Elisa Katharina Weiß
Dr. med.

Generation and Modulation of Memory-Related Network Oscillations in the Mouse Hippocampus *in vitro*

Promotionsfach: Physiologie
Doktorvater: Prof. Dr. med. Andreas Draguhn

The present thesis made use of the acute hippocampal slice preparation to address two major questions concerning the generation and modulation of hippocampal network activity.

In the first part, the functional role of the newly discovered neuronal connexin 30.2 in hippocampal circuits was examined. Electrical coupling via gap junctions is crucial for cell-to-cell communication within the central nervous system and is supposed to be involved in the generation of hippocampal network oscillations.

Field potential recordings in acute hippocampal slices of Cx30.2-deficient mice and control littermates were performed to investigate basal excitability, paired pulse behaviour, sharp wave-ripple complexes and gamma oscillatory activity.

Basal excitability and responses to paired stimuli were not different in the Cx30.2-deficient animals. Furthermore, the present study did not find any indication for a role of Cx30.2 in the generation of sharp wave-ripple activity. The structural correlate of the suspected underlying axo-axonal gap junctions remains hence to be elucidated. The interneuronal expression pattern of Cx30.2 suggested a possible role in the synchronisation of gamma oscillatory activity. However, only very mild alterations were observed for this oscillation pattern in Cx30.2-deficient animals. As a conclusion of this and recent other work, synchronisation of hippocampal gamma oscillations is mediated by several connexins, mainly Cx36 and Cx45, which seem to readily compensate for the loss of Cx30.2.

The second part of this thesis was dedicated to the studies of possible corticosteroid effects on the hippocampal network. The hippocampus is a key area involved in both, regulation of the stress response and memory formation, and there are abundant examples for the impact of corticosteroid levels on memory performance.

In order to study the acute effect on basal excitability, paired pulse behaviour, sharp wave-ripple and gamma oscillatory activities, the murine stress hormone corticosterone was bath-applied at different concentrations. In addition, the principal human corticosteroid, cortisol, and the solvent ethanol were tested. The most prominent effect was observed on sharp wave frequency, with low doses of corticosterone leading to increased frequency as compared to control measurements, whereas high concentrations induced a decrease. The effect showed hence the inverted U-shaped dose-dependency that is typically observed for corticosteroid effects. Basal excitability was only slightly affected by the hormone, but interestingly, the

highest concentration of corticosterone resulted in a transient desynchronisation of gamma oscillatory activity.

The canonical signalling pathway of corticosteroids involves two receptor systems, the mineralo- and the glucocorticoid receptor. In order to study their impact on the hippocampal network, mice deficient of one or both of the respective proteins were used. The results of the present thesis indicate that both receptors might exert some modulatory influence; however, none of the receptors proved to be indispensable for the generation of gamma oscillations or sharp wave-ripple complexes or the induction of long-term potentiation.

The present work provides evidence for fast and specific effects of acute corticosteroid application on hippocampal network oscillations and offers a possible mechanistic link between elevated stress hormone levels and altered hippocampal function. Whether mineralo- and glucocorticoid receptors are involved in mediating the observed acute effects requires further investigation.