A Network Interaction Perspective on Entorhinal Cortex–Hippocampal Theta Oscillations

Theta oscillations in the hippocampal-entorhinal cortex circuit play a central role in spatial navigation and memory consolidation [1]. Traditionally conceptualized as a global and homogeneous rhythm, theta activity is now understood to comprise multiple coexisting pathways that converge in the Cornu Ammonis layer 1 (CA1) [2]. These pathways include components associated with the trisynaptic circuits—namely projections from entorhinal cortex layer II (ECII) to the dentate gyrus, and from CA3 to the stratum radiatum of CA1—as well as a monosynaptic projection from ECIII to the stratum lacunosum-moleculare of CA1. Previous work has shown that theta-band synchronization across these pathways increases during tasks requiring the integration of internally generated memory representations with external sensory inputs [2]. However, direct contributions from the entorhinal cortex were not assessed in that study.

Here we analyzed simultaneous electrophysiological recordings from the hippocampus and EC in rats performing a T-maze task [3]. Applying Independent Component Analysis, we isolated the three hippocampal pathways along with two additional components corresponding to activity in ECII and ECIII. Functional connectivity analysis between the theta current generators showed coordinated activity within the EC and between the EC and hippocampal generators. Notably, synchronization between hippocampal and EC pathways did not follow anatomical connections, indicating a divergence between functional and structural connectivity. Finally, we identify the perforant pathway as the temporal leader of theta-band coordination across the entorhinal cortex–hippocampal network.

1. Buzsáki and Moser, Nature Neuroscience, 2013
2. López-Madrona et al, eLife, 2020
3. Zhou et al, iScience, 2022