Investigating Hippocampal Mossy Cell Circuits That Generate Avoidance Behavior

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The hippocampus, which comprises several sub-regions including the dentate gyrus (DG), CA1 and CA3, is critical to declarative memory, and emotion. Among the hippocampal sub-regions, the DG is the first relay station and is composed of glutamatergic principal neurons and GABAergic interneurons (INs). Unlike the CA areas, the DG contains two types of glutamatergic neurons, the granule cells (GCs) and the mossy cells (MCs). The GCs are the vast majority of principal cells and mediate feedback inhibition on the cells by exciting local GABAergic INs.
Relative to studies of GCs, our knowledge about the circuit functions of MCs in the DG network is not well established. The MCs mainly receive the excitatory drive from GCs and make feedback excitation on GCs as well as feedforward excitation on INs. The net effect of MCs onto GCs and INs throughout the DG long axis remains mysterious. Furthermore, the relevance of MCs in behavioral functions remains unexplored. Thus, we dedicate to investigating the in vivo effect of MC excitation at circuit and behavioral levels. Using Calcium fiber photometry, we find that ventral MCs (vMCs) are more active during open-arm exploration in the elevated plus maze. Chemogenetic activation of vMCs decreases the open-arm avoidance, suggesting a causal link between MC excitability and anxiety state. In agreement with this notion, vMC activation greatly decreases the anxiety-like behavior in a chronic pain mouse model. Finally, using juxtacellular recording and optogenetic approaches, we find that bilateral activation of MCs suppresses GCs, but mainly excites INs.

Keywords: Dentate gyrus, Hilar mossy cell, Fiber photometry, Anxiety, Avoidance behavior

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