Parallel signal transfer through hippocampal CA2 region following perforant-path stimulation and internally generated dentate spikes

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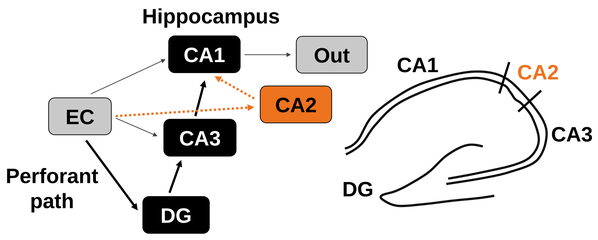
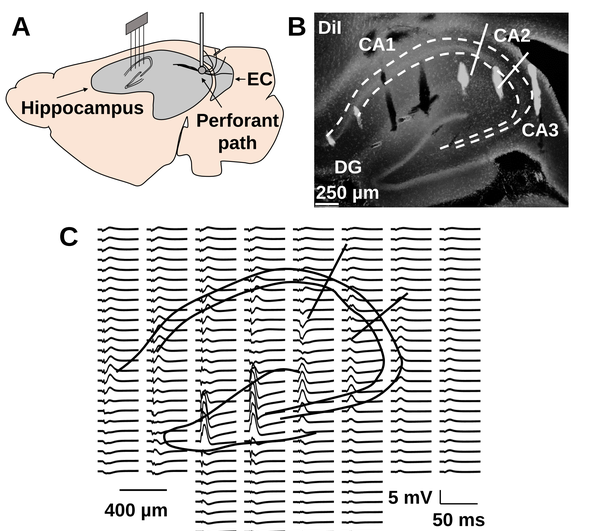
Abstract

- Most studies investigating signal propagation through the entorhinal cortex (EC) - hippocampal network focus on the tri-synaptic circuit (EC→ Dentate Gyrus (DG)→ CA3→ CA1).
- **The role of CA2 in the transmission of signals within the EC-hippocampal network remains unclear *in vivo*.**



- Using silicon probes, we studied EC signal transfer across the dorsal hippocampus in anesthetized and sleeping rats after perforant-path stimulation and dentate spikes, which are spontaneous DG field potentials evoked by EC input.
- Contrary to the tri-synaptic model, CA2 activation preceded CA3 following perforant-path stimulation and dentate spikes.
- Furthermore, peak activation of CA2 was significantly greater than activation of CA3 following both events.
- These data demonstrate a powerful transfer of signals from EC to CA2 *in vivo* that runs parallel to the tri-synaptic circuit.

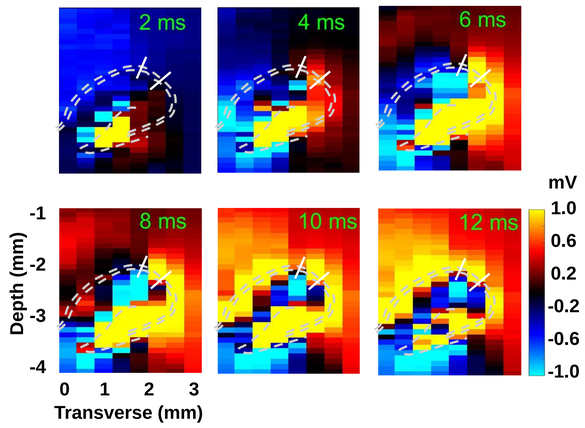
Stimulating the perforant-path



A) Stimulation and recording protocol.
B) Histological section of the dorsal hippocampus stained with DAPI (cell layers) and DiI (silicon probe tracks).
C) Electrophysiological mapping of perforant-path activation (750 µA stimulation intensity, average of 10 stimulations across 10 recording positions).

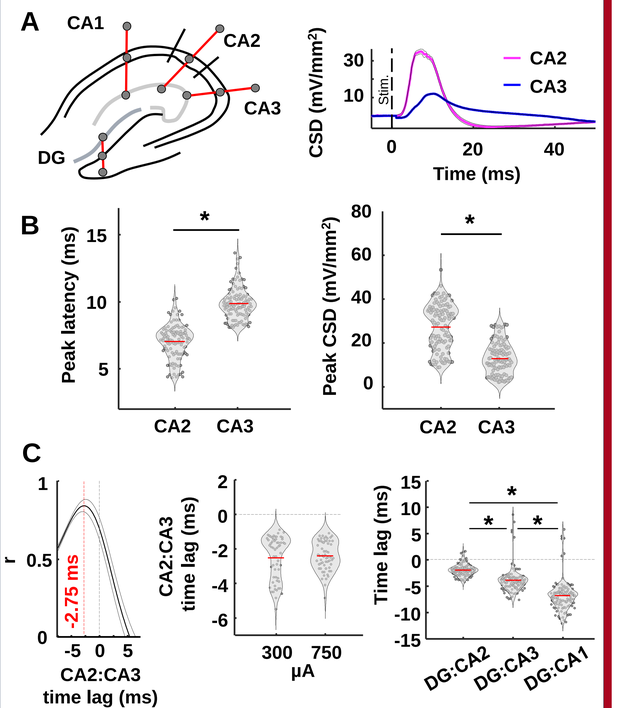
Strong activation of CA2 precedes CA3 following perforant-path stimulation

Voltage mapping



2D voltage maps over time of perforant-path activation of the dorsal hippocampus taken at 2-ms intervals after stimulation.

Current source density (CSD)



A) Left: electrode site orientations used for CSD analysis. Right: evoked peri-event CSD traces in CA2 and CA3.
B) Latency to peak CSD (left) and peak CSD amplitude (right) across all hippocampal sections (n = 120 stimulations, 3 rats).
C) Left: temporal cross-correlations taken from evoked CSD in A. Center, right: Temporal cross-correlations between CSD in CA2 and CA3 separated by stimulation intensity, and between DG and each hippocampal region (CA2, CA3, CA1).

Detecting dentate spikes

Data contributed by Azahara Oliva[3] and Antal Berényi[4,5]

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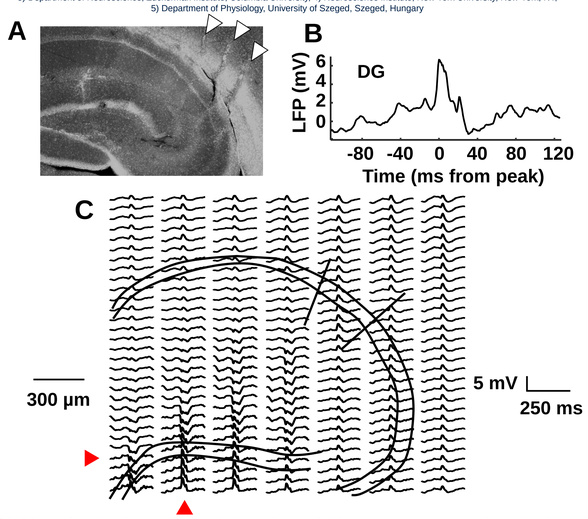
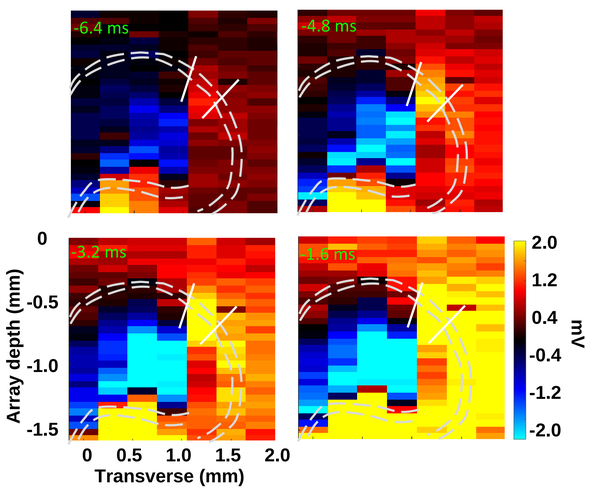


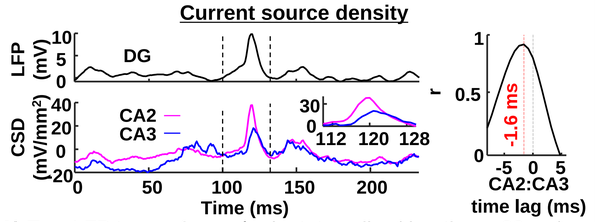
A) Histological section of the dorsal hippocampus stained with DAPI (cell layers). Probe tracks are indicated by white triangles.
B) Single dentate spike detected in DG during sleep at row and column marked by intersection of red triangles in C.
C) Electrophysiological mapping at time of dentate spike in B.

Voltage mapping



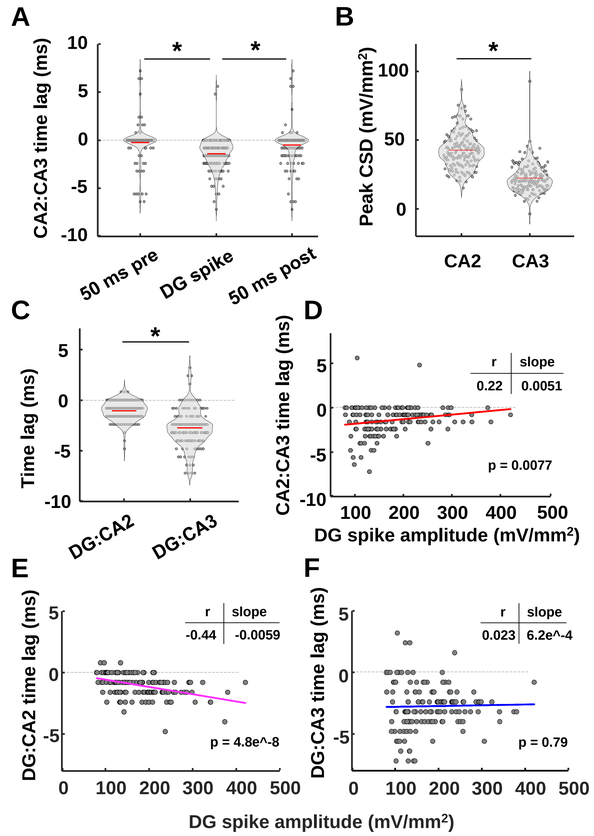
2D voltage maps over time taken at 1.6-ms intervals around the time of dentate spike peak in B and C above.

Current source density



A) Top: LFP trace of sample dentate spike (duration = 33 ms). Bottom: CSD traces in CA2 and CA3 during dentate spike.
B) Temporal cross-correlations taken from CSD in A.

Strong activation of CA2 precedes CA3 during dentate spikes



A) Temporal cross-correlations between CSD in CA2 and CA3 for all dentate spikes (n = 151 dentate spikes, 3 rats) at time intervals before, during, and after each dentate spike.
B) Peak CSD amplitude in CA2 & CA3 during dentate spikes.
C) Temporal cross-correlations between peak CSD in DG and CA2, and DG and CA3.
D-F) Effect of dentate spike amplitude on temporal cross-correlations between CA2 and CA3, DG and CA2, and DG and CA3.

Conclusion

- Peak activation of CA2 preceded and was higher in amplitude than CA3 after perforant-path stimulation and dentate spikes.
- These data show a **powerful transfer of signals from EC to CA2 *in vivo* that runs parallel to the tri-synaptic circuit.**
- These findings suggest a key role of CA2 in the initial and concurrent processing of cortical input within the EC-hippocampal memory network.

Acknowledgements

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