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The distribution of the proteins involved in inositol-1,4,5-trisphosphate-mediated calcium release in the hippocampus

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In this thesis, the distribution of the proteins involved in $InsP_3$-mediated Ca^{2+} release from the ER in hippocampal tissue was examined. The results presented here show a non-uniform distribution of the components of the Ca^{2+} signaling "toolkit" as elucidated by immunohistochemistry. Significant levels of type 1 inositol-1,4,5-trisphosphate receptor ($InsP_3R$ 1) as the main subtype in neuronal tissue were identified in the CA1 region of hippocampus whereas the CA3 region and dentate gyrus (DG) showed only moderate immunoreactivity. In contrast, chromogranin B (CGB), a protein binding to the $InsP_3R$ 1 on the luminal side of the endoplasmic reticular membrane, was enriched in the CA3 region, whereas DG and the CA1 region showed only faint CGB signals. The phosphoinositol kinases leading to the formation of inositol-1,4,5-phoshate ($InsP_3$), phosphatidylinositol-4-kinase (PI4K) and phosphatidylinositol-4-phosphate-5 kinase (PIPK), were found to be distributed in a much more homogenous pattern and showed strong immunoreactivity throughout all hippocampal cell fields with differences in the subcellular distribution. Moreover, a band of coinciding strong immunofluorescence for CGB and PIPK was observed in the CA3 stratum lucidum area. On a subcellular level, $InsP_3R$-like staining extended throughout the neuronal soma, whereas CGB and PIPK showed only weak immunofluorescence in neuronal cell bodies.
To set up a feasible model for the investigation of intracellular Ca^{2+} signaling in hippocampus, the distribution of proteins involved in $InsP_3$-dependent Ca^{2+} release was tested in hippocampal organotypic slice cultures. Comparing the results to the data obtained in acute tissue samples, strikingly similar distribution patterns of those proteins were found. The protein expression appeared to be very stable since its patterns could not be changed by treatment with immunophilins or Ca^{2+} release-modulating drugs.
The data presented in this thesis show a differential expression of the components of the signaling "toolkit" leading to $InsP_3$-mediated Ca^{2+} release and present organotypic hippocampal tissue cultures as a valuable model system for research into intracellular Ca^{2+} signaling as may be important for the understanding of various neuropathologic conditions such as Alzheimer's disease, temporal lobe epilepsia or schizophrenia.