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Thema der Dissertation: „**Modulation funktioneller Plastizität in der hippokampalen CA1 Region der frei beweglichen Ratte”**

Abstract

Processes of functional plasticity such as hippocampal long-term potentiation (LTP) and long-term depression (LTD) are regarded as cellular mechanisms underlying learning and memory formation. Synaptic plasticity is characterized by changes in the efficacy of synaptic transmission at synapses, can contribute to storage of information within neural circuits.

In these in vivo studies in freely moving rats it was studied the dopaminergic influence of the ventral tegmental area (VTA) on the excitatory postsynaptic potential (fEPSP) and the population spike (PS) in the CA1 region. The VTA, a modulatory input to the CA1 region, is a heterogeneous group of dopaminergic cells and a major component of the mesolimbic dopamine system. This brain structure was good qualified to test the influence on the synaptic plasticity in the CA1 region.

For these studies the method of double recording was now established in the CA1 region. It was able to record simultaneously the fEPSP and the PS in their places of generation in the same animal over a longer time, especially over 24 h like in this work.

It was shown that an early-LTP induction for the fEPSP and the PS of the CA1 can be induced using primed burst (PB) stimulation of the contralateral CA3 (cCA3). This transient form of LTP can be reinforce into a late-LTP by high-frequency stimulation of the VTA (VTAhfs) 15 min after PB-stimulation of the cCA3. For pharmacological studies we applied the D1/D5-receptor antagonist SCH23390, the protein-synthesis blocker anisomycin or emetine intracerebroventricularly (i.c.v.) 10 min before VTAhfs. Our results show that the reinforcement of an early- into a late-LTP is dependent on the dopaminergic D1/D5-receptor activation and the protein-synthesis in the CA1.

Further, the influence of VTAhfs on the early-LTD in the CA1 was studied. Early-LTD was induced in CA1 for fEPSP by the application of a low-frequency stimulation (LFS) at the cCA3 region. First, we stimulated the VTA 15 min after early-LTD induction and the result shows a reinforcement of an early-LTD into a late-LTD. The i.c.v. application of the D1/D5-receptor antagonist SCH23390 10 min before VTAhfs blocks the reinforcement into a late-LTD. These pharmacological studies show that the reinforcement is dependent on the dopaminergic activation of the D1/D5-receptors in the CA1. The VTAhfs 15 min before induction of an early-LTD shows no reinforcement into a late-LTD.

In addition to the modifications of an early-LTP/-LTD into a late-LTP/-LTD, the VTAhfs on test pulses led to the induction of a so-called “delayed-onset” potentiation for the fEPSP and the PS in the CA1 region. We applied i.c.v. the D1/D5-receptor antagonist SCH23390 or the NMDA-receptor antagonist AP5 10 min before VTAhfs. These pharmacological studies shows, that the delayed-onset potentiation is dependent on the synergistic activation of the glutamatergic and dopaminergic receptors. The necessity of synergistic activation of the D1/D5-receptors and the NMDA-receptors was not only checked by pharmacology studies but the other point to test the dependency of the synergistic activation was to stop the application of test pulses in the cCA3 for 3 h after VTAhfs. When the glutamatergic receptor activation was paused, the delayed-onset potentiation was not induced.

However, it seems to be, that the mesolimbic dopaminergic system is involved in the modification of LTP/LTD and plays an essential role by the induction of the delayed-onset potentiation in the CA1 region.