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Lamina-specific contribution of glutamatergic and GABAergic potentials to hippocampal sharp wave-ripple complexes

Fach: Physiologie

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My experiments were designed to study the cellular mechanisms underlying hippocampal sharp wave-ripple complexes (SPW-R). SPW-R are local field potential (LFP) transients reflecting multicellular activity. They are characterized by a low-frequency and a fast oscillatory component and are typically recorded during sleep or resting immobility. Interestingly, recent findings suggest that SPW-R might play a crucial role in memory consolidation.

Especially in the strictly laminated CA 1 subfield, the shape of SPW-R varies considerably across the layers. The genesis of this laminar profile is to date only partly understood. I tried to provide direct experimental evidence by combining a lamina-specific application of CNQX and gabazine with a high-resolution recording electrode array. Therefore a well-established murine slice model was used, which produces spontaneous network bursts that closely resemble SPW-R in behaving rodents.

The first main finding was that the shape of SPW-R is largely due to local active sinks and sources. Passive return currents, on the other hand, do not seem to play a major role. Besides, the contribution of GABAergic currents to SPW-R in stratum (s.) pyramidale is underlined. Notably, effects were relevant both on the slow and on the high-frequency component. My data also indicates that inhibitory inputs to s. oriens, in addition to pyramidal layer terminations, are involved in discharge timing. Glutamatergic afferents, in contrast, have a large impact on s. radiatum sharp waves. Surprisingly, I also detected a superimposed fast oscillation in this layer. Like the underlying low-frequency transient, these “radiatum ripples” seemed to have a relevant glutamatergic component. Interestingly, they were slightly slower than ripples in s. pyramidale. The pyramidal layer phase lag of about 1 ms at SPW-R onset thus decreased towards their end. As a consequence, recruitment of participating units might be facilitated during earlier ripple cycles.

The origin of these fibers remains unclear due to the limitations of the methods I chose. In my opinion, CA3 should be considered as a likely candidate region. GABAergic terminations rather originate from local circuit neurons and control action potential timing. Together these findings nicely illustrate the complementary role of spatially confined excitatory and inhibitory transmission.