Human entorhinal cortex represents visual space using a boundary-anchored grid

Joshua B. Julian*, Alexandra T. Keinath, Giulia Frazzetta and Russell A. Epstein

When participants performed a visual search task, functional MRI responses in entorhinal cortex exhibited a sixfold periodic modulation by gaze-movement direction. The orientation of this modulation was determined by the shape and orientation of the bounded search space. These results indicate that human entorhinal cortex represents visual space using a boundary-anchored grid, analogous to that used by rodents to represent navigable space.

During spatial navigation in rodents, grid cells fire when the body of the animal occupies a hexagonal lattice of spatial locations tiling the floor of the environment. These cells are believed to support a metric for navigational space that is anchored to environmental boundaries. Recent work with monkeys has expanded the variety of spaces that might be represented by grid cells, by demonstrating the existence of neurons in entorhinal cortex (EC) that fire in a hexagonal lattice of positions on a screen while animals explore visual space. However, it is currently unknown whether a similar grid-like coding of visual space exists in humans or whether putative grid representations of visual space obey the same boundary-anchoring principles as grid representations of navigational space.

To address these issues, we used functional MRI (fMRI) methods previously developed for identifying grid signals in humans during virtual navigation. These methods are motivated by the observation that firing patterns for grid cells within an individual tend to have the same orientation. Because of this common orientation, movements along a shared grid axis will yield a stronger grid-driven fMRI signal in EC than movements between grid axes, resulting in 60° periodic modulation by movement direction. We reasoned that if grid cells represent visual space in humans, then we should observe a similar 60° periodic fMRI signal as a function of gaze-movement direction while participants visually explore the environment. To test this idea, participants (n = 36) were scanned with fMRI and had their gaze tracked while they performed an unconstrained visual search task in which they had to find a target letter (L) among numerous distractors (Ts; Fig. 1a). A square border surrounded the search display for half the participants (n = 18) and a rectangular border surrounded the display for the other half (n = 18).

For each participant, we split the fMRI data into halves, identified the orientation of the 60° periodic signal as a function of gaze-movement direction within EC in one half of the data and tested the reliability of this visual grid orientation in the independent second half (Supplementary Fig. 1). Consistent with our prediction, we observed significant reliable sixfold modulation of the fMRI signal as a function of gaze-movement direction, bilaterally in EC (Fig. 1b).

This result reflects greater fMRI response when gaze-movement directions were aligned with the three grid axes than when they were misaligned (Fig. 1c and Supplementary Fig. 2). Conducting the same analyses for other rotational symmetries, we found no evidence of reliable 90° or 45° periodic signals across independent halves of the data in EC (Fig. 1d). Notably, across participants, the magnitude of the 60° periodic EC signal significantly correlated with self-reported navigational ability, suggesting that the same population of grid cells might support both vision and navigation (Spearman rank correlation, ρ = 0.28, P = 0.049; Supplementary Fig. 2). All gaze-movement directions were sampled during the visual search task, and we detected no sixfold bias in gaze behavior that could explain the presence of a sixfold symmetric fMRI signal (Supplementary Fig. 3). Thus, these results are evidence of a grid representation in human EC that codes for locations in visual space, complementing previous findings of grid representations in navigable space. Grid-like coding of visual space was also observed in a medial prefrontal region of interest previously reported to exhibit a grid-like response during navigation (Supplementary Fig. 4).

We next explored the coordinate system that EC uses to encode visual space. For grid cells to provide useful information about environmental locations, grid cell firing patterns must be stably anchored to features of the external world, such as environmental boundaries. In previous work examining grid cells tiling visual space in monkey EC, the head of the animal was fixed relative to the visual display, making it difficult to determine whether these cells coded locations in egocentric (head-centered) or allocentric (world-centered) coordinates. To address this issue, we tested whether EC grid representations of visual space exhibit two signatures of boundary-anchored coding that were previously observed in rodent grid cells.

First, we asked whether grid orientations are reliably aligned by search display shape. When rodents explore square environments, the grid lattice aligns to ±7.5° from the cardinal axes defined by the borders (Fig. 2a). We looked for a similar effect in the participants who searched square displays (Fig. 2b). Across these participants, the average EC visual grid orientations were significantly clustered around ±7.5° offsets from the square display border (Fig. 2c).

Moreover, of the 14 participants who showed significant clustering of grid angles across voxels in bilateral EC (of 18 total participants), 12 had voxel-wise grid angles that were significantly clustered around offsets of 6°–9° from the display borders (Fig. 2d and Supplementary Fig. 5). By contrast, visual grid orientations for the rectangular-display participants were not clustered around ±7.5° from the rectangular borders across participants (Fig. 2e). Indeed, grid orientations were closer to 7.5° offset from the display borders in the square-display participants than in the rectangular-display participants (one-tailed t test, t41 = 2.26, P = 0.015). Because the shape of the display was the only stable environmental feature that differed between these participants, these results confirm that visual grid orientations were affected by the geometry of the visual environment.

Second, we examined whether rotation of the search display would induce a corresponding rotation of the visual grid. To address this question, each participant who performed the search task with the upright rectangular search displays also completed...
Fig. 1 | Visual grid-like representation in human EC. a, Left: example square visual search display (for display purposes, example display has fewer letters than actual displays and relative letter size is increased). Right: schematic of the scene visible during scanning. b, Reliable grid-like coding of visual space was observed in bilateral EC (t test, P < 0.05, small-volume family-wise error (FWE)-corrected (SVC) in bilateral EC; peak Montreal Neurological Institute (MNI) coordinates: 40, –4, –38; peak Z = 3.09). LH, left hemisphere; RH, right hemisphere. c, fMRI response in a 2-mm sphere centered on the peak EC voxel from b for periods of gaze-movement aligned to grid orientation φ (within ±15° of a φ axis) and misaligned (more than ±15° from all φ axes; aligned: t test, t_{55} = 1.95, P = 0.030, sign-test P = 0.033; misaligned: t test, t_{55} = -2.60, P = 0.014, sign-test P = 0.029; all tests two-tailed). d, Split-half orientation consistency (beta weight) in the spherical EC voxel region of interest (ROI) from c for 90° and 45° periodicities (magnitude of 60° plotted for scale). Neither 90° nor 45° showed significant orientation consistency (90°: t test, t_{55} = -1.15, P = 0.87, sign-test P = 0.56; 45°: t test, t_{55} = -1.02, P = 0.84, sign-test P = 0.93). Note that these null effects were not specific to the EC ROI based on the 60° periodicity analysis, as we saw no effect for 90° or 45° in the entire EC at P < 0.05 (SVC). Throughout the figure, all statistical tests are one-tailed unless otherwise noted, and n = 36 participants; error bars show ±1 s.e.m.; *P < 0.05; ***P < 0.001; ns, not significant.

Fig. 2 | Visual grid orientation is anchored to the search display geometry. a, The grid orientations of rodents navigating through square environments are offset 7.5° from the environment walls. (The example cell shown is adapted with permission from ref. 3, Nature Publishing Group.) b, We tested whether the visual grid orientation φ was similarly offset 7.5° from the square display borders. Specifically, because the possible range of φ is between 0° and 60°, we examined whether grid orientations cluster around four possible angles, each 7.5° from one of the two cardinal axes of the display. c, Grid orientations of the square display participants. Left: average grid angle in each participant (blue squares), on the range of 0°–60°. Middle: histogram of average grid orientations across participants, modulo 15°, showing clustering around 7.5° (n = 18; V test, V = 5.18, P = 0.042). Right: average percentage of grid orientations, modulo 15° ± 1 s.e.m., across all bilateral EC voxels. The average grid angle and standard error reported above the middle histogram were computed in circular space. d, Polar histograms of all EC voxel grid orientations for two example square-display participants. Note clustering of grid orientations around ±7.5° from the display border (left participant: n = 285 voxels, V-test, V = 80.42, P = 3 × 10^{-11}; right participant: n = 289, V = 205.54, P = 5 × 10^{-13}; Bonferroni corrected for multiple grid angles tested). e, Grid orientations of the rectangular-display participants (red rectangles), organized as in c. Across rectangular-display participants, grid orientations were not clustered around 7.5° (n = 18; V test, V = -2.48, P = 0.796).
two additional scan runs in which the displays were rotated 30° clockwise (Fig. 3a). If the visual grid code is anchored to the borders of the search display, then rotation of the search display should yield a corresponding 30° rotation of the visual grid orientation, as observed in navigating rodents when chamber boundaries are rotated. We found that the fMRI signal in EC during rotated runs was predicted by a grid angle that was rotated 30° relative to the upright-display-fit grid orientation better than by a grid angle that was not rotated (Fig. 3b and Supplementary Fig. 6). Furthermore, the average grid orientation during rotated runs was offset 28.33° ± 2.87° (mean angle ± s.e.m.) relative to the grid orientation during upright runs (Fig. 3c). Notably, six participants showed little grid angle rotation (Fig. 3d). Unexpectedly, these nonrotating participants were faster at finding the target letter during the rotated-display runs than the participants whose grid orientations rotated (Fig. 3e). Thus, although visual grids were anchored to the borders of the search display on average, there were individual differences in which external reference frame was selected, and these differences had consequences for search behavior.

In sum, we report the first evidence (to our knowledge) that human EC represents locations in visual space using a grid code. This visual grid code exhibited two signatures of boundary-anchoring previously observed in rodent grid cells—alignment to boundaries based on the shape of the environment and rotation when the environmental borders are rotated—indicating that similar computational principles anchor primate and rodent grid cells to the external world, even across different spatial domains. These results may illuminate a longstanding controversy over the representation of visual space. Previous evidence suggests that the mammalian visual system represents space in retinotopic coordinates, which are updated before each eye movement based on information about the intended direction of the upcoming saccade. Although nonretinotopic spatial codes are observed under some circumstances, it is often unclear whether these codes are egocentric (head-centered) or allocentric (world-centered), and evidence for an allocentric map that represents where a viewer is looking relative to stable visual environmental cues has remained sparse (although see refs. 14, 15). The current results provide evidence for such a map and suggest a mechanism by which it might be generated. During navigation, grid cells are thought to perform path integration by using self-motion inputs to update allocentric representations of location. We hypothesize that visual grid cells may use a similar path-integration mechanism to update an allocentric representation of the current gaze position based on eye-motion signals present in the hippocampus and EC. Beyond navigation, recent work has also shown that a grid-like code is used to represent both imagined and conceptual spaces. Our data add to this growing body of work by showing that grid cells may provide the mechanism by which locations in visual space are coded, thus allowing us to form durable visuospatial representations that are stable across eye movements.

**Methods**

Methods, including statements of data availability and any associated accession codes and references, are available at [https://doi.org/10.1038/s41593-017-0049-1](https://doi.org/10.1038/s41593-017-0049-1).

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Author contributions

J.B.J., A.T.K. and R.A.E. designed the study. Data collection was performed by J.B.J., A.T.K. and G.F.; J.B.J. and A.T.K. analyzed data. The manuscript was drafted by J.B.J., A.T.K. and R.A.E.

Competing interests

The authors declare no competing financial interests.

Additional information

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Methods

Participants. Thirty-six participants (14 male) took part in this experiment (mean age: 23; range: 18–32). All participants gave written consent and were paid for participating, in compliance with procedures approved by the University of Pennsylvania Institutional Review Board. All had normal vision and reported that they were in good health with no history of neurological disease. Data from seven additional participants were collected but discarded before analysis of fMRI data due to poor eye tracking quality (six because of inaccurate gaze reconstructions; one because of poor sampling of all gaze angles). From data of one additional participant was discarded due to excessive head motion during scanning (>3 mm average absolute head motion). Following scanning, each participant completed the Santa Barbara Sense of Direction (SBSOD) questionnaire, which provides a standardized measure of self-reported navigational ability.

Visual search task. Participants completed a series of 6.5-min fMRI scan runs, during which they performed a visual search task. Square-display participants completed four runs and rectangular display participants completed six runs. Participants were randomly assigned to display shape groups. During each run, participants viewed visual search displays consisting of a single target letter ‘L’ shown amongst distractor ‘T’ letters (letter height = 0.74°). Participants were instructed to use their eyes to search for the target letter and to press a button as a binary response when they found the target letter. Each trial was self-paced and lasted an average of 0.58 s (mean ± s.e.m.). Stimuli were presented using Matlab (2016a, The MathWorks Inc., Massachusetts) and the Psychtoolbox2 (Version 3.0.11). A pseudorandom search display was generated on each trial, such that all letters had a random location on the borders of each display shape, subject to the constraint that only partial overlap between the letters was permitted and a random orientation. Note that this meant that the shape implied by the array of letters was the same as the shape defined by the drawn border. Each search display had one of three possible densities ([100, 144, 169] or [81, 100, 121] letters total in the square and rectangle conditions, respectively). The search display density was randomly selected on each trial, with the constraint that each of the three possible densities was presented once before repeating. Search displays subtended a visual angle of 17.0° × 17.0° (square participants) or 11.0° × 17.0° (rectangular participants), and the search display border line thickness was 0.21°. There was a variable intertrial interval of 2–6 s, randomly selected on each trial, during which participants fixated on a centrally located fixation cross. The onset of each trial was time-locked to the onset of an fMRI acquisition.

For the rectangular-display participants, four scan runs consisted of upright rectangular displays and two runs consisted of rectangular displays rotated by 30° clockwise. For these participants, the presentation order of the displays was URUURU, where U and R correspond to upright and rotated displays, respectively. This ordering ensured that any effect of display rotation could not be due to general drift across runs.

Eye tracking methods and preprocessing. Participant’s gaze position during scanning was monitored and recorded using a LiveTrack AV MR-compatible eye tracking camera (Cambridge Research Systems, Rochester England). The gaze position of the right eye was recorded at 30 Hz. Prior to each scan run, gaze position was calibrated using a series of nine fixation points evenly spaced between –8° and +8° in the horizontal and vertical dimensions relative to screen center. The average calibration error across all runs was 0.332° ± 0.018° (mean ± s.e.m.). The estimated angles of gaze movements from periods of fixations within each run were calculated as a movement-velocity-thresholding procedure, as follows. To reduce misattribution of gaze movements to eye tracking noise, the gaze position time course was first temporally smoothed with a boxcar filter (half width = 0.185 s). Gaze movements were then identified based on a median split of the smoothed gaze movement instantaneous velocity. Gaze position measurements in the horizontal and vertical velocity were treated as no movement, as were samples during which participants blinked. Gaze movements with velocities in the upper median half tended to be long saccades relative to the size of the search displays, with an average ballistic gaze trajectory length of 1.60° ± 0.60° (mean ± s.d.). Note that this velocity-thresholding procedure is conservative, in that it excludes short saccades, gaze movements, during which we would not expect to observe a strong grid-like fMRI signal, based on previous fMRI studies of human navigation. Based on this method of classifying gaze movements, 7.1° ± 0.57° (mean ± s.e.m.) of all fMRI acquisitions contained no gaze movements whatsoever for the entire duration of the acquisition, which served as the implicit baseline relative to which fMRI signal change was measured.

fMRI acquisition. Scanning was performed at the Center for Functional Imaging at the University of Pennsylvania using a 3T Siemens Prisma scanner equipped with a 64-channel head coil. High-resolution T1-weighted images for anatomical localization were acquired using a three-dimensional magnetization-prepared rapid-acquisition gradient-echo pulse sequence (repetition time (TR), 1,620 ms; echo time (TE), 3.09 ms; inversion time, 950 ms; voxel size, 1 × 1 × 1 mm; matrix size, 192 × 256 × 160). T2*-weighted images sensitive to blood oxygenation level–dependent contrasts were acquired using a gradient-echo echoplanar pulse sequence (TR, 1,000 ms; TE, 25 ms; flip angle, 45°; voxel size, 2 × 2 × 2 mm; field of view, 192°; matrix size, 96 × 96 × 78; multiband acceleration factor of 4). Ten additional fMRI volumes, which were excluded from data analysis, were also collected at the start of each scan run to account for signal steady-state transition. Visual stimuli were displayed at the rear bore face in an InVivo SensaVue Flat Panel Screen at 1,920 × 1,080 pixel resolution (diameter = 80.0 cm, w × h = 69.7 × 39.2 cm). Participants viewed the stimuli through a mirror attached to the head coil. Behavioral responses were collected using a fiber-optic button box.

fMRI analysis: preprocessing. fMRI data analysis was carried out using FSL FEAT (FMRIB’s Software Library, version 6.00, https://fsl.fmrib.ox.ac.uk/fsl/fslwiki). The following standard data preprocessing was performed: motion correction using MCFLIRT, non-brain removal using BET, spatial smoothing using a Gaussian kernel of FWHM = 8 mm, grand-mean intensity normalization of the 4D dataset by a single multiplicative factor for each scan run, and high-pass temporal filtering (Gaussian-weighted least-squares linear regression fitting, with sigma = 50.00 s). For second-level group analyses, EPI images were registered to the high-resolution anatomical image using boundary-based reconstruction and then normalized into standard space (MNI 305) using nonlinear registration. All data normalization was performed using Freesurfer (version 5.3.0, http://surfer.nmr.mgh.harvard.edu/).

fMRI analysis: identifying grid-like coding of visual space. We performed a split-half analysis to estimate the orientation of the visual grid code during periods of gaze movement, following procedures used previously to identify grid-like codes during virtual navigation. To test whether grid orientations across participants

fMRI analysis: identifying grid-like orientation in the visual search displays. To test whether grid orientations across participants

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centered around 7.5°. The V-test is similar to Rayleigh's test for circular uniformity, with the difference that under the alternative hypothesis the distribution is nonuniform, centered at a particular hypothesized angle (in this case, 7.5°).

To test whether grid orientations in voxels within individual participants clustered around 7.5° offset from cardinal axes, we first evaluated whether EC voxels in each participant showed orientation clustering around any angle. To do so, we averaged the grid angle derived from each voxel across runs, yielding a distribution of voxel-wise grid orientations. Next we tested these voxel-wise grid orientations for nonuniformity using Rayleigh's test for circular data. Note that because grid orientations were averaged voxel-wise across fMRI runs for this analysis, significant orientation clustering also required temporal stability across runs of the grid orientation across voxels. This analysis identified participants who had significant nonuniformity, i.e. orientation clustering, of grid angles in EC (P < 0.05, accounting for spatial smoothing). Finally, we tested whether the voxel-wise grid orientations in participants with significant clustering were specifically clustered around 6.0°–9.0° in 0.5° increments (via folding and V-tests, as described above; P values were Bonferroni corrected for the seven grid angles tested).

fMRI analysis: rotation of the grid-like representation orientation with rotation of the search display. To test whether the visual grid orientations of rectangular-display participants rotated in concert with the rotated displays, we first computed the circular average of the grid orientation derived from each upright-display run. Next we rotated this average grid orientation, \( \phi \), by 30° and used this rotated orientation to predict the fMRI signal during rotated-display runs with a GLM. Specifically, a single PM to was used to model the effect of gaze-movement direction on the fMRI signal during the rotated-rectangle runs: a cosine of gaze-movement angle aligned to the 30° rotated grid orientation, \( \cos(6(\theta + 30° - \phi)) \). Positive weights from this analysis indicated that the 60° periodic fMRI signal was better predicted when the orientation of the grid axes was rotated 30° from \( \phi \) during rotated-display runs, whereas negative weights indicated that rotated-display runs were better predicted by the original grid orientation \( \phi \) without rotation. The weights for this PM were first combined across both rotated-display runs in each participant and then tested across participants with small-volume FWE-correction within the group-level bilateral EC ROI.

To examine the distribution of rotation effects across EC voxels, we first identified the grid orientation for each voxel during the rotated scan runs in the same fashion as we did for the upright scan runs. We then compared the distribution of grid orientations across all EC voxels when the display was upright to the distribution when the display was rotated. Specifically, for each participant, we subtracted \( \phi \) from each EC voxel's grid orientation, separately for the upright and rotated display runs, so that the average grid orientation across voxels were aligned relative to \( \phi \) in each participant. We then calculated the distribution of voxels with grid orientations occurring from 0° to 60° in 2° increments, separately for the upright and rotated scan runs, and subtracted the upright distribution from the rotated distribution. If grid orientations across voxels rotate in concert with rotation of the search display, then there should be a higher percentage of voxels with grid angles around \( \phi + 30° \) when the display is rotated than when it is upright.

Statistics. No statistical methods were used to predetermine sample sizes, but our sample size was similar to those reported in previous publications\(^{18–20}\). Parametric \( t \) tests and nonparametric sign-tests were used throughout the paper. For each parametric test, unless otherwise noted, data values met normality assumptions (Lilliefors test, \( P > 0.05 \)). If data did not meet normality assumptions, only sign-tests are reported. Rayleigh's tests and V-tests were also used, as described in detail in the two preceding fMRI analysis methods sections. Data collection and analysis were not performed blind to the conditions of the experiment.

Life Sciences Reporting Summary. Further information on experimental design is available in the Life Sciences Reporting Summary.

Code availability. The code that supports the findings of this study is available from the corresponding authors upon request.

Data availability. The data that support the findings of this study are available from the corresponding authors upon request.

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Experimental design

1. Sample size
   Describe how sample size was determined.
   We used a sample size greater than the norm for the field, plus the sample size was larger than was required to detect similar effects in recent fMRI studies using similar analysis methods (e.g., refs 18-20).
   Moreover, we demonstrate that the effect of grid-like coding of visual space replicates in two independent samples. Thus, our total sample size is more than adequate to measure an effect of this size.

2. Data exclusions
   Describe any data exclusions.
   No fMRI data were fully processed and then subsequently excluded. However, subjects were excluded before analysis of fMRI data due to poor eye tracking quality. Data were also excluded due to excessive head motion during scanning (>3 mm average absolute head motion) identified during fMRI pre-processing. Exclusion criteria, and number of subjects excluded, are described in methods.

3. Replication
   Describe whether the experimental findings were reliably reproduced.
   We replicated the effect of grid-like coding of visual space in two independent groups of participants (Supplementary Fig. 2). No other replications were attempted.

4. Randomization
   Describe how samples/organisms/participants were allocated into experimental groups.
   Participants were randomly assigned to groups (square display vs. rectangle display).

5. Blinding
   Describe whether the investigators were blinded to group allocation during data collection and/or analysis.
   Data collection and analysis were not performed blind to the conditions of the experiment.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.
6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

- The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
- A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- A statement indicating how many times each experiment was replicated
- The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
- A description of any assumptions or corrections, such as an adjustment for multiple comparisons
- The test results (e.g. P values) given as exact values whenever possible and with confidence intervals noted
- A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
- Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Describe the software used to analyze the data in this study.

Data analysis was carried out using FSL (version 6.00), FreeSurfer (version 5.3.0), and Matlab (2016a). Psychtoolbox (Version 3.0.11) was used for stimulus presentation.

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). Nature Methods guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

All materials are available from the author or standard commercial sources

No antibodies were used in the study.

No eukaryotic cell lines were used in the study.

Animals and human research participants

Provide details on animals and/or animal-derived materials used in the study.

No non-human animals were used in this study.
12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

36 participants (14 male) took part in this experiment (mean age: 23; range: 18-32). All had normal vision and reported to be in good health with no history of neurological disease.
## MRI Studies Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

### Experimental design

1. Describe the experimental design.

   - Task event-related

2. Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.

   - Participants completed a series of 6.5 min fMRI scan runs during which they performed a visual search task. Each trial was self-paced, and lasted an average of 7.50±0.58 seconds (mean±s.e.m.). There was a variable inter-trial interval of 2-6 seconds, randomly selected on each trial.

3. Describe how behavioral performance was measured.

   - Eye tracking data were collected, and constituted the main dependent measure. Participants pressed a button when they found the visual search target. Behavioral search performance was assessed in terms of response latency.

### Acquisition

4. Imaging

   a. Specify the type(s) of imaging.

   - functional

   b. Specify the field strength (in Tesla).

   - 3T

   c. Provide the essential sequence imaging parameters.

   - T2*-weighted images sensitive to blood oxygenation level-dependent contrasts were acquired using a gradient-echo echoplanar pulse sequence (TR, 1000 ms; TE, 25 ms; flip angle 45°; voxel size, 2x2x2 mm; field of view, 192; matrix size, 96x96x78; multiband acceleration factor of 4).

   d. For diffusion MRI, provide full details of imaging parameters.

   - N/A

5. State area of acquisition.

   - whole-brain

### Preprocessing

6. Describe the software used for preprocessing.

   - fMRI data analysis was carried out using FSL FEAT (version 6.00). Data preprocessing included motion correction using MCFLIRT, non-brain removal using BET, spatial smoothing using a Gaussian kernel of FWHM 8mm, grand-mean intensity normalization of the 4D dataset by a single multiplicative factor for each scan run, and highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma=50.0s).

7. Normalization

   a. If data were normalized/standardized, describe the approach(es).

   - For second-level group analyses, EPI images were registered to the high-resolution anatomical image using boundary-based reconstruction and then normalized into standard space using non-linear registration. All data normalization was performed using FreeSurfer (v5.3.0).

   b. Describe the template used for normalization/ transformation.

   - MNI305

8. Describe your procedure for artifact and structured noise removal.

   - Six nuisance regressors were included in all GLMs to account for head motion-related artifacts.
9. Define your software and/or method and criteria for volume censoring, and state the extent of such censoring. | N/A

## Statistical modeling & inference

10. Define your model type and settings.

| Mass univariate; fixed-effects within subject to combine fMRI data across scan runs; random-effects across subjects for second-level analyses. |

11. Specify the precise effect tested.

| Our main effect tested was whether entorhinal cortex (EC) exhibits grid-like coding of visual space during the visual search task. To do so, we performed a split-half analysis to estimate the orientation of the visual grid code during periods of gaze movement. Data were first split into halves by run. For each half of the data, we identified the angular orientation of the putative visual grid axes in each participant’s bilateral EC. The grid orientation thus obtained was then subsequently used to test whether there was a significant EC grid signal during the other independent half of the runs. |

12. Analysis

| Main analyses were ROI-based |

a. Specify whether analysis is whole brain or ROI-based.

| Entorhinal cortex was defined anatomically, based on automatic anatomical parcellation of the cortex using FreeSurfer |

b. If ROI-based, describe how anatomical locations were determined.

| Voxel-wise |

13. State the statistic type for inference. (See Eklund et al. 2016.)

14. Describe the type of correction and how it is obtained for multiple comparisons.

| Small-volume correction for the number of functional voxels in a group-level EC ROI. |

15. Connectivity

| N/A |

a. For functional and/or effective connectivity, report the measures of dependence used and the model details.

| N/A |

b. For graph analysis, report the dependent variable and functional connectivity measure.

16. For multivariate modeling and predictive analysis, specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.

| N/A |