CA3

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1 Connection

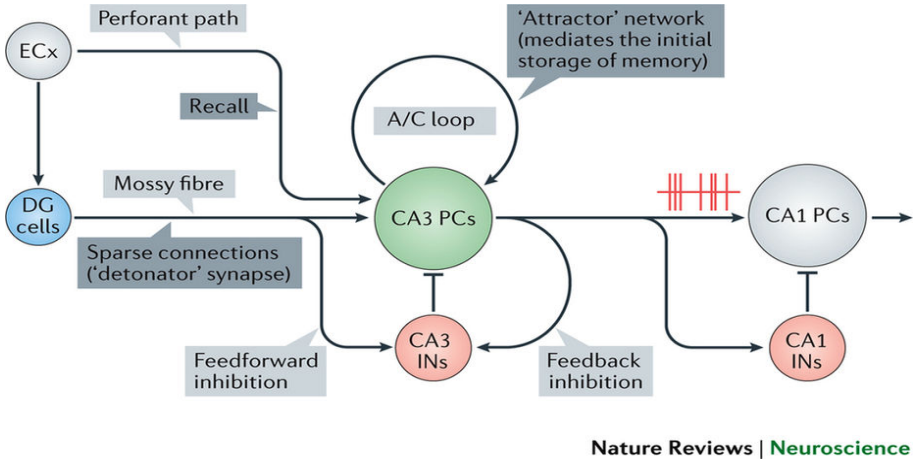

Figure 1: "This schematic illustration shows the different elements of CA3 circuits and their hypothesized involvement in memory encoding and recall.The extensive excitatory interconnections between CA3 pyramidal cells (PCs) known as the associative/commissural (A/C) loop are proposed to work as an attractor network, in which associative memories are stored and recalled through pattern completion. Mossy fibres originating from the dentate gyrus (DG) provide sparse and powerful excitatory connections (known as 'detonator' synapses) to CA3 PCs; these connections are proposed to assist in the encoding of new patterns of activity (representing new memories) in CA3 through pattern separation. The direct connections from the entorhinal cortex (ECx) to CA3 are thought to provide the cues for retrieval (recall) of information from CA3, especially when incomplete information is provided. Feedforward inhibition via CA3 interneurons (INs) strongly controls information transfer between DG and CA3 depending on the pattern of presynaptic activity, and may be involved in the precision of memory. Inhibitory loops in CA3 control the generation of oscillatory activities and are amenable to substantial structural plasticity upon learning. Within the hippocampus, the main outputs from the CA3 region (illustrated by the red schematic trace) are the axons of CA3 PCs, which make contact with CA1 PCs and CA1 INs." [1].

1.1 Input

- Recursive ipsilateral (associational) and contralateral (commissural) excitatory inputs, mediate the pattern completion process. "Unlike most cells in other cortical regions, CA3 cells are predominantly connected to themselves, and receive less than one-third of their inputs from other cell populations" [2].
- From dentate gyrus (DG) granule cells via mossy fibres: sparse excitatory input to CA3 pyramidal cells. pattern separation in CA3 may be "based on the low probability that any two CA3 neurons will receive projections from a similar subset of DG cells" [3]. There are also the feed-forward inhibition from DG as shown in Figure 1.
- From entorhinal cortex (EC) layer II (similar as the dentate gyrus but no input form layer III, as contrast to the dentate gyrus). Convergent input from medial and lateral EC. which is "in contrast to the parallel point-to-point projections between layer III of entorhinal cortex, CA1, and subiculum" [2]
- Inhibitory input from interneurons in CA1 and(or) the widespread intrahippocampal GABAergic system.

- Extrahippocampal input: "from the septal complex, in that CA3 receives bilaterally input from the medial septum/diagonal band of Broca. Other inputs to CA3 apparently originate from the amygdaloid complex and endopiriform nucleus and some of the aminergic nuclei in the brain" [4].

1.2 Output

- To CA1 and CA2: direct projection via Schaffer collaterals from CA3a,b & c separately.
- To dentate gyrus: backprojections to the mossy cells in DG, and inhibit granule cells in DG via the mossy cells. CA3 is thought to be possible to modulate DG firings, maybe even facilitating sensory input from DG. [4].
- To the lateral septal nuclei: 75% of CA3 cells output to CA1 and the lateral septal nuclei. Some single CA3 cells can output to CA3, CA1 and lateral septum, ipsilaterally and contralaterally.[4].

Note: generally CA3 do not connect to the subicular complex and the peri-/post-rhinal cortices [4].

1.3 Main Components

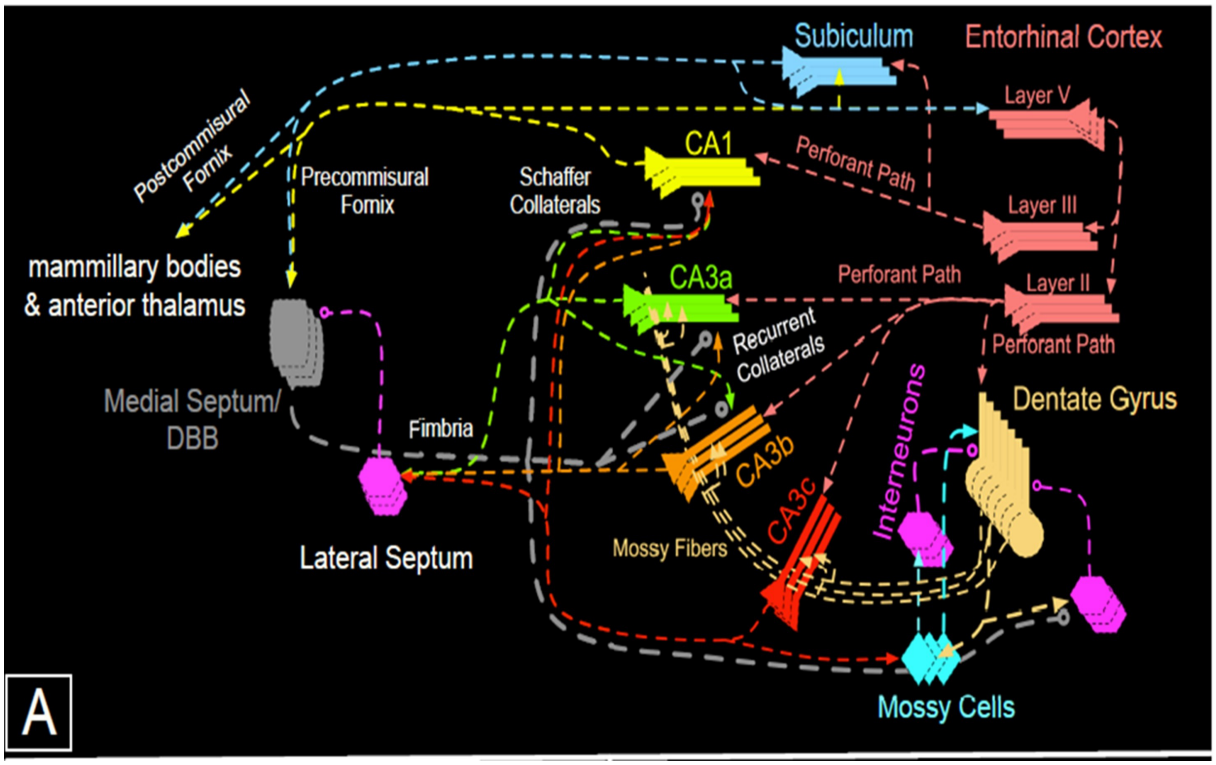

Figure 2: "The colors in the circuit diagram correspond to the colors used to outline the different hippocampal subregions." [3].

- CA3a & b: have recurrent connections, receive input from DG and EC layer II, and output to CA1.
- CA3c: does not have much recurrent connections, but project robustly to CA1, as shown in Figure 2; backproject to the dentate gyrus [3, 4].
- Pyramidal cells (in CA3a, b &c): has bursting firing pattern.
- Interneurons (in CA3a, b &c): recurrent inhibition loops formed by basket CA3 inhibitory cells with CA3 pyramidal cells as shown in Figure 1. [1].

2 Function

- Pattern Separation: different groups of CA3 place cells fire in different environments with similar set-ups. (The firing cells in CA1 overlaps, and the overlap increases with more similarities in the

environment.) [2] Also, the place fields stabilize more slowly in CA3 than CA1 when the rat entering a novel environment, suggesting that the spatial representations in two areas emerge independently. It may also because of the predominantly recurrent connection in CA3, "which may require that a stable orthogonalized representation of a new context is reached iteratively".[5]. And CA3c are shown to detecting the relative location change of objects (not an overall change in the arena) [6].

- Pattern Completion: the same subgroup of CA3 cells will be activated when the rat is in the same room but with partial or different cues [2, 7]. This function mainly rely on the recurrent connections in CA3, which is proposed to work as an attractor network to store and recall memories [8].
- Rate remapping: during the pattern completion process, if the cues are not the same (but the room is the same), the firing fields do not change but firing rate changes a lot [9].
- Control of oscillations: Gamma rhythm can be intrinsically generated in vivo in CA3. Sharp waves (SPWs) can be intrinsically generated in vitro in CA3. The inhibitory neurons in CA3 seems to contribute in synchronizing the local neuron oscillations [1].

2.1 Scales

- Spatial Scales: The place field of CA3 area is around $800cm^2$, with radius of $30cm^2$, which is the the smallest grid spacing.
- Temporal Scales: CA3 cells start to fire simultaneously as the CA1 cells when the animal started to explore an environment. However, the firing patterns of CA3 cells stabilized more slowly than CA1 cells, and some of the place cells in CA3 did not stabilize even after 10-20min. [7]

2.2 Evidence of Building Blocks / Modularization

CA3a, b & c receives similar input from the entorhinal cortex and the dentate gyrus, but they react differently to different spatial changes.

2.3 Evidence of Lateralization

N/A

2.4 Empirical Lesion studies

- Rats with intermediately damaged CA3c could not detect the change in object locations or the geometry of the arena. Rats with damaged CA3a & b only impaired rats in detecting the geometry change of the arena. (However the impairments caused by CA3c lesions is much less severe than by DG lesions).[6]
- CA3 lesion enabled he theta oscillation in CA1, and led to less accurate spatial encoding in gamma rhythms in CA1, which mease CA3 affect the temporal encoding in CA1 [10].

3 Computational Model

The attractor network model mentioned before: [8].

Note: quite a few studies look into the detail interneuron connections, recurrent connections and plasticity mechanism among the mossy fibres from the dentate gyrus to CA3, see [1, 11] for a review of recent discoveries.

References

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