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Tittle of Dissertation: "Late-LTP in apical CA1 dendrites of hippocampal slices in vitro"

Abstract

The major forms of hippocampal synaptic plasticity such as long-term potentiation (LTP) and long-term depression (LTD) are regarded as cellular correlates of learning and memory formation. In recent years, an impressive research effort has been devoted to understanding the cellular and molecular mechanisms of hippocampal synaptic plasticity, particularly LTP.

During my initial studies I could reproduce electrically induced LTP in apical dendrites of pyramidal neurons within CA1 region of hippocampal slices in vitro. Depending on different induction protocols distinct forms of LTP such as a transient, protein synthesis-independent early-LTP (with duration of 3-4 h) or a de novo protein synthesis-dependent late-LTP (lasting for at least 6 h) could be induced. Both forms of LTP required NMDA-receptor activation and especially the late-LTP required synergistic activation of glutamatergic and dopaminergic inputs during its induction.

It has been reported that the LTP in CA1 region is characterized by processes of synaptic tagging. During LTP induction the activated synapses are marked by a “synaptic tag/ tag complex” which can capture plasticity-related proteins (PRPs). During synaptic tagging, early-LTP induced in one synaptic input can be transformed into a late-LTP, if late-LTP was induced in an independent synaptic input of the same neuronal population within a distinct time window. The synthesis of process unspecific plasticity-related proteins (PRPs) by late-LTP induction in the second synaptic input is sufficient to transform/reinforce the early-LTP into a late-LTP, which is marked by a synaptic tag/ tag complex.

Next, I was interested to investigate whether actin network function is essential for the maintenance of LTP in hippocampal CA1 region. It has been reported that the dynamics of actin cytoskeleton is essential for the maintenance of LTP. Here we found that the inhibition of actin polymerization affects the protein synthesis-independent early-LTP and protein synthesis-dependent late-LTP. But interestingly, the application of actin inhibitors after the induction of late-LTP was unable to block LTP at all, suggesting an early mechanism that is required for the induction and maintenance of LTP.

In the last series of experiments I have investigated, whether inhibition of actin network interferes with processes of synaptic tagging. The transformation of early-LTP into late-LTP was blocked by the application of structurally different actin polymerization inhibitors, latrunculin A and cytochalasin D. We suggest that the actin network is required for early “house keeping” processes for inducing and maintaining early-LTP. Furthermore, inhibition of actin dynamics negatively interacts with the setting of synaptic tag complex. We propose actin as a tag-specific molecule in apical CA1 dendrites, where it is directly involved in the tagging/capturing machinery and inhibition of actin network thus prevents the interaction with plasticity-related proteins. This results in the prevention of late-LTP by inhibition of the actin network during LTP induction.