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Hyperactivity of ventral hippocampal mossy cells degrades dorsal hippocampal mnemonic function via longitudinal projections

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The anterior hippocampus of individuals with early psychosis or schizophrenia is hyperactive, as is the ventral hippocampus in many schizophrenia-related rodent models. Mossy cells (MCs) of the ventral dentate gyrus (vDG) target both dorsal DG (dDG) granule cells and inhibitory interneurons along the hippocampal long axis. Furthermore, MCs respond to stimulation throughout hippocampal subfields, and consequently may be suited to detect hyperactivity at its origin. Here we hypothesized that vMC hyperactivation activates dDG granule cells to influence dorsal hippocampal function. In CD-1 mice, we targeted dDG-projecting vMCs using an intersectional viral strategy. vMCs were recorded during exploratory behaviors using in vivo fiber photometry. We used excitatory chemogenetic constructs to investigate how vMC hyperactivation affects long-term spatial memory during an object location memory (OLM) task. Photometry revealed vMC activation during exploratory rearing. Furthermore, vMCs innervated dDG granule cells, and vMC chemogenetic activation modestly increased dDG granule cell activity and associated c-Fos. Finally, vMC chemogenetic activation during the OLM training phase impaired performance 1-day later, without affecting locomotion or object exploration. These data suggest that vMC activation can directly excite dorsal granule cells and interfere with dDG function, supporting future study of this circuitry in schizophrenia-related animal models featuring ventral hyperactivity.

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