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Subcellular distribution of TRPC6 channel proteins in the hippocampus.

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Activation of group I metabotropic glutamate receptors (mGluR) leads to formation of second messenger molecules including IP3 and DAG as well as to a long lasting depolarization of postsynaptic membrane potential. This latter effect might be brought about by the opening of a classical type of transient receptor potential channel (TRPC) the operation of which is gated by DAG. However, it is currently unknown whether DAG sensitive channels are in a position to accomplish this function. In the present study our aim was to clarify the subcellular localization of one of the DAG sensitive TRPC channels, TRPC6. Immunostaining using a specific antibody developed against this channel revealed that TRPC6 channels were densely expressed on the dendrites and spines of dentate granule cells as well as in their preterminal axon segments. TRPC6 immunoreactivity was also found on the dendritic surface of mGluR1- or parvalbumin- immunopositive interneurons. Electron microscopy using immunogold labeling uncovered that the distribution of TRPC6 channels on spines of dentate granule cells mimics the spatial occurrence of mGluR5, PLCbeta1 and DAG lipase, proteins that may form a molecular cascade controlling the function of TRPC6 channels. Our results suggest that TRPC6 channels are located close to those proteins that are involved in endocannabinoid signaling, thus this channel with a substantial permeability for Ca2+ may contribute to the synthesis of endocannabinoids.