VISUOSPATIAL COGNITION

Grid cells map the visual world

Neuroimaging studies of human entorhinal cortex activity revealed 60-degree spatial periodicity, a hallmark of grid cells, as gaze movements were made throughout the visual field. This activity may serve as a framework for organizing visuospatial memory.

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How do our brains achieve the remarkable feat of building vivid memories that allow us to recall past experiences? During our waking hours, we receive vast amounts of visual information and form memories of these visual experiences as consciously accessible episodic memories. We know that the brain structures critical for episodic memory do not work by storing the entire raw contents of an experience, like saving a digital movie file on a disk drive. Instead, memories are formed with many parallel layers representing object features and spatial relations within a context and are modulated by attention and emotion. Cells involved in episodic memory receive information from cognitive structures and from all available sensory systems, but the mechanisms by which this information is used to support mnemonic functions are not well-understood.

In this issue of *Nature Neuroscience*, Julian et al.[1] and Nau et al.[2] bring us closer to understanding the mechanisms underlying visuospatial memory. Their work shows that one brain structure, the entorhinal cortex (EC), maps the visual world in a manner that may provide a framework for the formation of memories of visual information. Taking these results together with previous results in monkeys[3], it is apparent that neurons exist in the primate EC that have comparable properties to the grid cells in rodent EC, which tile the physical location of the animal[4].

While there is much that we know about how the brain processes sensory input, the representation of sensory information among neurons that are critical for visual memories is less clear. In many brain structures, a discernible arrangement of visual information can be mapped to signals from our retinae. By contrast, retinotopic maps are not evident in the neuronal structures that are critical for visuospatial memory functions, such as the EC and hippocampus. Instead, researchers have found that these areas, and the brain areas with which they are strongly connected, contain neurons that respond to information such as specific objects, regions of space, object–place associations, and relative positions in the environment[5]. Thus, the cells involved in episodic memory must use coding schemes based on compressed and relational representations of the world and its contents. In this model, the function of grid cell activity may be to represent the relations among elements of an environment within a stable organizational framework.

Julian et al.[1] and Nau et al.[2] integrated eye tracking with behavioral tasks and high-resolution functional MRI (fMRI) to examine how coordinated movements of the eyes, reflected in the gaze location, relate to changes in the blood oxygenation level–dependent (BOLD) response in the human EC. Both studies showed that activity in the human EC has 60° spatial periodicity as gaze movements are made throughout the visual field (Fig. 1a). Their results suggest that individual grid cell neurons produce this periodicity, demonstrating the presence of visual grid cells in the human EC for the first time. These putative grid cell responses in the EC were determined by eye movements, in contrast to previous studies examining physical movement through real[4] or virtual[6,7] space. The findings from both Julian et al.[1] and Nau et al.[2] are consistent with reports from single-unit recordings in the monkey EC[3,8] and connect with recent studies demonstrating a broader scope for a grid-like code[9–13].

A grid cell increases its firing rate when the organism is sampling information near the nodes of a triangular grid, yielding a hexagonal firing pattern that has sixfold symmetry, meaning it is identical after any 60° rotation. The pattern of grid cell activity also has a corresponding phase or orientation between 0 and 60°. Although the fMRI technique is limited to population-level assessments of brain volumes that might contain hundreds to thousands of grid cells, if grid cells in a local population all have a similar orientation, then a measure of activity in the population will be enhanced for sampling that occurs along that orientation (Fig. 1b). This property has been used to suggest the presence of grid cells using fMRI to measure activity in the EC of humans performing a virtual reality navigation task[6]. Julian et al.[1] and Nau et al.[2] used this same principle in the context of visual exploration, predicting that the BOLD signal would be enhanced when gaze moved along directions aligned with the grid.

Both groups recorded BOLD signals while subjects made gaze movements to perform a task. Julian et al.[1] asked subjects to search a display for an L glyph among a randomized array of T glyphs, and Nau et al.[2] asked subjects to track a displayed target that moved smoothly along predefined directions and occasionally jumped to a new spot before moving along a different set of directions. Grid patterns were identified in both experiments, even though gaze movements were directed by the subject in Julian et al.[1] versus by the experimenter in Nau et al.[2] Julian et al.[1] found that the grid orientation was anchored to the display bounds, such that the grid rotated when the bounding region rotated, and the grid retained the same relative alignment with the border. This result demonstrates that the visual grid is allocentric, meaning it is anchored to the external world and adapts to changes in context. Julian et al.[1] also found that grid activity was strongest in the medial posterior part of the EC, supporting the idea that this region is functionally analogous to the area of the EC where grid cells are found in other species.

Neurons in the monkey EC have been shown to encode spatial information, including cells that represent saccadic eye movements[14] and cells that map viewed locations[3,8]. The cells that encode eye-movement attributes may signal the direction of visual exploration or attention. In support of this idea, it was recently shown that EC grid cells are driven by visual attention to regions of space, even without direct sampling of a region[9]. The findings of visual grid cells, in comparison to physical location–based grid cells, suggests that EC neurons may have the ability to perform the same computations, independent of specific sensory or environmental dimensions. Indeed, it has been suggested

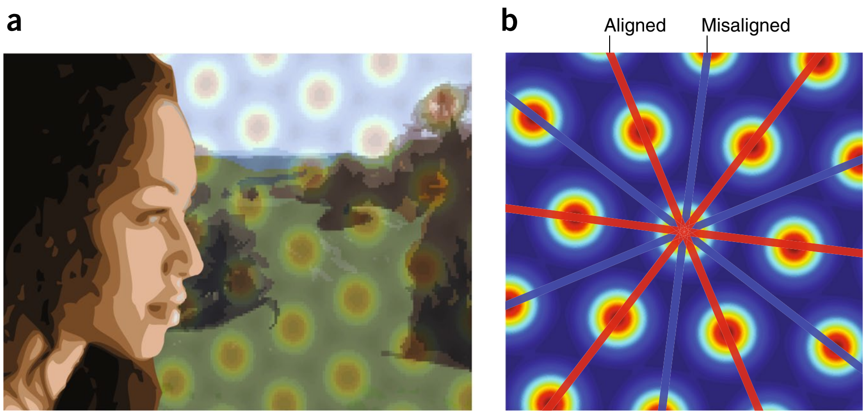

Fig. 1 | Entorhinal grid cells tile the visual world. a, When we explore the world by changing the location of our gaze with coordinated eye movements, grid cells in the entorhinal cortex map the environment with activity that increases near the nodes of a triangular grid. This spatially periodic neuronal activity arises remotely, without physical visits to any locations within the environment. **b**, Because grids have similar orientations within a subject, gaze movements aligned with the grid will tend to yield greater activity by passing through more firing fields, compared to misaligned gaze movements. This principle was used to identify visual grid cells in humans[1,2].

that grid cells can map the passing of time[10], auditory space[11], imagined space[12] and conceptual cognitive space[13]. Furthermore, the underlying neuronal circuitry may have been conserved in the evolution of mammalian species, such that grid cell responses may function in fundamentally the same way across species.

Considering the decades of research on the hippocampal formation in rodents, nonhuman primates and humans, we seem to have arrived at a parsimonious explanation for results that at first glance may appear in conflict. The elegant activity patterns of spatial representation neurons such as place cells, grid cells, border cells and head-direction cells observed in the rodent hippocampal formation are known to be allocentric, and the observations that fundamentally characterize these cells and dominate their interpretation are based on the physical location of the animal. This perspective has led to theories that the EC subserves navigation, with neuronal activity generated primarily through egocentric self-motion signals in a process termed 'path integration'. The discovery of visual grid cells in the primate EC[1–3] highlights the importance of considering the range of behaviors an organism uses to sample its environment to understand the structure of this neuronal activity. All species explore and sample their environments in ways that are driven by their unique physiologies and may not involve smooth movement through space. When we explore our environment with eye movements, for example, we make several saccades every second, rapidly moving from one location to another. This method of sampling the environment may support visual path integration, which may help drive the firing patterns of visual grid cells, with the aid of allocentric spatial view cells[15] and cells that represent the direction of eye movements[14].

Path integration may help explain how grid cell patterns arise; however, visual exploration experiments have provided additional insights into how grid cell patterns may be involved in memory. Visual grid cells can conjunctively encode memory signals and are robust to changing environment content[3]. Julian et al.[1] have shown that visual grids adapt to changing environment bounds, and both Julian et al.[1] and Nau et al.[2] identified grid patterns across dynamic visual content. These observations suggest that grid cells in the EC provide a flexible and consistent framework for memory processes. This framework may assist in the formation and recollection of the relations among the physical and abstract content within a context that form the basis of our episodic memories. ❒

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Competing interests
The authors declare no competing financial interests.