Artificially enhancing or suppressing hippocampus-mediated fear memories

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Introduction

• Cognitive and emotional disruptions underlie many stress-related disorders

• The hippocampus processes cognitive and emotional aspects of learning along its dorsal-ventral extent and functional changes along this axis may differentially contribute to cognitive and emotional impairments

• Here, we asked if artificially activating a positive or negative memory in the dorsal or ventral hippocampus can promote appetitive or aversive-related behaviors

• We also examined the behavioral effects of chronic reactivation of a negative memory on fear behavior and the necessity of BLA involvement during chronic activation of the dorsal hippocampus.

Method

• We infused AAV9-cFos-tTA and AAV9-TRE-ChR2-mCherry or AAV9-TRE-mCherry into the dorsal (dDG) or ventral dentate gyrus (vDG) and implanted optic fibers above the injection site

• When mice are off doxycycline (Dox) diet, neuronal activation (via c-Fos) promotes the transcription of ChR2, allowing for targeting of cell ensembles active during positive or negative memory formation

• Tagged cell ensembles can then be reactivated via light-stimulation (i.e., ChR2) or CNO (hM4Di)

Conclusions

• Activation of dorsal and ventral hippocampus cells were sufficient to drive freezing, avoidance, and preference

• The ventral, but not dorsal, hippocampus is sufficient to modulate anxiety-like states

• Chronic activation of the dorsal hippocampus cells produces extinction-like reductions in fear responses, whereas ventral hippocampus stimulation induces a context-specific enhancement of a fear memory

Future Directions

We will examine if optogenetic reactivation of a fear memory prior to extinction facilitates extinction and mitigates renewal (c) and reinstatement (d) in EtOH mice

Acknowledgements

This work was supported by NIH DP5, NARSAD, Harvard Milton Fund, & The Ludwig Family Foundation, and the Center for Memory and Brain at BU. Thanks to the labs of Howard Eichenbaum and Joshua Sanes for assistance.

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Additional Data

• vDG eYFP/c-Fos overlap to examine context specificity

• vDG chronic activation of positive, negative, or neutral memories

• dDG chronic activation of * or / effects

• BLA chronic activation

Conclusions

BLA Silencing During Chronic dDG Activation of Negative Memories

Inactivation of tagged BLA cells during chronic dorsal hippocampus activation does not prevent context-specific extinction-like fear behavior