Inter-dentate Gyrus Inhibition Supports Contextual Memory

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Excitatory cortical inputs enter the dentate gyrus (DG) and recruit memory ensembles, while activating local inhibitory interneurons (INs) to constrain their size. A subset of GABAergic cells mediates long-distance inhibition between the bilateral DG. However, their function at the cellular and behavioral levels has remained enigmatic. Combining electrophysiological and optogenetic approaches, we demonstrated that somatostatin-expressing contralateral-DG (SOM+ cDG)-projecting neurons preferentially engage dendrite-targeting INs over principal neurons (PNs). Single-unit recordings from freely moving mice revealed that the optogenetic stimulation of SOM+ cDG-projections modulates the activities of GABAergic INs and PNs over multiple timescales. Importantly, we demonstrate that the optogenetic silencing of SOM+ cDG-projections during contextual fear conditioning results in compromised DG-dependent memory tasks. Moreover, the optogenetic stimulation of SOM+ cDG-projections is sufficient to disrupt contextual memory recall. Collectively, our findings reveal that SOM+ long-range-projections mediate inter-DG inhibition and contribute to learning and memory.

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