

CA2

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1 Connection

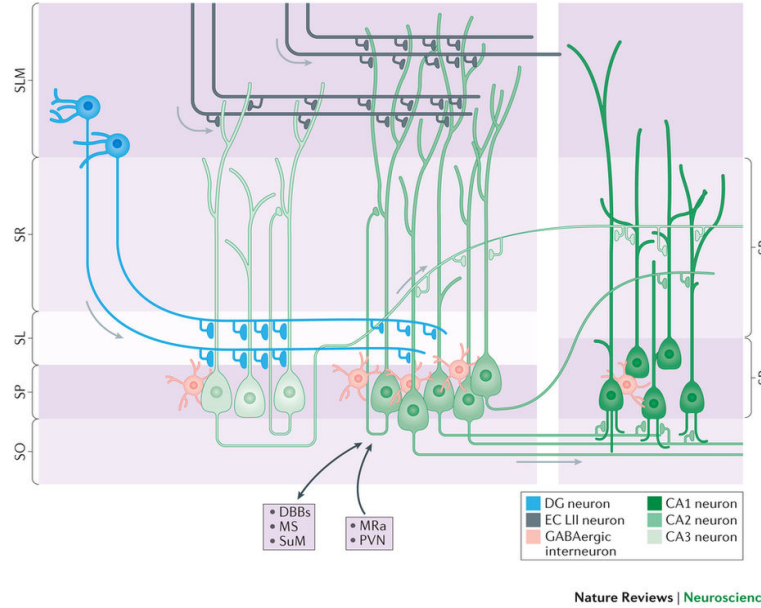


Figure 1: “Connectivity of CA2 neurons within the rodent hippocampal circuit. The CA2 region (medium green) is located between the CA3 region (light green) and the CA1 region (dark green) and is an integral part of the hippocampal circuitry. In rodents, the primary afferents contacting CA2 pyramidal neurons arise from three primary sources: 1. dentate gyrus (DG) granule cells (shown in blue) that target the stratum lucidum (SL), 2. CA3 neurons that target the stratum radiatum (SR), and 3. medial and lateral entorhinal cortex layer II (EC LII) neurons (shown in dark grey) that target the stratum lacunosum-moleculare (SLM). This part of the perforant path was found to dip far into the area normally considered to be SR in monkeys and humans¹⁴³. The main projection target of CA2 pyramidal neurons is deep calbindinimmunonegative CA1 neurons with dendrites in stratum oriens (SO); CA2 neurons target the CA1 SR to a lesser extent. Extrahippocampal inputs to CA2 (indicated by black arrows) include those from vasopressinergic neurons in the paraventricular nucleus (PVN) of the hypothalamus and from the median raphe (MRa), and reciprocal connections with the supramammillary nucleus (SuM), medial septum (MS) and diagonal bands of Broca (DBBs). Many different types of inhibitory interneurons are found in area CA2 and form synapses on CA2 pyramidal neurons. The density of reelin- and parvalbumin-immunopositive interneurons (shown in pink) is several-fold higher in area CA2 stratum pyramidale (SP) than in CA1 SP and CA3 SP. Not all the connectivity among these DG, CA3 and CA1 are shown here.” [1]

Note: the definition of CA2 region is revised recently - some of the previously defined CA3a region are redefined as CA2 in some recent studies using gene and protein expression patterns.

1.1 Input

- From MEC and LEC layer II and III : strong convergent excitation input (the input from EC layer II is stronger than layer III)
- From CA3 Schaffer collaterals: weaker bilateral input

- Extrahippocampal inputs: from vasopressinergic neurons in PVN (may be the reason of the role that CA2 plays in social behavior), the median raphe, and reciprocal connection from SuM and medial septum
- Recurrent ipsilateral and commissural contralateral inputs [1, 2].

1.2 Output

- To CA1: mediate the information from dorsal/intermediate DG to be transferred to intermediate/ventral hippocampus [1] And the “CA2-CA1 stratum oriens and CA2-CA1 stratum radiatum projections are heavily biased to be ipsilateral, with the ipsilateral fibers representing approximately 70 and 90% of the respective CA2-CA1 projections. (By contrast, the CA3-CA1 stratum oriens projection is dominated by the contralateral projection, and the contralateral projection represents approximately 60%. The CA3-CA1 stratum radiatum projection is between 60 and 70% ipsilateral connections.)” [3]
- Reciprocal connections to MEC, SuM and medial septum.

1.3 Main Components

- Pyramidal cells: The peak firing rates are similar to the pyramidal cells in CA1 and CA3, around 5Hz. Some studies reported a delay in firing [1].
- Interneurons: The interneurons is three to ten times denser in the stratum pyramidale (SP) in CA3 than in CA1 or CA3 . The long-term depression plasticity is normal at inhibitory synapses. [4].

Note: CA2 neurons have two distinct features: resistant to long-term potentiation plasticity at excitatory synapses (mainly in SR region); resistant to injury (hippocampus is generally extremely vulnerable). The mechanisms underlie these two may overlap. [1]

2 Function

- Temporal coding: CA2 do not have stable place cells, and its firing patterns gradually become dissimilar over hours or days. Therefore, CA2 could be a region for temporal coding, or act as a prerequisite for “providing a unique input pattern to CA1 at different time points” [5].
- Spatial contextual encoding: The spatial firings in CA2 are more sensitive to small changes in contexts such as new objects than CA1 and CA3 [6, 7],
- Social behaviour: The spatial firing pattern alters significantly according to different social input [7]. The mice with damaged CA2 becomes indifferent to familiar or novel mice, but can still perform social task [8].

Note: “The firing rates and immediate early gene expression were unaffected by social experience and novel objects. Thus, it is suggested that CA2 neurons can update their spatial representations online, possibly as a means to encode social and novel contextual information” [7]

2.1 Scales

- Spatial Scales: Place field size (around $1000cm^2$) of CA2 cells are larger than CA1 and CA3 (around $800cm^2$) [5].
- Temporal Scales: also modulated by theta rhythms and not much different from CA1 and CA3 [5].

Note: there is higher percentage of active cells in an environment in CA2 than in CA1/CA3, and each cells have more multiple firing fields [5]. Therefore, there is less spatial information registered in CA2 than that in CA1/CA3.

2.2 Evidence of Building Blocks / Modularization

The temporal/contextual/social encoding could be regarded as different modules for different building blocks.

2.3 Evidence of Lateralization

N/A

2.4 Empirical Lesion studies

- CA2 damages impair social recognition and social memory, but do not impact object recognition or other spatial memory. [9, 8, 10, 11].

3 Computational Model

N/A

References

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