Crosstalk between the L-type Ca^{2+} channel and the mitochondria

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The L-type Ca^{2+} channel is responsible for initiating contraction in the heart. Mitochondria are responsible for meeting the cellular energy demands. We examined whether activation of the L-type Ca^{2+} channel alone is sufficient to alter mitochondrial function in guinea-pig ventricular myocytes. We performed experiments in quiescent myocytes with consistent ATP utilisation or where we held ATP concentration constant (in the patch pipette) since this allowed us to more readily explore the effects of channel activation on mitochondrial function. The L-type Ca^{2+} channel was activated directly with the dihydropyridine agonist BayK(−) or voltage-clamp of the plasma membrane. We also activated the channel by depolarization of the plasma membrane with 45 mM KCl. Activation of the channel increased superoxide production (assessed as changes in dihydroethidium fluorescence), mitochondrial NADH production and metabolic activity (assessed as formation of formazan from tetrazolium) in a calcium-dependent manner. Activation of the channel also increased mitochondrial membrane potential assessed as changes in JC-1 fluorescence. The response was reversible upon inactivation of the channel during voltage-clamp of the plasma membrane. Actin filaments can regulate the function of the L-type Ca^{2+} channel. Actin also associates with mitochondria *via* phalloidin binding sites to stabilise mitochondria within the cell. We tested whether changes in mitochondrial membrane potential were mediated through the cytoskeleton by movement of the channel. Depolymerization of actin or exposing cells to a peptide directed against the α-interacting domain of the α1C subunit of the channel (thereby preventing movement of the β subunit) attenuated the increase in mitochondrial membrane potential. We conclude that activation of the L-type Ca^{2+} channel can regulate mitochondrial function and the response also appears to involve movement through the cytoskeleton.