Mossy Cells in the Ventral Hippocampus Differentially Impact on Granule Cell Activity along the Longitudinal Axis

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The hippocampus is an elongated brain structure which runs along a dorsal-to-ventral axis in rodents, corresponding to the posterior-to-anterior axis in humans. A glutamatergic cell type in the hilus of the dentate gyrus (DG) called mossy cells (MCs) establishes extensive excitatory collateral connections with the primary DG cell type, the granule cells (GCs) in both hippocampal hemispheres along the longitudinal axis. MCs are thought to mediate interhemispheric inhibition through commissural projections. However, how MCs regulate the GC activity along the hippocampal longitudinal axis remains unclear. The goal of this study is to investigate the action of ventral MCs on ventral and dorsal GCs in mice and their synaptic transmission modes. Combining optogenetic and electrophysiological approaches, we show that ventral MC excitation results in a low synaptic excitation/inhibition (E/I) balance in ventral GCs, but a high synaptic E/I balance in the translamellar dorsal GCs. In agreement with the differential E/I balance along the ventrodorsal axis, activation of ventral MCs either enhances or suppresses the local GC response to the cortical input, but primarily promotes the distant GC activation. Moreover, activation of ventral MCs enhances the spike timing precision of the local GCs, but not that of the distant ones. Collectively, these findings suggest that MCs differentially regulate the local and distant GC activity through distinct synaptic mechanisms.