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Spatial Cognition: Grid Cells Support Imagined Navigation

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Grid cells in the entorhinal cortex represent an animal's current location during navigation. A new study indicates that grid cells in humans also represent information about imagined movement and spatial orienting, suggesting that the entorhinal network has a flexible role in spatial representation.

The network of grid cells in the entorhinal cortex (EC) appears to play a key role in how animals navigate. The activity of each grid cell provides information about the animal's current location by spiking when the animal is present within a set of positions that form a regularly spaced grid across an environment. A new study by Horner *et al.* [1] reported recently in *Current Biology* provides striking evidence that grid cells also support other types of spatial processing, most notably imagined movement and orientation. These results imply that entorhinal grid cells support a flexible neuronal code for space that can be dynamically targeted according to thoughts and mental simulations.

Grid Cells in Humans

Grid cells were first discovered in rodents by recording neuronal activity as animals ran through laboratory arenas [2]. The

discovery of grid cells was an important advance in understanding how the brain supports navigation, not only because these cells reliably signal the animal's current location but also because the regular spacing of each cell's activity across the environment was evidence of a metric code for space that could theoretically support various types of spatial cognition [3].

For obvious ethical reasons it is challenging to record directly from individual grid cells in humans. In fact, the first evidence for grid cells in humans came from a cleverly designed functional magnetic resonance imaging (fMRI) study by some of the authors of the current paper [4]. Grid cells have several attributes that allow them to be observed with fMRI in spite of this method's lack of resolution at the single-neuron level. First, each grid cell represents space via a triangular grid that has six-way (60°)

rotational symmetry. Second, each grid cell fires at a higher mean firing rate when the animal travels in a direction that is aligned to its grid versus a misaligned direction. Third, multiple neighboring grid cells in one individual generally represent grids with the same orientation. As a result of these attributes, Doeller *et al.* [4] expected the activity of grid cells to be visible in fMRI as sites that exhibited increased fMRI activity when a person moved in any of six directions that were spaced at 60° intervals (six-way rotational symmetry).

Doeller *et al.* [4] tested this approach by having subjects perform a virtual-reality navigation task during fMRI scanning. Consistent with predictions, the fMRI response from the EC was modulated to a person's current heading in a manner that exhibited six-way rotational symmetry. The presence of six-way symmetric fMRI heading

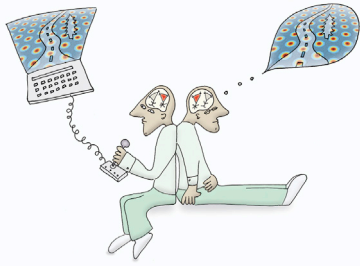


Figure 1. Entorhinal grid cells have a diverse role in spatial cognition.

This illustration demonstrates that an entorhinal grid cell might have a single grid representation that supports spatial navigation in a virtual video game environment (left) as well as imagined navigation of that same environment (right). (Courtesy of M. Jacobs and B. Jacobs.)

responses in the EC is strong evidence for human grid cells, because they are the only known cell type, in any animal, that would generate this pattern. Subsequent research supported this approach by demonstrating direct electrophysiological evidence for grid-like single-neuron activity in neurosurgical patients [5]. The Doeller *et al.* [4] study was important because, in addition to the merit of its scientific findings, it demonstrated a general technique for studying the grid-cell system noninvasively. This technique is the foundation of the new findings by Horner *et al.* [1].

Role in Spatial Cognition Without Movement?

It is without question that, as humans, we engage in imagination and mental travel, not only through paths we have traveled before but also those we have never actually physically experienced. To what extent might entorhinal grid cells mediate such processes in humans? Horner *et al.* [1] have made substantial progress answering this question by taking advantage of the fact that humans, unlike rodents and other simpler animals, can simply be instructed to imagine moving through space. First, as in Doeller *et al.* [4], subjects undergoing fMRI scanning were trained on a virtual-reality spatial task where they first learned the locations of objects in a virtual environment. Then, in the memory phase of the experiment, they rotated to face the direction of a given object's location.

The key new feature of Horner *et al.*'s [1] work is their task's imagination phase. Here, subjects closed their eyes and imagined moving in a straight line toward the remembered location of an object. This provided controlled data on the neural basis of imagined movement across a particular path. Data from this period were then compared with the subsequent movement phase, where patients drove along the same path that they had previously imagined, with their eyes open so that they receive visual feedback.

The researchers examined the data to compare directional patterns in the fMRI response between real and imagined movement. First, they replicated Doeller *et al.*'s [4] earlier finding of six-way symmetric directional responses during virtual movement. Then, critically, they examined the pattern of entorhinal activations during the imagination phase. Notably, imagined movement also generated six-way symmetric directional responses, consistent with the activity of grid cells. Furthermore, these directional patterns were the same between real and imagined movement, suggesting that the same grid representations that support actual movement along a (virtual) path also activated during imagined movement along that path.

The findings from these studies are exciting because they indicate that grid cells have a broad role in representing spatial information beyond its established role in movement and path integration [6]. Nevertheless, it is important to bear in mind the inherent limitations of using virtual reality with fMRI to characterize grid cells. First, because fMRI indirectly measures the aggregate activity of neuron groups, it cannot provide insights into particular detailed properties of grid cells, such as the spacing of grid fields or spike timing [2]. Second, there is a possibility that the observed symmetric directional fMRI responses are actually driven by an entirely different, undiscovered orientation-dependent cell type rather than grid cells. Third, although virtual reality experiments have uncovered many parallels with the known electrophysiology of real-world navigation [5,7,8], there is some evidence

from rodents of neural differences between real and virtual navigation [9]. Because of these caveats, it will be important to continue to compare fMRI findings from virtual-reality experiments to electrophysiological data from real-world navigation.

Grid and Place Cells beyond Navigation

These new discoveries provide important evidence that the grid cell network, at least in humans, is not exclusively coupled to locomotion, self-motion, or sensory information, but can also be activated from internal brain processes, such as voluntary recall, imagery, and planning. This suggests that the grid cell network could have a general, unifying role in spatial cognition by allowing a single spatial 'map' to support multiple types of behaviors (Figure 1).

The findings from Horner *et al.* [1] raise key questions concerning the potential role of entorhinal cells in various types of spatial representation. To what extent do the other elements of the navigational system, such as head-direction and border cells [10–13], also support spatial cognition beyond movement? The EC is also implicated in representing non-spatial information such as object identity [14,15] — does imagination also reinstate these representations? Finally, how does the brain distinguish real from imagined spatial representations? Addressing these questions will be essential to understanding the functional role of grid cells and will open new doors for research on how this network supports high-level cognition.

To fully understand the functional role of entorhinal grid cells, it is necessary also to examine the role of hippocampal place cells, which is the hub of spatial inputs from EC [16]. Although place cells are best understood as representing where an animal is currently located, new research has demonstrated that place cells also transiently represent remote locations to support route planning [17,18]. In humans, there is evidence from episodic memory tasks that the place cells that represent the location where an event occurred also activate during memory retrieval [19]. More recently, hippocampal theta

oscillations resulting from synchronized activity of ensembles of neurons have been shown to be involved in mentally updating one's spatial location in the absence of sensory information [20]. Including the findings from Horner *et al.* [1], this rapidly growing and exciting body of work suggests that the entorhinal cortex and hippocampus operate in a flexible way to allow a single set of spatial representations to support various types of behaviors.

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Anthropology: The Long Lives of Fairy Tales

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Anthropologists, borrowing techniques from evolutionary biology, have demonstrated that some common fairy tales can be traced back 5,000 years, or more, long before the development of written traditions.

“Near a great forest there lived a poor woodcutter and his wife, and his two children; the boy’s name was Hänsel and the girl’s Gretel. They had very little to bite or to sup, and once, when there was great dearth in the land, the man could not even gain the

daily bread....” Hänsel and Gretel, Grimm’s Fairy Tales

When we read our children the story of Hänsel and Gretel, the names give away that it is a story of German origin. Or is it? Although *Hänsel and Gretel* is recorded in Grimm’s Fairy Tales [1],

versions of the story exist in Baltic countries and in France. It’s been suggested that the story might have its origins in the 14th century great famine that struck Europe [2], or even earlier as a rite-of-passage tale in proto-Indo-European society [3]. The prospect of oral traditions dating back

