RHYTHMIC ACTIVITY OF THE HIPPOCAMPUS IN MICE WITH A MODEL OF ALZHEIMER'S DISEASE AND MODULATION OF ASTROCYTE MORPHOLOGY

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Rhythmic electrical activity in the brain is essential for information processing in neural networks. The theta rhythm (4-12 Hz) of the hippocampus is the leading low-frequency oscillation, orchestrating the phase for the emergence of faster gamma cycles, which underlies the mechanism of cross-frequency connectivity. This rhythm is directly linked to the animal's active movement in space and ensures the temporal encoding of information through the positioning of spikes relative to the phase of the theta wave. A key function of neuronal activity in the gamma range (20-200 Hz) is the organization of precise interactions between various inputs: for example, from the CA3 area and the entorhinal cortex, which is necessary for memory consolidation and retrieval, as well as for the formation of spatial and episodic memories.

Modulation of rhythmic hippocampal activity is disrupted in neuropathologies, particularly Alzheimer's disease (AD). However, it remains unclear what is the underlying cause of the observed disturbances: neuronal death, vascular pathology, or functional (morphological or metabolic) impairments of astrocytes. In this study, we investigate the influence of specific morphological changes in astrocytes on the modulation of theta and gamma rhythms and their interactions in the mouse hippocampus.

Part of the study was conducted in an animal model of AD (5xFAD line), while another involved C57BL/6 animals. A functional viral construct modulating the expression level of ezrin, a protein responsible for membrane-cytoskeletal coupling, was injected into both hemispheres of each animal. Two viral constructs were used: one that causes proliferation of astrocyte processes and an increase in their volume (OE) or, conversely, a decrease in the average cell size (KD), or a virus with a non-coding sequence (NC) for control mice. Animals in all groups also had nichrome electrodes implanted bilaterally in the hippocampi. The electrical activity of hippocampal CA1 neurons in freely moving animals during the Open Field and Barnes Maze tests was recorded using a telemetry system (MultiChannel Systems).

We analyzed hippocampal rhythmic activity in mice with a model of Alzheimer's disease and modulated ezrin levels. Analysis of electrophysiological recordings from 5xFAD mice revealed characteristic disturbances in oscillatory activity in the Alzheimer's disease model. The data obtained from animals with altered astrocyte morphology may indicate that both a decrease and an increase in astrocyte volume lead to pathological changes in the theta and gamma rhythms separately, as well as disruption of their phase-amplitude coupling.

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