Mossy Cell Longitudinal Projections Differentially Regulate Granule Cell Activity Via Distinct Excitation/inhibition Balances

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The hippocampus is a long, curved brain structure, which runs along a dorsal (septal)-to ventral (temporal) axis in rodents, corresponding to a posterior-to-anterior axis in humans. It is comprised of the dentate gyrus (DG) and areas CA3 and CA1. The DG granule cells (GCs), which are the vast majority of the principal cells, receive multimodal sensory input from the cortex and relays it to downstream brain areas along the hippocampal transverse axis. In contrast, hilar mossy cells (MCs), which are the second population of principal cells in the DG, establish extensive divergent projections along the hippocampal longitudinal axis. However, little is known about the MC longitudinal connectivity between the dorsal and ventral DG. Here, we investigated MC connections with GCs along the longitudinal axis. Selective activation of MC associational fibers shortens spike latency of both local and distant GCs, but only enhances the spike timing precision of GCs located in the same lamella. Furthermore, MCs exert direct excitatory and indirect inhibitory conductances in GCs. Depending on the GC location, MC activation leads to a low excitation/inhibition (E/I) balance in GCs in the same lamellae, but a high E/I balance in GCs located in distant lamellae. Our study reveals that MCs differentially regulate the GC activity along the hippocampal longitudinal axis through distinct synaptic mechanisms.

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