Differential Regulation of Anxiety and Memory Formation by Dentate Hilar Mossy Cells

Kai-Yi Wang[1] and Cheng-Chang Lien[1, 2]

[1]Institute of Neuroscience & [2]Brain Research Center, National Yang-Ming University, Taipei 112, Taiwan.

Hilar mossy cells (MCs) have long been associated with dentate gyrus (DG) network function by providing excitatory feedback to granule cells, the vast majority of principal cells in the DG. Extensive degeneration of MCs throughout the hippocampal long axis in mice leads to impaired pattern separation and increased anxiety-like behaviors. However, aberrant rewiring and plasticity changes of the DG network may occur under pathological conditions. Moreover, lesion studies fail to address the causal relations between MC activity and various behaviors under physiological conditions. In this study, a chemogenetic approach was used for reversible and bidirectional control of MC excitability. In behaving mice, chemogenetic inhibiting MC activity increased the innate anxiety-like behavior, whereas elevating MC activity decreased both their innate and defensive anxiety-like behaviors. In great contrast to regulation of anxiety, both elevating and reducing MC activity impaired short-term but not long-term object recognition memory. Together, our data indicate that fine-tuned MC excitability is required for short-term recognition memory, whereas bidirectional modulation of MC activity has either an anxiolytic or an anxiogenic influence.

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