Distinct characteristics of CA1 place cells correlated with medial or lateral entorhinal cortex layer III input.

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INTRODUCTION

- Place fields of CA1 pyramidal cells can be affected by spatial and non-spatial information. Activity patterns can change in magnitude, shift to new locations in an environment, or disappear when changes to the environment or the animals' behavior occur. In general, this phenomenon is called "remapping" (see Colgin et al., 2008) for review).
- The principal gateway for sensory and spatial information to the hippocampus is the entorhinal cortex. The lateral entorhinal cortex (LEC) is involved in the coding of non-spatial information, such as objects, motivation or goal and the medial entorhinal cortex (MEC) codes for spatial information (e.g. Hargreaves et al., 2005).
- The medial and lateral entorhinal cortices send projections to CA1, but the axon terminals coming from LEC terminate on the portion of CA1 closest to the subiculum ("distal to CA3") whereas the axon terminals coming from MEC terminate in the CA1 region "proximal" to CA3 (Steward O et al., 1976). See Fig1.
- We hypothesized that neurons showing remapping in response to changes in non-spatial information will be primarily located in the distal portion of CA1, whereas neurons that show a remapping as a consequence of changes in spatial information will be located in the proximal region of CA1.

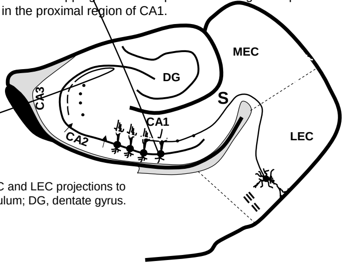

Figure 1: MEC and LEC projections to CA1. S, subiculum; DG, dentate gyrus.

METHODS

Subjects: Four adult male Brown Norway/Fischer 344 hybrid rats (350-400g) were used. Animals were stereotaxically implanted with a hyperdrive consisting of a bilinear bundles of 6 independently movable tetrodes targeted to the dorsal hippocampus with the goal of recording simultaneously in the proximal and distal portions of CA1 (Fig. 2).

Task and apparatus: Rats ran 3 tasks:

- **Constant place and variable cue condition:** Rats were trained to explore a square box in which walls were configured in two ways: 3 black walls and 1 white wall or 3 white walls and 1 black wall. Previous work showed that this task induced rate remapping (Leutgeb et al., 2005) .
- **One environment with two visually identical regions:** Animals were trained to travel between two visually identical boxes connected by a corridor. When the boxes are in a parallel configuration, linear path-integration and external cue information are in conflict. When they are oriented 180 deg opposite, both linear and angular (HD) path integration are in conflict with external cues. (Fuhs et al. 2005, Skaggs et al. 1998).
- **Sensory cues and place field directionality:** Animals were trained to run bidirectionally on a circular track (Battaglia, et al. 2004). Half of the track was enriched by the presence of objects. Cells that are more strongly influenced by path-integration are expected to have a higher probability of bidirectional fields; cells more influenced by external cues are expected to have fewer bidirectional fields.

Histology: After the recording was completed an electrolytic lesion was made by passing current (5µA for 10 seconds) on every electrode. The position of the tip of each tetrode was determined by Nissl staining.

Data analyses: Spatial and firing rate correlations were computed as in Leutgeb et al. (2005).

RESULTS

Figure 2: Top and flat unfolded view of hippocampus, showing the actual positions of the bilinear bundles in four animals. The white dashed line separates distal from proximal CA1. The arrow indicates the tip of the tetrode shown in the inset.

Distal CA1 neurons have more rate remapping than proximal CA1 neurons during a constant place and variable cue task.

Figure 3: Rate change of the place fields of distal and proximal CA1 neurons during a constant place and variable cue task.
A: Schematic representation of the task.
B: Example of changes in rate.
C: Mean +/- SEM across sessions of rate changes for the two configurations. * p<0.05 Mann-Whitney test. The selected cells were required to have a field in at least one condition. The % rate change is computed as an absolute value.

RESULTS

Proximal CA1 neurons show more remapping in an environment with two visually identical regions.

Figure 4: Changes in the place fields' spatial correlation and rates of distal and proximal CA1 neurons in an environment with two visually identical regions. The % rate change is computed as an absolute value.
The task spanned 4 consecutive days with different configurations of the boxes. The corridor configuration did not produce strong global remapping; however, when on trial 2 of Day1 and Day3 there was a significant difference between distal and proximal CA1. The face-to-face configuration produced strong global remapping (Day4), unless it was preceded by the corridor configuration (Day2). Rate changes and changes in spatial correlation swere evaluated across all conditions for proximal an distal CA1 neural populations. Correlations for face-to-face conditions were computed after rotating the data to the parallel configuration.

RESULTS

Neurons with bidirectional (Bi) place fields are more numerous in proximal CA1, whereas neurons with multiple place fields (MPF) are more prominent in distal CA1.

Figure 5: Distribution of bidirectional (Bi), multiple place field (MPF) and non-bidirectional (Non-Bi) neurons during a circular track task, across different sessions and animals.
A: Schematic representation of the task.
B: Different types of neurons detected during this task.
C: Distribution of the different types of cells in the medial an lateral portions of CA1. Red dots: boot-strapping test indicating chance levels (100 shuffles).
D:

CONCLUSIONS