

Calcium-dependent halothane activation of sarcoplasmic reticulum calcium channels from frog skeletal muscle

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The effect of halothane on calcium channels present in sarcoplasmic reticulum membranes isolated from frog skeletal muscle was studied at the single channel level after fusing the isolated vesicles into planar lipid bilayers. Addition of 91 μM halothane to the cytosolic compartment containing 1 μM free calcium activated the channel by increasing fractional open time from 0.11 to 0.59, without changing the channel conductance. The activation of the channels by halothane was calcium dependent. At resting calcium concentrations in the cytosolic compartment, halothane failed to activate the channel, whereas maximal activation was found at 10 μM calcium. The free energy of halothane binding to the channel decreased from -5.8 kcal/mol at 1 μM calcium to -6.6 kcal/mol at 10 μM calcium. Halothane increased the open time constants and decreased the closed time constants, indicating that it binds to both the open and the closed configurations of the channel.