Human markers of grid cell coding of non-spatial cognition

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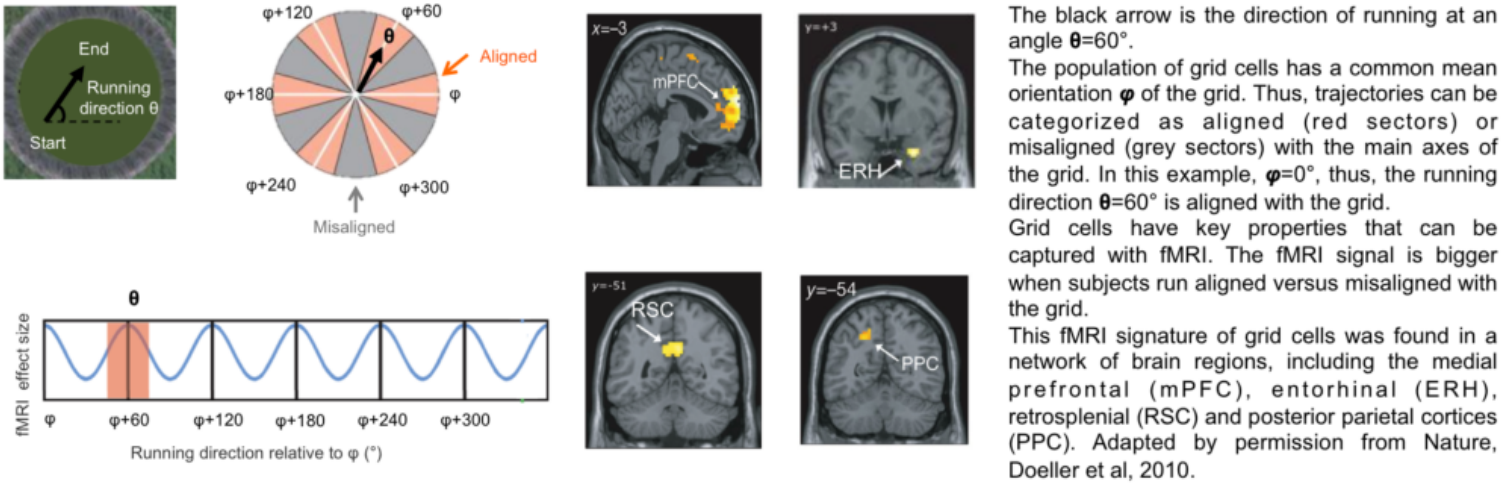
E-Poster

Introduction:

Grid cells in the entorhinal cortex use very specific computations to organize spatial knowledge into continuous maps (Hafting, et al., 2005). Non-spatial knowledge was also hypothesized to be organized in similar continuous maps (Buzsaki and Moser, 2013; O'Keefe and Nadel, 1978; Tolman, 1948), but tests of this hypothesis have proved elusive. Markers of grid cells can be measured non-invasively in humans using functional magnetic resonance imaging (fMRI), as a signal that varies with running–direction with 6-fold (hexagonal) symmetry (Doeller, et al., 2010). This has led to the critical discovery that human grid cells are not unique to the entorhinal cortex, but they are also observed in a network of brain regions commonly activated in memory and conceptual reasoning tasks (Binder, et al., 2009; Kumaran, et al., 2009; Schacter, et al., 2012). Direct intra-operative recordings of grid cells in humans validated this finding (Jacobs, et al., 2013). However, whether such non-spatial knowledge is also organized by a grid cell code remains unknown. Here, using these precise fMRI markers of grid cells, we tested whether the same periodic signal could be identified when subjects navigated through abstract semantic dimensions.

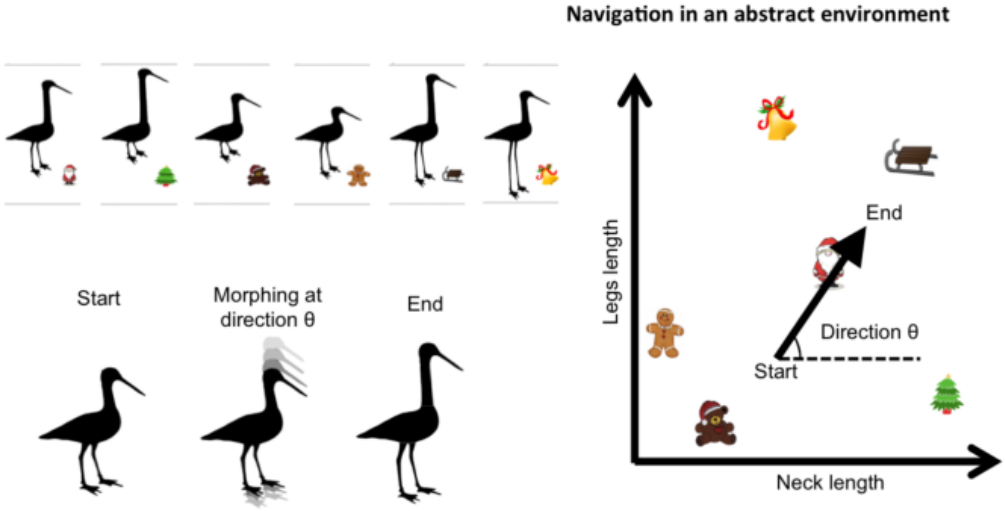
Measuring the grid cell signal with fMRI during navigation in a spatial environment



The black arrow is the direction of running at an angle **θ**=60°.
The population of grid cells has a common mean orientation ***φ*** of the grid. Thus, trajectories can be categorized as aligned (red sectors) or misaligned (grey sectors) with the main axes of the grid. In this example, ***φ***=0°, thus, the running direction **θ**=60° is aligned with the grid.
Grid cells have key properties that can be captured with fMRI. The fMRI signal is bigger when subjects run aligned versus misaligned with the grid.
This fMRI signature of grid cells was found in a network of brain regions, including the medial prefrontal (mPFC), entorhinal (ERH), retrosplenial (RSC) and posterior parietal cortices (PPC). Adapted by permission from Nature, Doeller et al, 2010.

Methods:

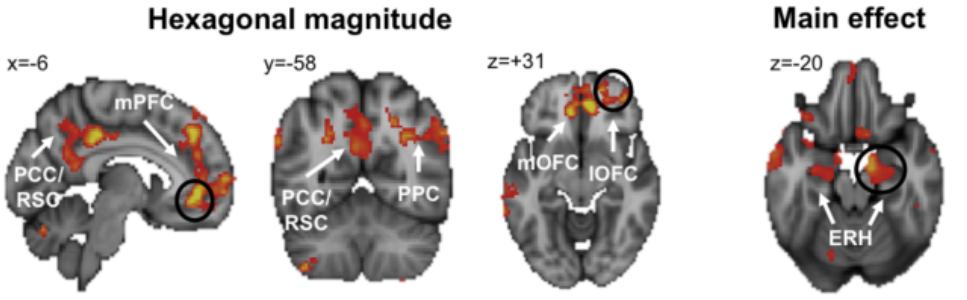
Human participants (n=35) performed a novel behavioural task developed by us, while their brains were scanned with fMRI. They repeated the experiment during 2-6 independent scanning sessions, spanned across 1-3 separate days (145 datasets).
Our task that was equivalent to the one used for real spatial navigation, with the notable difference that our environment was not spatial, but abstract. This continuous abstract environment had two dimensions, the length of the neck and the length of the legs of a bird. In each trial, participants watched a video of a bird morphing into another, which was equivalent to a trajectory in this abstract environment. Using methods for finding signatures of grid cells with fMRI, that were previously established during spatial navigation (Doeller, et al., 2010), we defined multiple trajectories with different directions in the abstract environment and we tested whether the fMRI signal was bigger for trajectories aligned with the grid compared to those misaligned with the grid.



Subjects were firstly trained to associate stimuli (birds) with rewards (Christmas symbols)
In each trial they saw a video of a bird that morphed into a different bird. They had to choose which reward they got in that trial.
Unknown to them, these bird stimuli could also be organized into a continuous abstract environment where rewards acted as landmarks. Thus, the example morphing trial has an equivalent trajectory $\boldsymbol{\theta}$ that can be shown in this abstract environment. For comparison, the trajectories in the spatial and abstract environment have the same direction $\boldsymbol{\theta}$.
A location in this abstract environment is represented by a bird stimulus. A trajectory is equivalent to morphing one bird shape into another. The direction $\boldsymbol{\theta}$ is the ratio between how much the neck and legs are changing relative to each other.

Results:

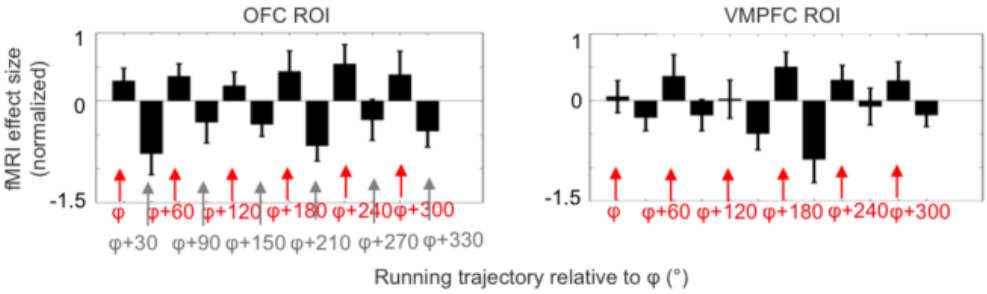
We firstly tested for a magnitude effect, that is, we looked for brain regions where there was more 60° modulation than expected by chance. We found a significant magnitude effect in the medial prefrontal extending into the orbitofrontal cortices and the posterior parietal, cingulate and retrosplenial cortices. This network was strikingly similar to the one found during spatial navigation. We also found a significant main effect of the task in the entorhinal cortex.
We then aimed to test if the grid angle φ was consistent between independent experimental sessions. We created unbiased regions of interest (ROIs) in the orbitofrontal, ventromedial prefrontal and entorhinal cortices, from the voxels that showed the highest magnitude and main effect of the task. Next, we estimated φ from these ROIs and we aligned the direction of the trajectories from one session to the grid angle φ from another independent session. We found that the grid angle was consistent in the orbitofrontal, ventromedial and entorhinal cortices, suggesting that the hexagonal symmetry effect was robust across independent experimental sessions.
Finally we found a significant hexagonal adaptation effect in the ventromedial prefrontal and entorhinal cortices, for trajectories that reactivated the same population of grid cells, close in time.



fMRI hexagonal magnitude. Significant 60° modulation ($p<0.05$, cluster corrected) in the medial prefrontal (mPFC; peak MNI coordinates 6/44/-10; peak Z-score = 4.49), posterior cingulate and retrosplenial (PCC/RSC; 8/-52/26; Z = 4.57), posterior parietal (PPC; 30/-62/28; Z = 4.88), medial and lateral orbitofrontal cortices (mOFC, lOFC; 6/44/-10; Z = 4.49).

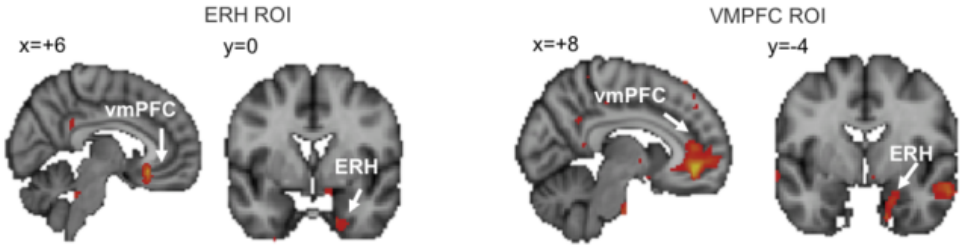
Main effect. Significant main effect of the task ($p<0.05$) showing activity in the entorhinal cortex (ERH; 12/-8/-22; Z = 3.71). Black circles mark the regions of interests where the grid angle was extracted for the grid angle consistency analysis.

Grid angle consistency between different sessions and same brain region



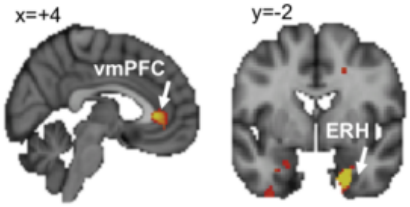
When we used the orbitofrontal cortex (OFC) ROI to estimate the grid angle from on session, we found the same grid angle in the other session, in the same brain region. Similarly, we found the grid angle to be consistent between independent sessions when we estimated the grid angle from the ventromedial prefrontal cortex (VMPFC). Note that the fMRI effect size is higher for trajectories aligned than those misaligned with the grid, illustrating the hexagonal symmetry effect.

Grid angle consistency between different sessions and different brain regions



We used the ERH ROI to estimate the grid angle from one session and we found the same grid angle in the other session ($p<0.05$) not only in the ERH (18/0/-36; Z = 2.5), but also in the vmPFC (8/24/-12; Z = 3.52). Similarly, when using the VMPFC ROI, we found significant consistency ($p<0.05$) not only in the vmPFC (10/38/-8; Z = 3.8), but also in the ERH extending in the subiculum (28/-10/-18; Z = 3.12).

Hexagonal adaptation



fMRI activity as a function of the time since the last trajectory at any multiple of 60° from the current trajectory. Significant adaptation ($p<0.05$) in the ventromedial prefrontal cortex (vmPFC; -8/38/-4; Z = 3.78) and effect of the task performance on adaptation in the entorhinal cortex (ERH; 20/-4/-36; Z = 4.63).

Conclusions:

Using multiple independent datasets and analyses, we show that non-spatial information is organized with a grid-cell code into a continuous map in the same brain network as the one found during real spatial navigation. Our study illustrates the potential power of sophisticated fMRI analyses to non-invasively investigate precise neuronal computations in behaviours that are most easily accessible in humans.

Higher Cognitive Functions:

Imagery

Space, Time and Number Coding [1]

Higher Cognitive Functions Other

Imaging Methods:

BOLD fMRI [2]

Learning and Memory:

Long-Term Memory (Episodic and Semantic)

Poster Session:

Poster Session - Monday

Keywords:

Cognition

Computational Neuroscience
FUNCTIONAL MRI
Memory
Other

[1|2]Indicates the priority used for review

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Yes

Please indicate below if your study was a "resting state" or "task-activation" study.

Task-activation

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Internal Review Board (IRB) or Animal Use and Care Committee (AUCC) Approval. Please indicate approval below. Please note: Failure to have IRB or AUCC approval, if applicable will lead to automatic rejection of abstract.

Yes, I have IRB or AUCC approval

Please indicate which methods were used in your research:

Functional MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

FSL

Provide references in author date format

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