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Synchronized activity between the ventral hippocampus and the medial prefrontal cortex during anxiety.

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Recommendations:

Very Good 24 Mar 2010

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CONTROVERSIAL | NEW FINDING

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This exciting study shows that 1) medial prefrontal cortex (mPFC) theta is much more coherent with ventral than with dorsal hippocampal CA1 theta, and 2) exposure to anxiety-provoking environments increases ventral hippocampal/mPFC theta coherence (with the suggestion that the ventral hippocampus drives mPFC, rather than the reverse). The findings have important implications for our understanding of the organisation of hippocampal theta and its role in the generation of anxiety.

The hippocampus has long been thought to play a role in anxiety (reviewed {1,2}) in addition to its well-established role in spatial memory {3}, and the two may be linked {4}. In the present study, Adhikari et al. recorded EEG from dorsal and ventral hippocampus and mPFC while mice were exposed to two anxiety-provoking environments (a bright open field and an elevated plus maze [EPM]) and a familiar control environment. Even in the control environment, ventral CA1/mPFC theta coherence was much higher than dorsal CA1/mPFC coherence, and exposure to anxiety-provoking environments further increased ventral CA1/mPFC theta power correlations, as well as the phase locking of mPFC multi-unit activity to ventral CA1. Importantly, anxiety-induced increased theta coherence likely reflected hippocampal-to-mPFC influence, rather than the reverse; this is because a) ventral CA1/mPFC theta power correlation was maximal when the mPFC EEG signal was shifted backwards by 8ms; b) theta frequency increased in mPFC during anxiety, approaching the frequency seen in ventral CA1; c) phase locking of mPFC multi-unit activity to ventral CA1 theta was maximal when mPFC spikes were shifted backwards by 32ms. These results are in line with anatomical tracing data showing that direct CA1-mPFC projections come from the ventral, not dorsal, CA1, while prefrontal influence on CA1 is multi-synaptic. They are also consistent with a dorso-ventrally decreasing importance of spatial information in hippocampal electrophysiology {5}. The higher frequency of dorsal compared to ventral hippocampal theta seen in this study is consistent with the oscillatory interference model of grid cell firing and theta proposed by one of us (see {6}, on which Neil Burgess is the author), given the increasing spatial scale of place {4} and grid cell {7} responses with dorso-ventral location, and with concomitant changes in intrinsic neuronal rhythmicity {8}. The authors also analysed theta power in serotonin-1A receptor knockout (5HT-1AR KO) mice, a genetic model of anxiety. On exposure to the open field and EPM, relative to baseline levels in a familiar environment, 5HT-1AR KO mice showed significantly higher theta power in mPFC, but not in ventral and dorsal hippocampus. The latter result did not replicate their earlier finding of increased theta power in the dorsal CA1 pyramidal layer in the anxiogenic open arms of the EPM in these mice {9}. The authors suggest this may be due to the reduced sample sizes and/or decreased EPM anxiogenicity in the present study. In across-subject comparisons of power, orso-ventral location. This important study further undermines previous eneration of anxiety.

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Disclosures
None declared

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Abstract:

ABSTRACT

The ventral hippocampus, unlike its dorsal counterpart, is required for anxiety-like behavior. The means by which it acts are unknown. We hypothesized that the hippocampus synchronizes with downstream targets that influence anxiety, such as the medial prefrontal cortex (mPFC). To test this hypothesis, we recorded mPFC and hippocampal activity in mice exposed to two anxiogenic arenas. Theta-frequency activity in the mPFC and ventral, but not dorsal, hippocampus was highly correlated at baseline, and this correlation increased in both anxiogenic... more »
environments. Increases in mPFC theta power predicted avoidance of the aversive compartments of each arena and were larger in serotonin 1A receptor knockout mice, a genetic model of increased anxiety-like behavior. These results suggest a role for theta-frequency synchronization between the ventral hippocampus and the mPFC in anxiety. They are consistent with the notion that such synchronization is a general mechanism by which the hippocampus communicates with downstream structures of behavioral relevance.

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