]_i$ and insulin secretion, but the action of FFAs on electrophysiological properties of β-cells is largely unknown. Moreover, the mechanism of increase in $[Ca^{2+}]_i$ induced by FFAs is not fully understood. We used primary cultured rat pancreatic β-cells to test the effect of linoleic acid on $[Ca^{2+}]_i$ and membrane potential. Linoleic acid (20 μM) induced an increase in $[Ca^{2+}]_i$ under 3.5 mM glucose, which was eliminated by pretreatment of the cells with thapsigargin, but not blocked by removal of extracellular Ca^{2+}. Simultaneously with the increase in $[Ca^{2+}]_i$, membrane potential was hyperpolarized by linoleic acids significantly (Mean±SD, -48±13.7 mV to -76±6.8 mV after linoleic acids, n=12, $P<0.01$). Only a very small component of calcium-activated potassium currents was involved, as apamin and charybdotoxin did not deter the hyperpolarization induced by linoleic acid. In contrast, the blockade of ATP-sensitive potassium channels (K_{ATP} channels) by tolbutamide totally abolished the hyperpolarization induced by linoleic acid. K_{ATP} current was then recorded by nystatin-perorated patch clamp. It was strongly increased by linoleic acid. We concluded that linoleic acid-induced increase in $[Ca^{2+}]_i$ is due to calcium release from intracellular calcium stores of rat β-cells but not through voltage-dependent calcium channels. Electrophysiologically, linoleic acid induces hyperpolarization by activating K_{ATP} channels, but not calcium-activated potassium channels. This hyperpolarization may prevent insulin secretion induced by a high level of glucose.