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„State-Dependent Activity and Plasticity of Neuronal Assemblies in Oscillating Networks of the Hippocampus“

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The hippocampus plays a central role in the context of learning and memory. Network oscillations at different state-specific frequencies distinguish and mediate different steps of information processing. Gamma oscillations during active behavioural states contribute to acquisition of new memory represented by neuronal assemblies. Subsequently, sharp-wave-ripple-oscillations (SPW-R) during rest periods promote long-term consolidation of acquired memory and memory storage to neocortical areas. Consequently, on the one hand, the hippocampal network has to guarantee flexibility of neuronal assemblies for encoding of new information while, on the other hand, formed neuronal assemblies have to be stable enough to survive changes in network states.

The first aim of the thesis was to investigate the participation of the dentate gyrus (DG) in hippocampal network oscillations and changes in network states. The DG is implicated in spatial processing during memory acquisition as it provides means of distinguishing between partly similar but distinct information patterns (“pattern separation”). However, its role during subsequent memory consolidation has not yet been comprehensively clarified. For this purpose, experiments were conducted making use of an *in vitro* model of hippocampal oscillations in mouse hippocampal slices. These experiments reveal that SPW-R-activity in CA1 is associated with coherent network activity in the DG. Moreover, even on cellular level, precise long-range coupling of unit activity in the DG to fast oscillations in CA1 and CA3 is seen. This coupling is found to be mediated via recurrent connections from the CA-areas to the dentate gyrus. After local pharmacological blockage of $GABA_A$-receptors SPW-coupled firing in the DG is diminished, which points to a role of inhibitory interneurons in establishing this long-range phase-coupling. The inclusion of units in the dentate gyrus into active assemblies during SPW-R may implicate different important advantages during memory consolidation: hippocampal storage capacity is increased and reverberating activity involving potent synapses may strengthen connections within the trans-regional assemblies. By conveying pattern separation mechanisms onto the CA-regions the DG would promote correct readout to neocortical areas.

The second aspect examined in this thesis is the effect of switching between different network states on the stability and plasticity of neuronal assemblies. Spontaneous SPW-R-activity in hippocampal slices was interrupted by a period of gamma oscillations. This was achieved by pharmacological activation of cholinergic receptors modelling septal influences *in vivo*. Afterwards, SPW-Rs were re-established. Changes in unit and field activity after a transient phase of gamma oscillations were compared to data from prolonged SPW-R-recordings.

Interestingly, the group of active units remains remarkably stable in spite of an intermittent, drastic change in oscillatory rhythm. Furthermore, also the precise temporal coupling to the underlying fast ripple oscillations persists after a cholinergically induced gamma period. On closer examination, an increase in SPW-related firing is observed after cholinergic activation. This effect is not seen in prolonged SPW-recordings. Therefore, it can be specifically attributed to the intermittent gamma period under cholinergic influence. In contrast, firing outside of SPWs is stable and even diminished in CA1. In this region the degree of modulation of SPW-related firing is correlated to the gamma power. As one potential mechanism contributing to this plasticity effect an induction of long-term-potentiation of synaptic transmission is seen after cholinergically induced gamma. As a further intriguing observation, plastic changes in unit-to-field-coupling are even mirrored in changes in SPW-waveforms. These have been supposed to constitute macroscopic fingerprints of defined neuronal assemblies. In contrast, during prolonged SPW-R-oscillations, SPW-waveforms remain rather constant over time. Thus, a single episode of muscarinic receptor-induced gamma oscillations leads to specific changes to hippocampal cellular assemblies and strengthens coupling between units and the underlying network. In contrast, SPW-R-oscillations render the structure of hippocampal assemblies remarkably stable. As a conclusion, the present work reveals important insight into the balance of stability and plasticity in the hippocampus by which memory consolidation and formation can be achieved.