Intro to Behavioral Neuroscience (B)
Lecture 5: Spatial Memory / Navigation

Richard Veale

Graduate School of Medicine
Kyoto University

https://youtu.be/XFHs2n612qs

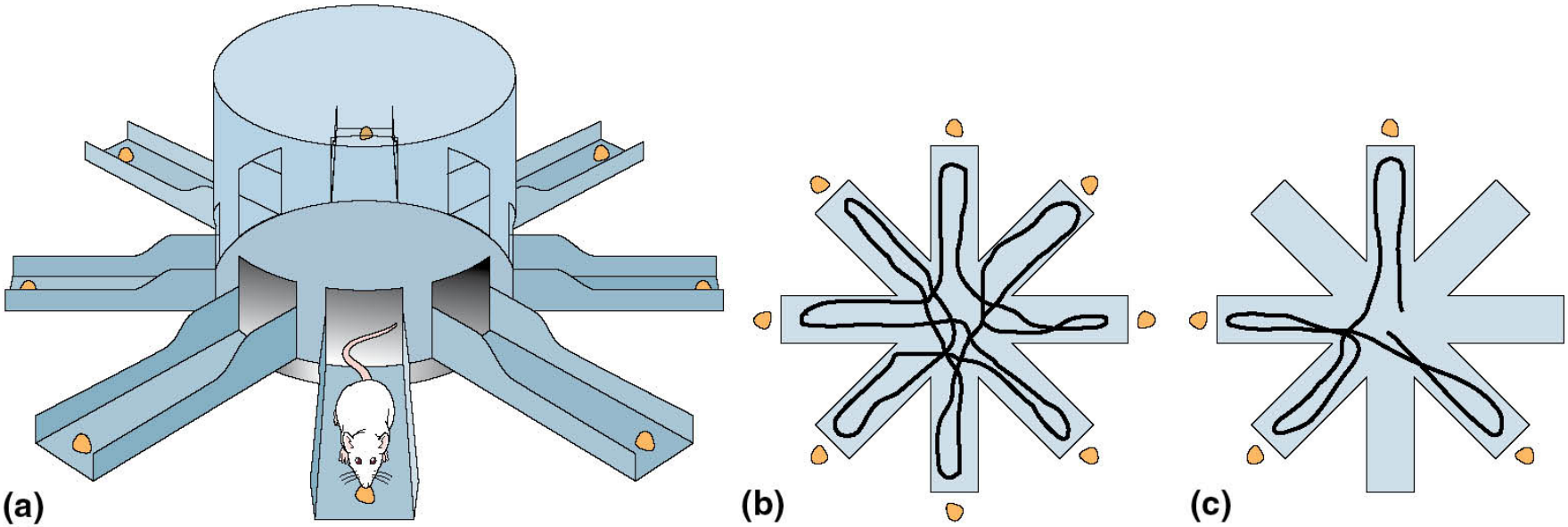
Lecture video at above link.

Today:
Spatial Memory & Navigation

Spatial Memory and Navigation

1) Place cells in the hippocampus
2) Grid cells in the entorhinal cortex
3) The function of the hippocampus
4) Procedural memory and basal ganglia
5) Curiosity, exploration and navigation

Spatial Memory: Radial Arm Maze

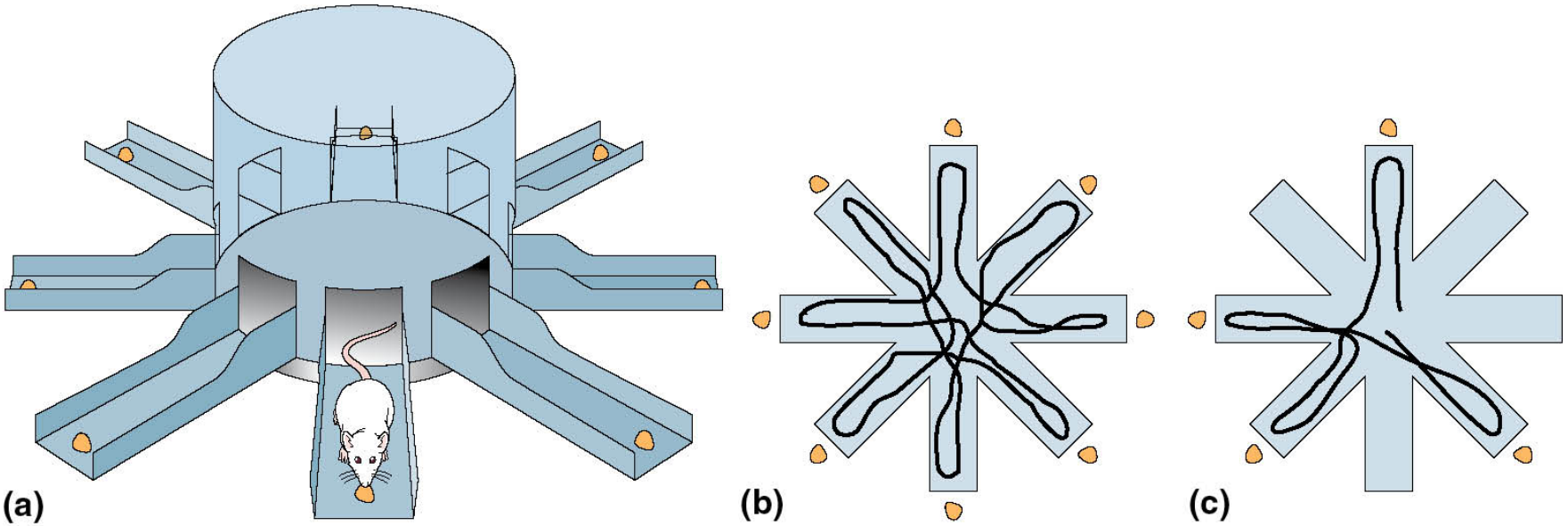


Radial arm maze:

a), b) Food is placed at each arm, and the rat learns to search efficiently, i.e., not to visit an arm twice. The rat uses visual or other cues to orient itself.

After hippocampal lesions, the rats can still learn to go down the arms for food, but they will visit arms more than once -> they cannot retain the memory where they have already been (spatial working memory).

Spatial Memory: Radial Arm Maze

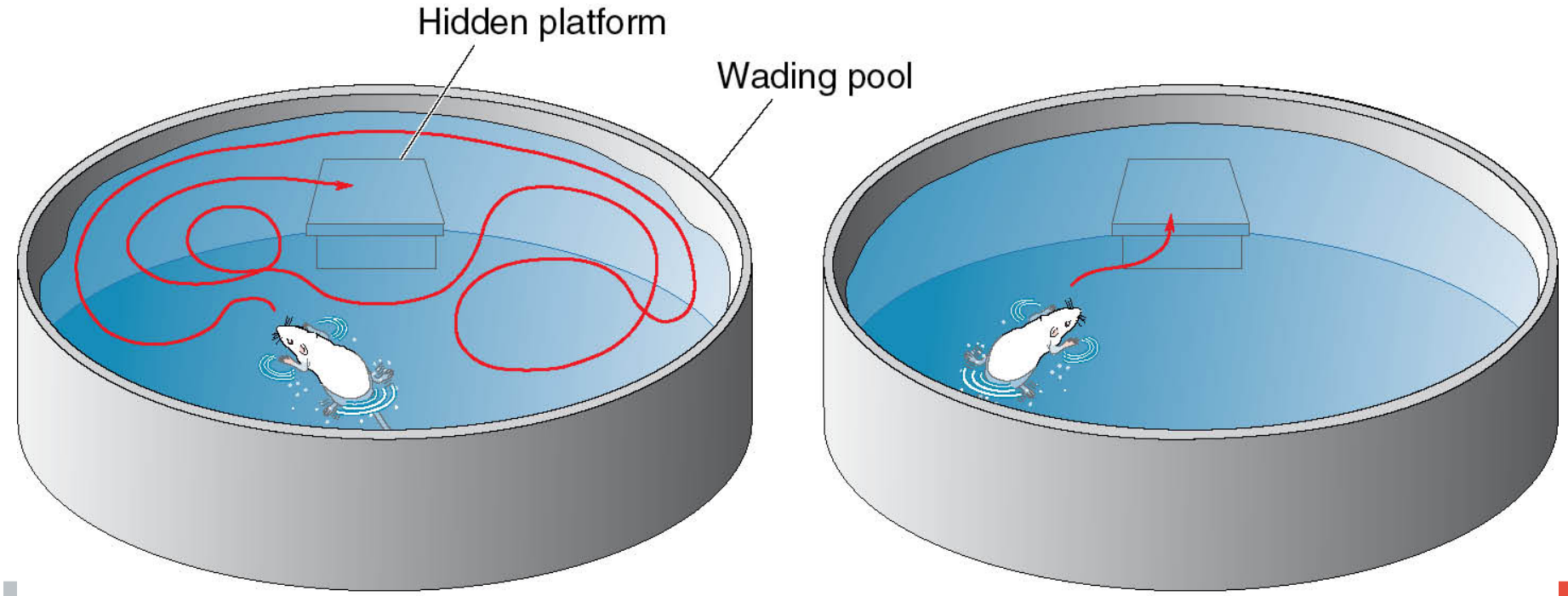


c) If food is placed in just a few arms, the rat learns not to visit the arms that never had food. This is also true for rats with hippocampal lesions, but these rats will visit the arms with food several times.
So, they learn the procedure (avoiding the no-food-arms), but have a deficit in spatial memory (revisiting already visited arms).

Spatial Memory: Morris Water Maze

Morris water maze:

If rats are placed into a water pool with a hidden platform, they try to get to the platform quickly (swimming is uncomfortable for them). Normal rats will learn the position of the platform after some trials, rats with bilateral hippocampal lesions will not.

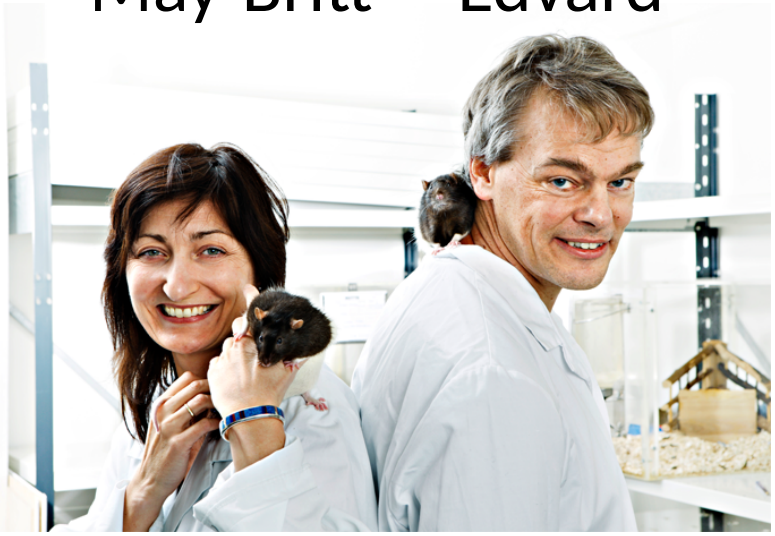


Nobel Prize 2014

Place cells

Moser

May-Britt Edvard

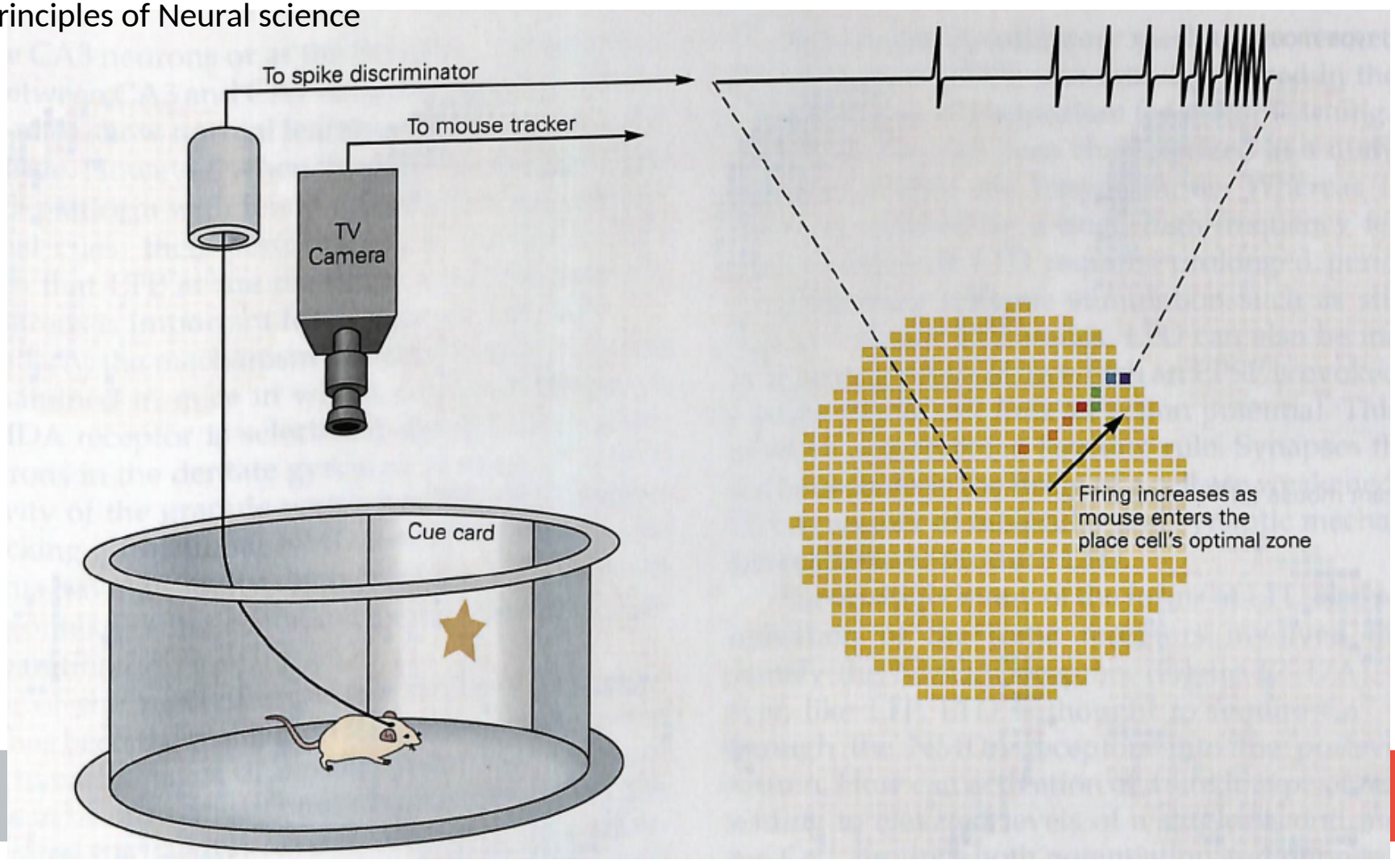


Grid cells

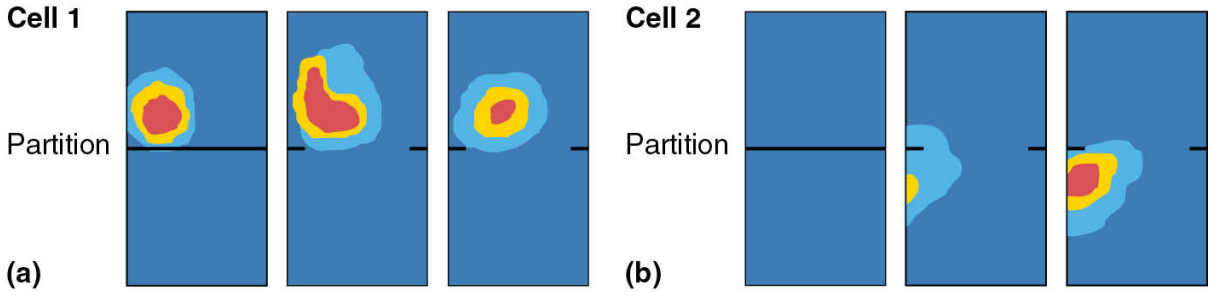
Place Cells

A rat is placed into a space with visual cues (cue card, etc.). When neural firing is recorded during exploration, place cells in hippocampus fire when the rat approaches a specific position.

Kandel, Principles of Neural science



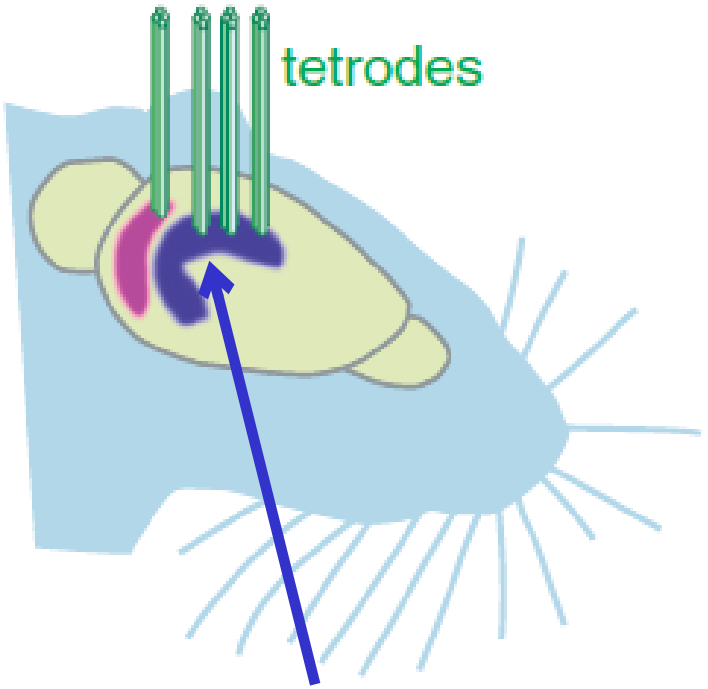
Place Cells: Hippocampus



Different place cells encode different positions in an environment.
For example, cell 1 (a, above) responds to a position in the lower left corner of a box (left panel). If a hole is opened to another box, this cells keeps its firing behavior. Cell 2 starts to respond to a position in the new environment.

Thus, place cells are dynamic, i.e., cells will adapt their response behavior to new environments.

(e.g. O'Keefe and Dostrovsky, Brain Research, 1971)



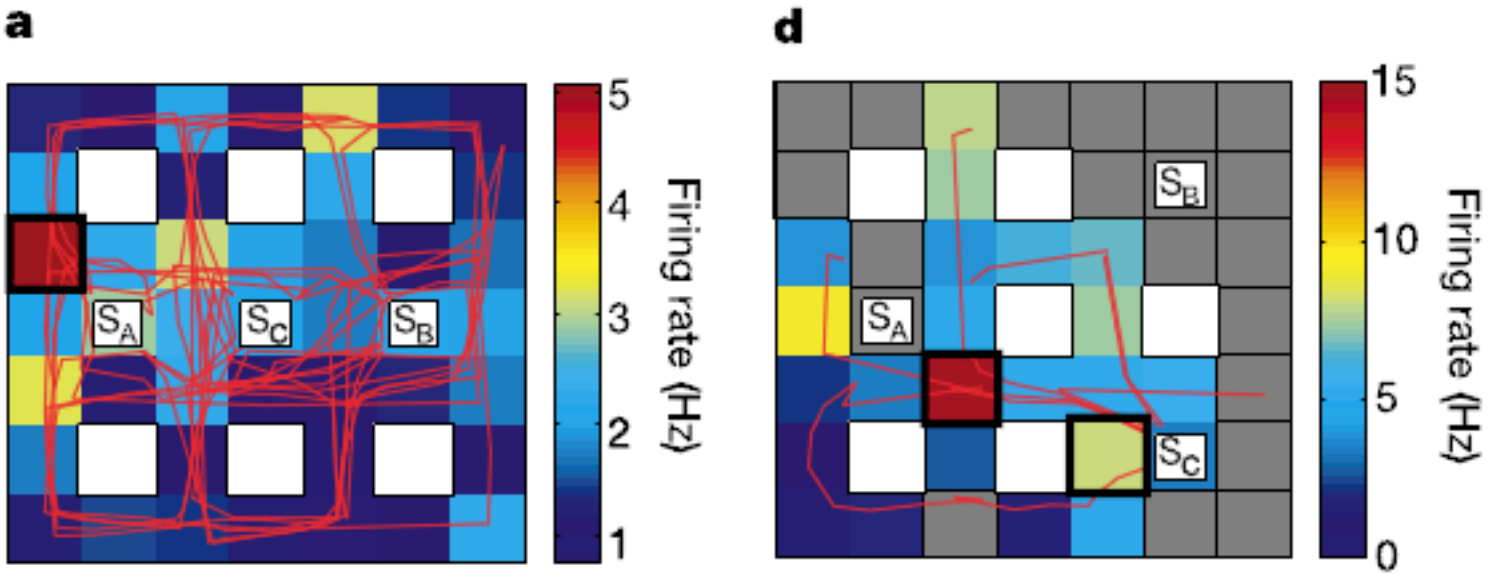
Place Cells: In Human?

7 Patients with intractable epilepsy were prepared for surgery with invasive recordings of neural activity to determine the importance of specific loci in the brain.

During this preparation, they underwent a taxi driver task: they navigated a virtual environment (a) with 9 buildings, picking up virtual customers and driving them to one of the three targets (b-e).

Ekstrom et al., Nature, 2003

Place Cells: In Human?



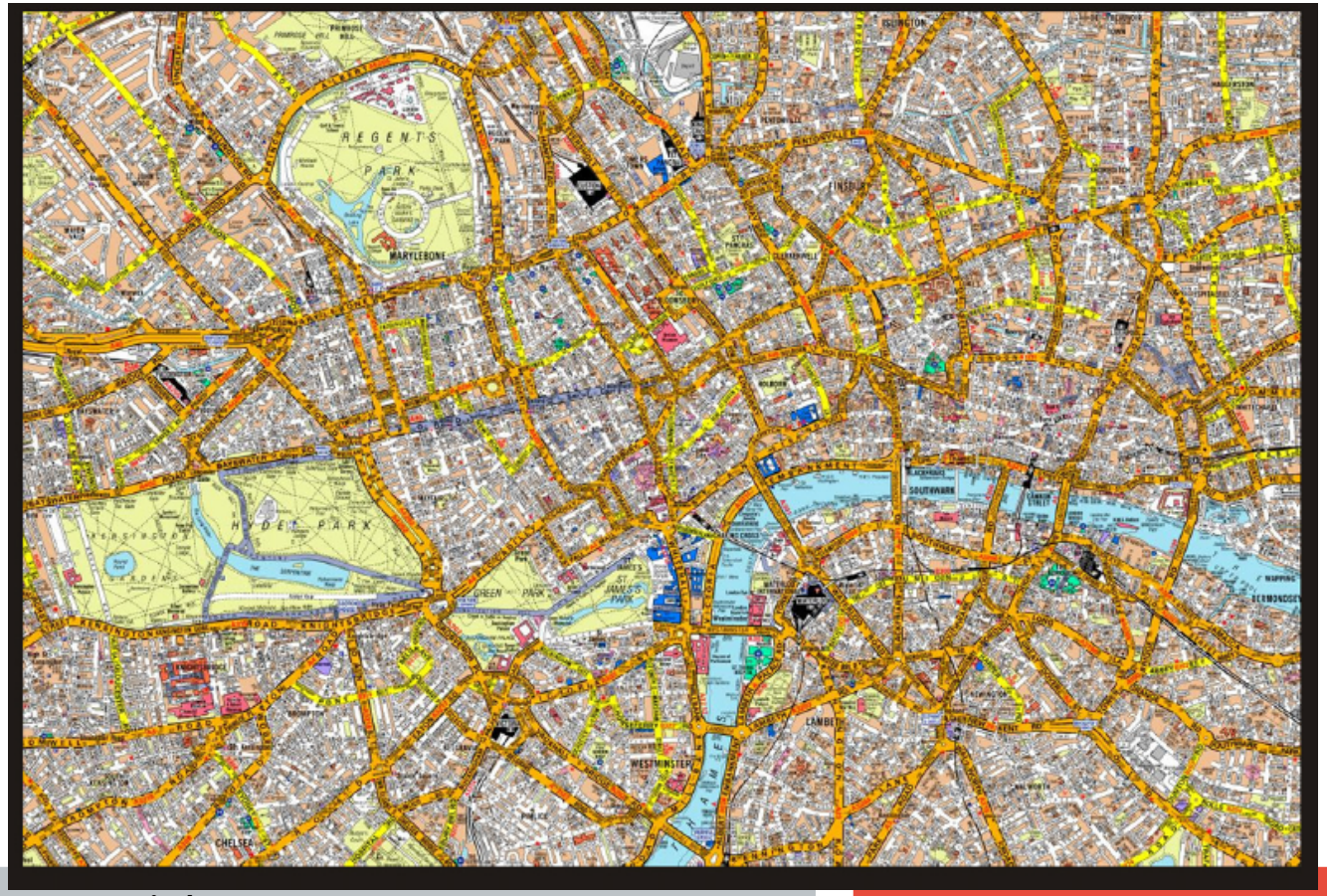
Two examples of place-cells in the hippocampus: the red square shows a position at which these cells respond strongly.

In an area near the hippocampus, the parahippocampal area, many cells responded to visual views of landmarks rather than positions.

Ekstrom et al., Nature, 2003

Human Hippocampus: London Taxis

London taxi drivers need four years to acquire the “knowledge” of ~25,000 streets in London and to pass exams.
In this study, such apprentice taxi drivers underwent structural MRI measurements and were compared to a control group and to failed trainees.

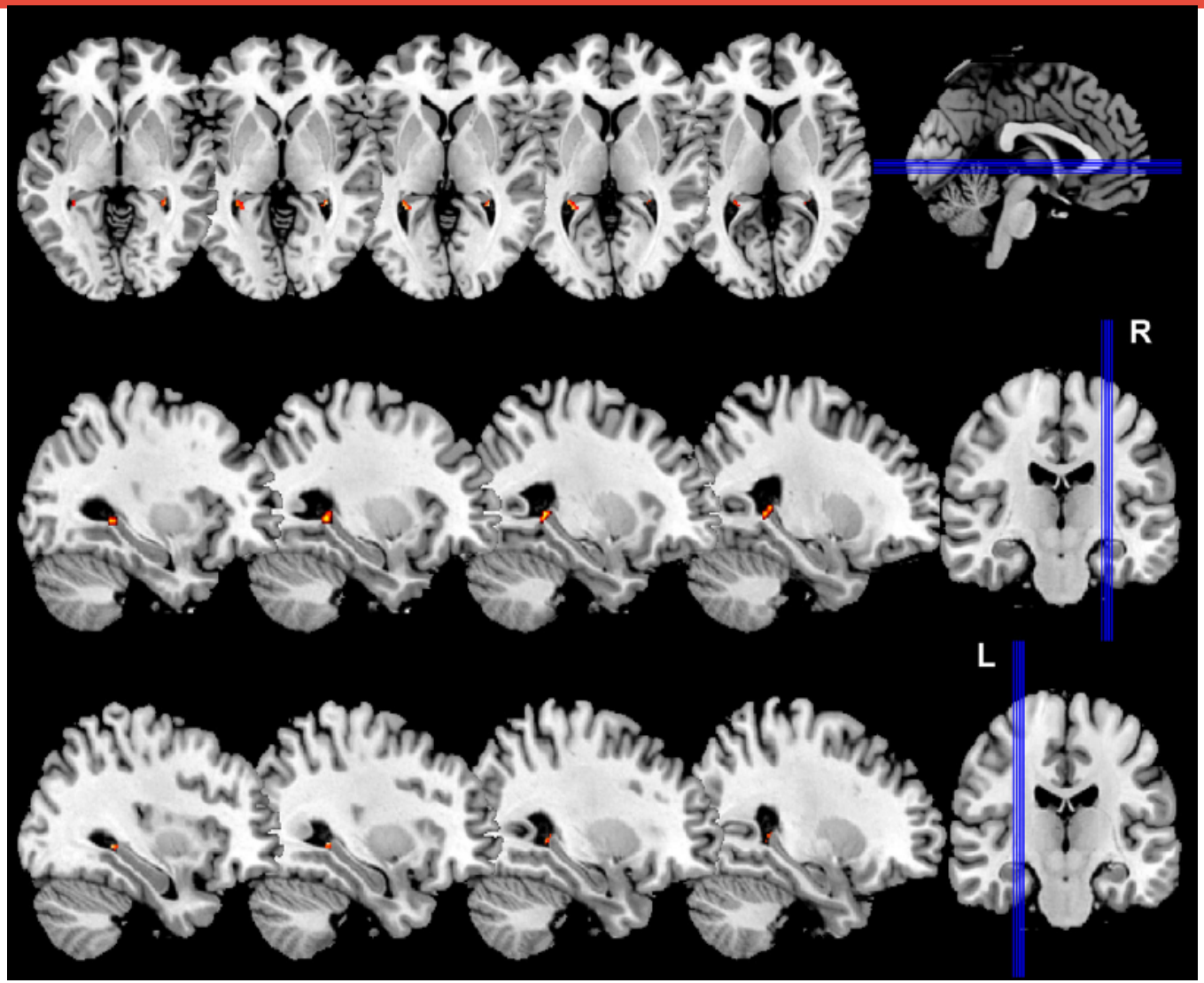


Woollett & Maguire, Current Biology, 2011

Human Hippocampus: London Taxis

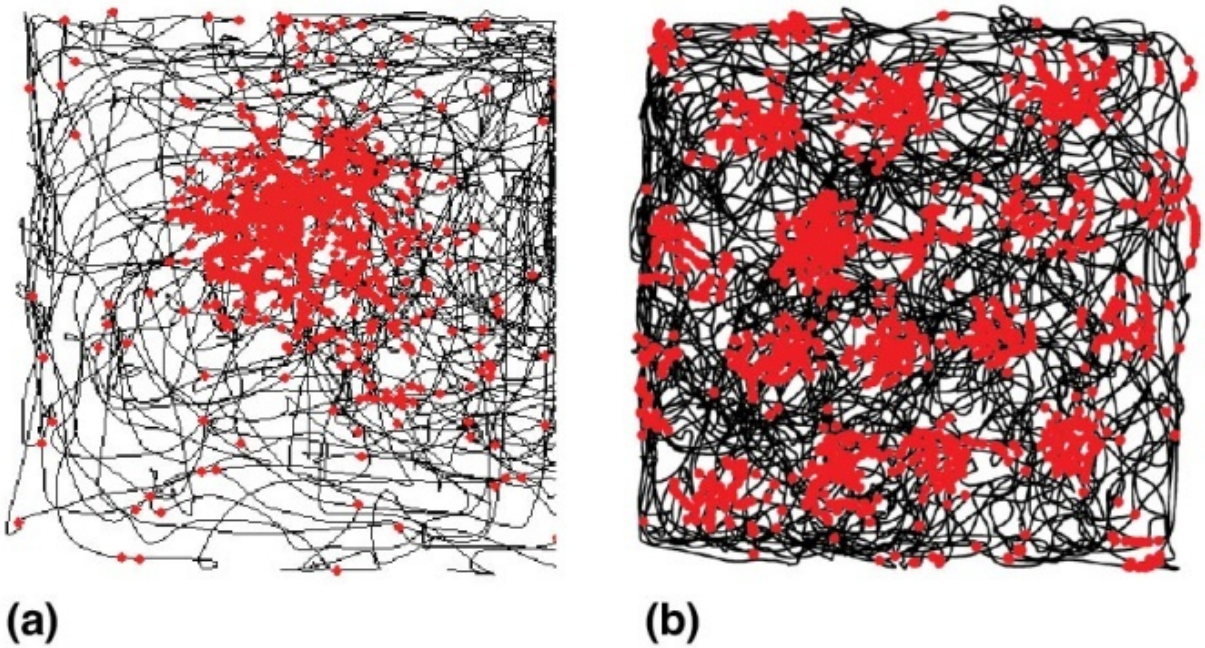
Bilateral posterior hippocampus (red and yellow) increased in size in successful taxi driver trainees.

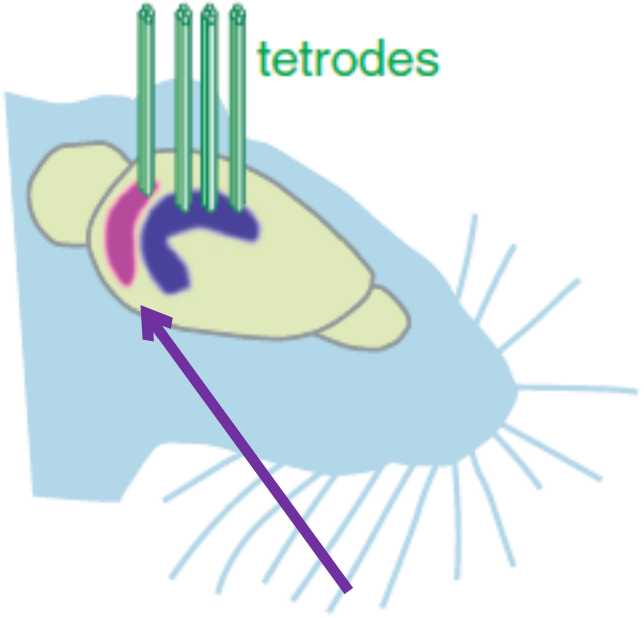
Interestingly, a long-term taxi-driver (37 years) with bilateral hippocampal lesion was still able to navigate the major streets of London, but got lost in side-streets, when fine details were needed (Maguire et al., Brain, 2006).



Woollett & Maguire, Current Biology, 2011

Grid Cells





a) Hippocampal place cell: responds to a single position and gets input from entorhinal cortex.

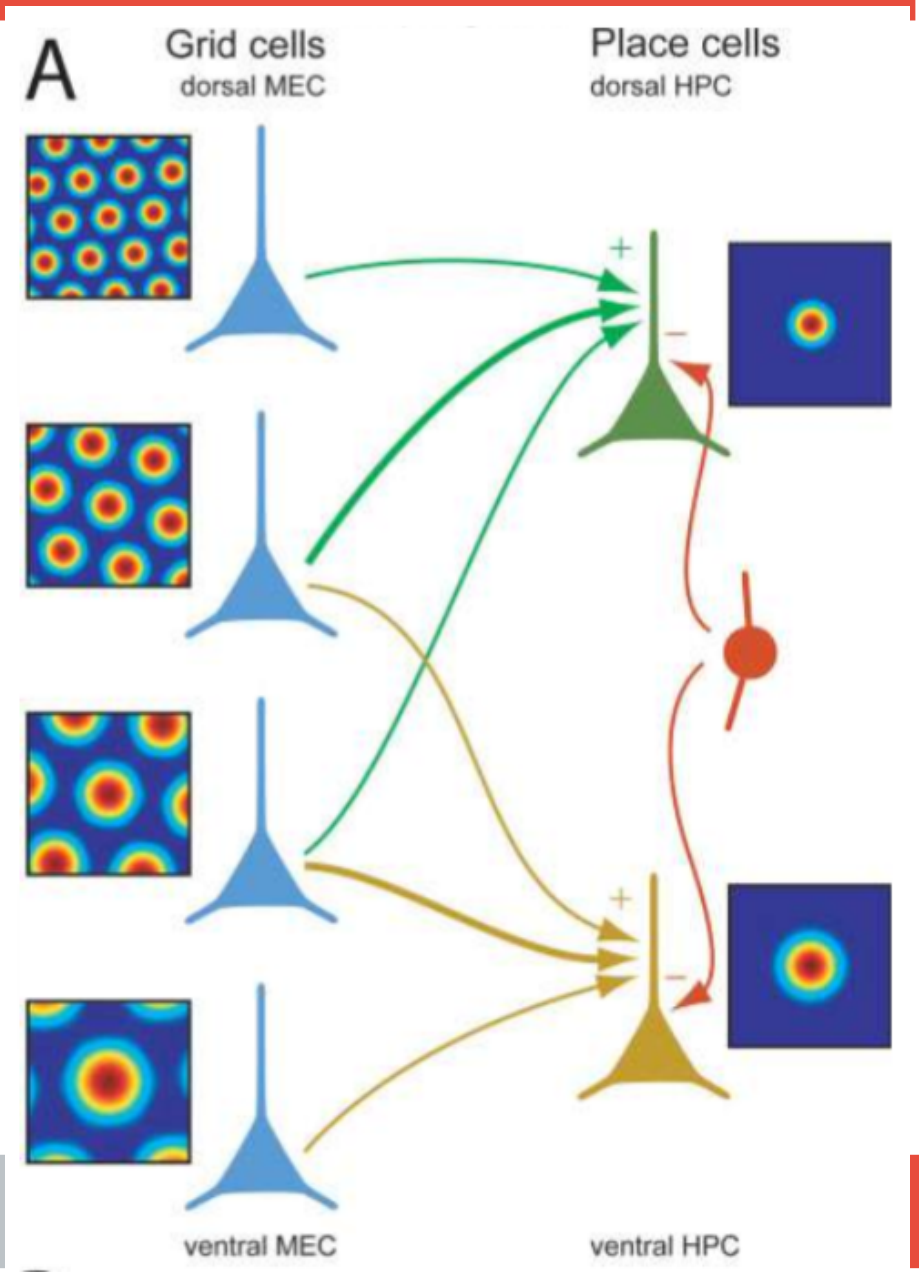
b) Entorhinal grid cell: responds to several positions in the environment with regular spacing. Different cells have different spatial frequencies , orientations, and phases.

Grid Cells → Place Cells?

Place cells in hippocampus (HPC) receive input from grid cells in medial entorhinal cortex (MEC) and integrate it. The input comes from many cells with different grid spacing (distance between grid points), orientations, and phase.

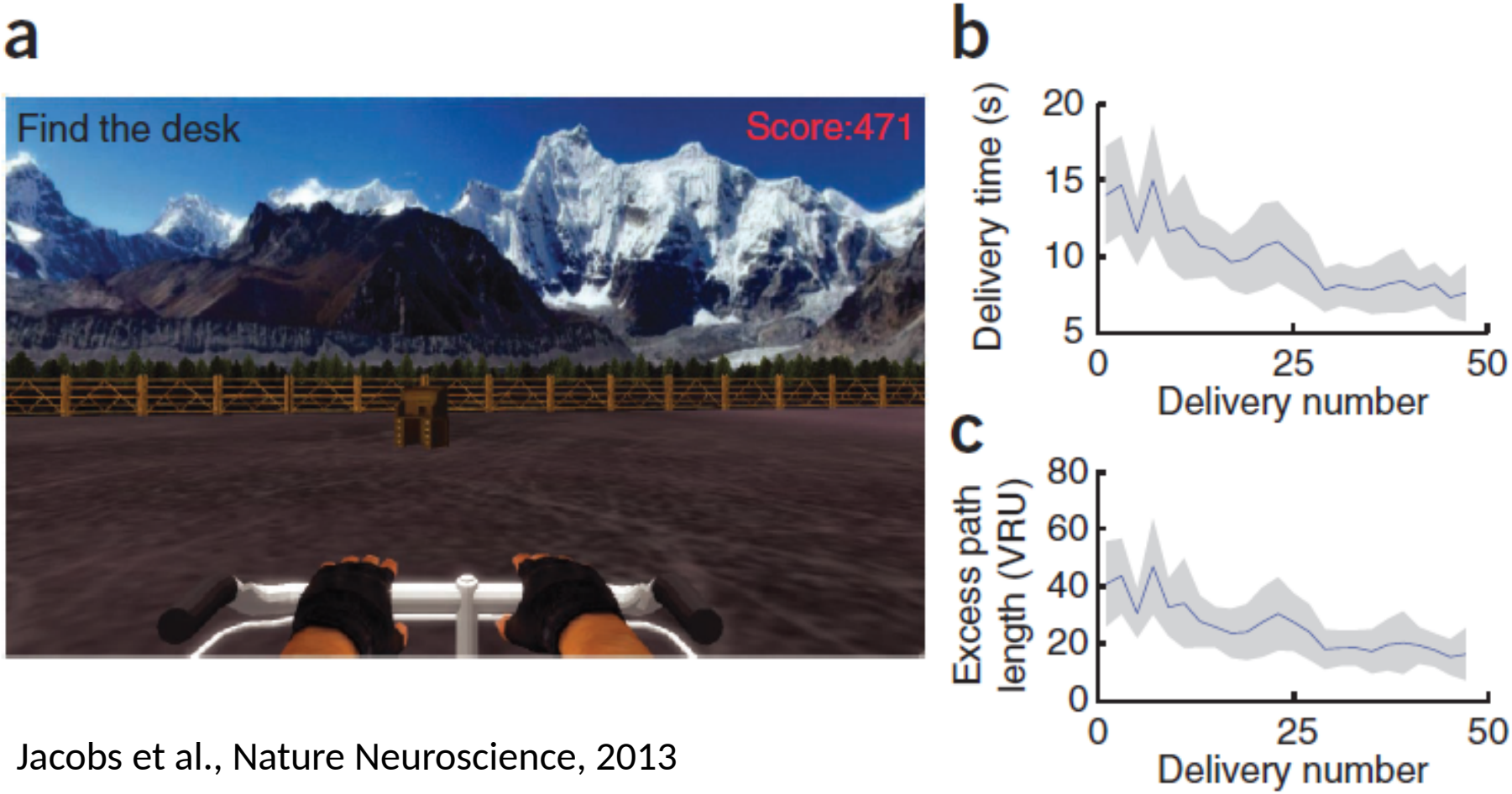
Grid and place field size increases from dorsal to ventral (right image).

Solstad et al., Hippocampus, 2006



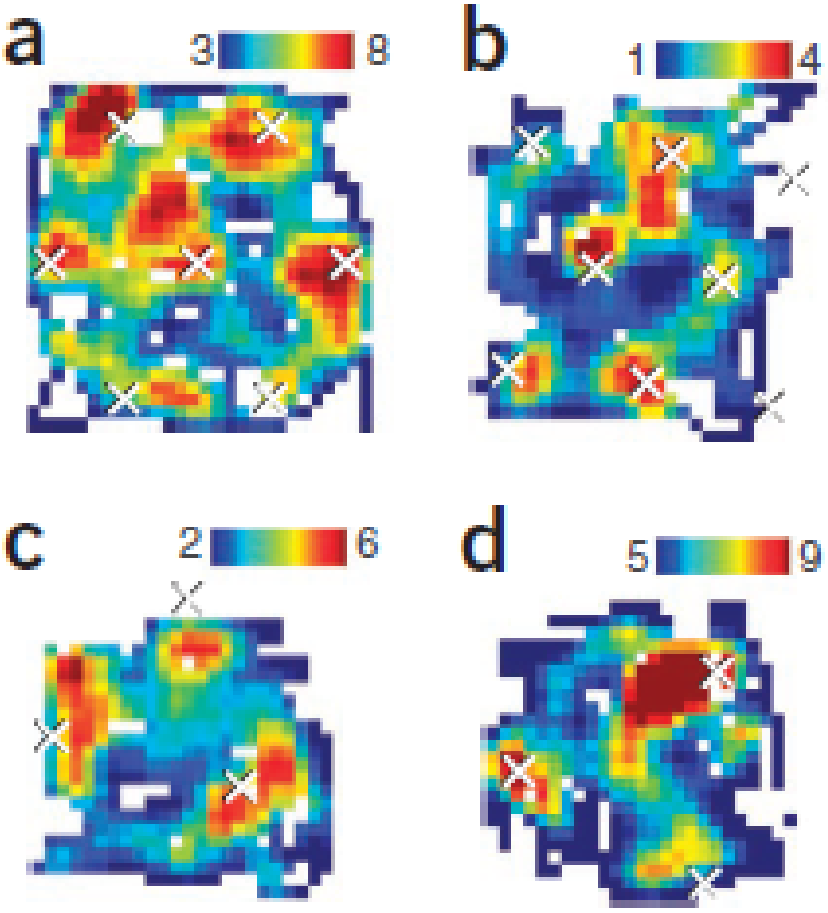
Grid Cells: In Human?

14 Patients with intractable epilepsy underwent invasive recordings during a virtual delivery task. They had to learn the positions of 4 objects (e.g., desk) in a virtual arena with visual landmarks (mountains etc.).



Jacobs et al., Nature Neuroscience, 2013

Grid Cells: In Human?



Example cells from different patients' entorhinal cortex.

In red: high firing rates at specific positions in the virtual world.
The white crosses indicate the estimated grid spacing provided by a model.

The combined input of several grid cells is assumed to provide the basis of neural coding in hippocampal place cells.

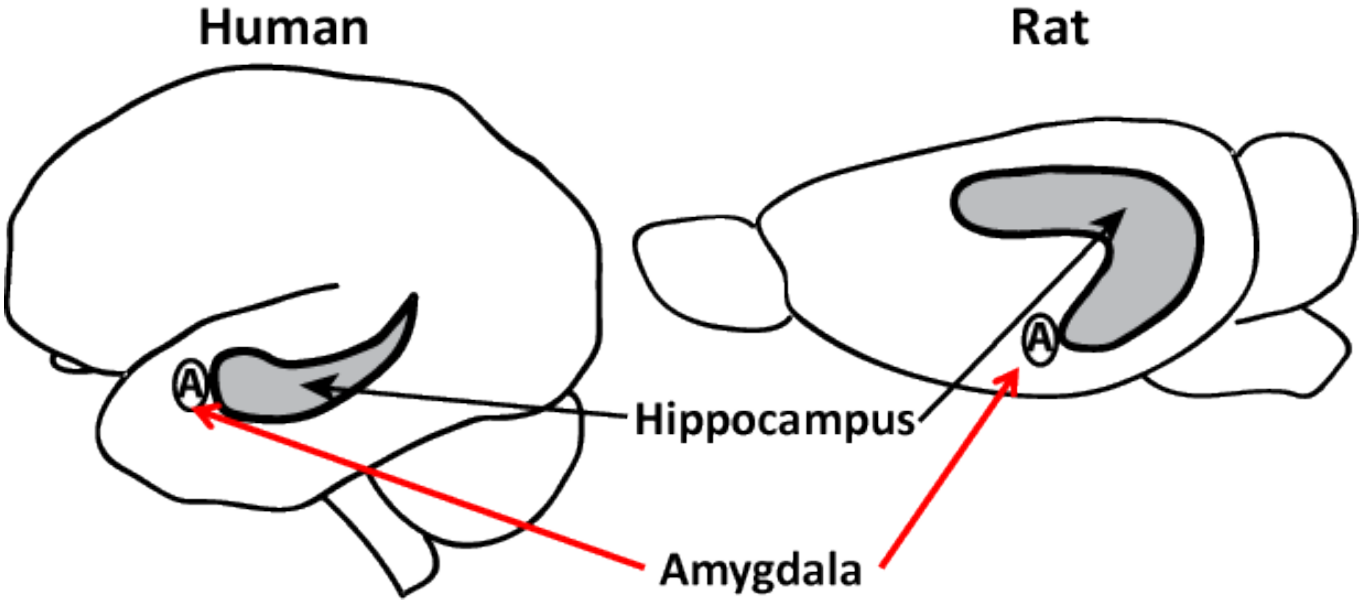
(To a lesser degree, grid cells were also found in hippocampus and cingulate cortex in this study.)

Jacobson, Nature Neuroscience, 2013

But…I thought hippocampus was for episodic memory (patient H.M.)?

It is confusing: in human studies (H.M.), hippocampus seems to be mainly important for the acquisition of declarative/episodic memories, but in rats its function is mainly spatial memory?

Possibly, the difference occurs because human and rodent hippocampus have different shapes: posterior human hippocampus corresponds to rat dorsal (upper) hippocampus. Anterior human hippocampus corresponds to rat ventral (lower) hippocampus.
Rat dorsal hippocampus has place cells with small place fields (high spatial resolution), ventral hippocampus has much larger place fields and also a role in context and fear learning.



Joe Manns' homepage, Emory University

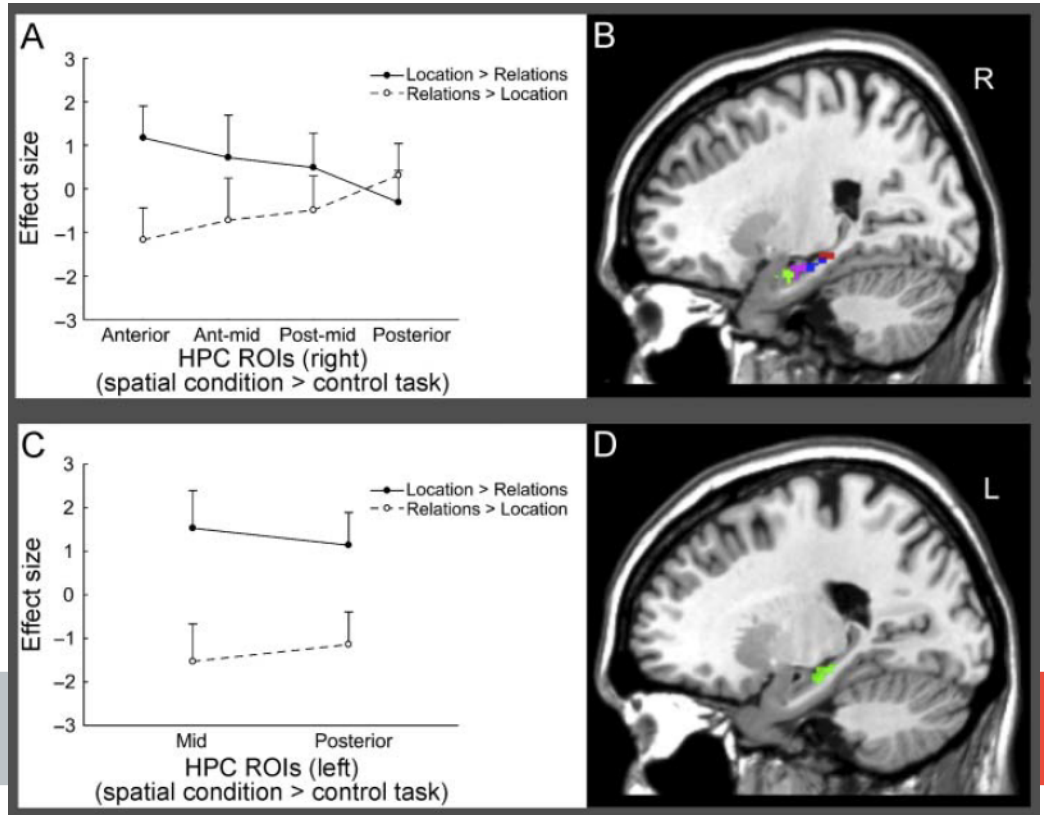
Role of hippocampus in human spatial navigation

Similarly, in humans there seems to be a gradient of a role for reactivation of spatial memory in posterior hippocampus and episodic memory in anterior hippocampus (Nadel et al., Journal of Cognitive Neuroscience, 2012).

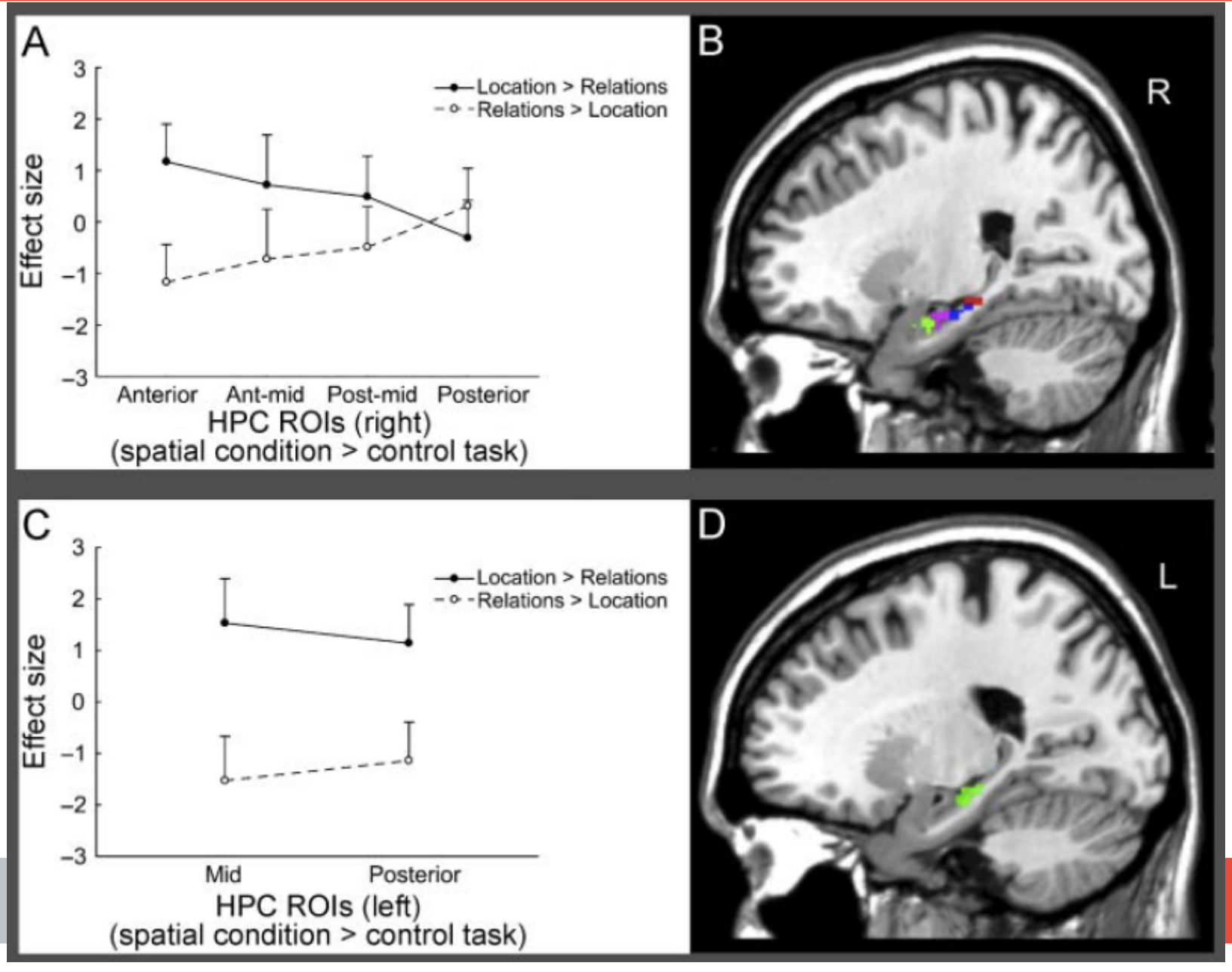
Below is material and results of a functional magnetic resonance imaging study that shows an anterior-posterior gradient in the human hippocampus with location information (context) activating anterior and spatial relationship posterior hippocampus.

Table 1. Two Spatial Conditions Used for "True or False" Recognition Task in the Scanner

Location	The location of a past experienced event.
	e.g., "Your parents' 25th wedding anniversary party was held at the Marriott Resort."
Spatial relations	The spatial relationship between the rememberer and/or a person or object present during a past experienced event.
	e.g., "When your mom spilled her wine at dinner, your dad was sitting to your left."



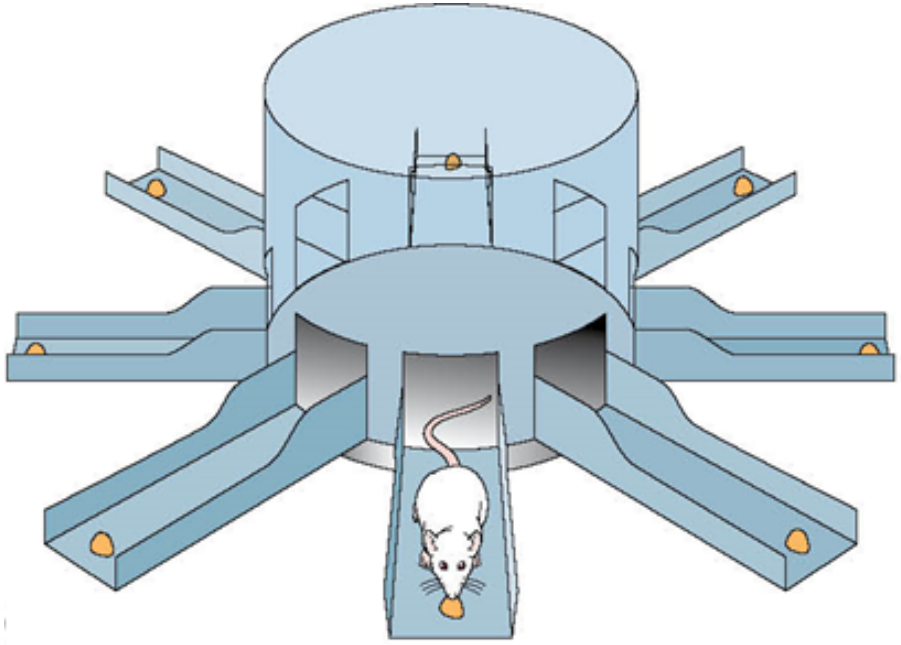
Hippocampal function in humans



Procedural Memory: Basal Ganglia

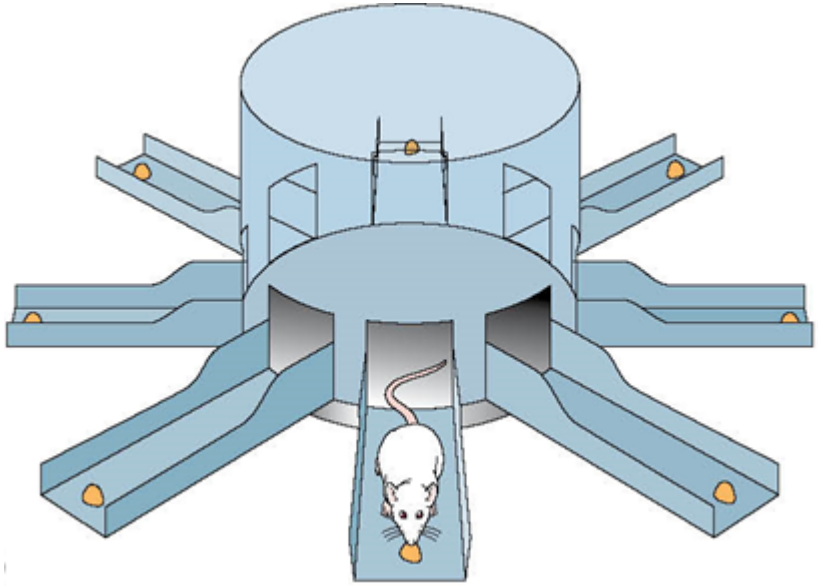
Patient H.M.'s bilateral hippocampus lesions prevented him from forming new declarative memories, but he was able to learn a procedural task.

To test what neural circuit is responsible for procedural learning, researchers adapted the radial arm maze task for rodents.



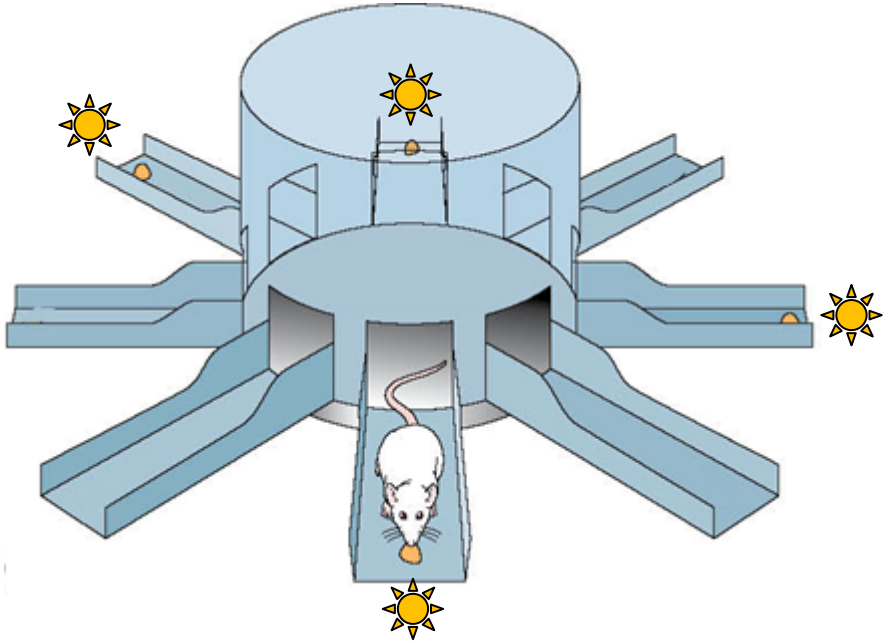
Spatial vs Procedural Task

1) Spatial task: just like the original radial arm maze task, food was put at each arm, the most efficient strategy was to visit each arm once and to remember where one already went.



Rats could not do this task when the hippocampal system was damaged.

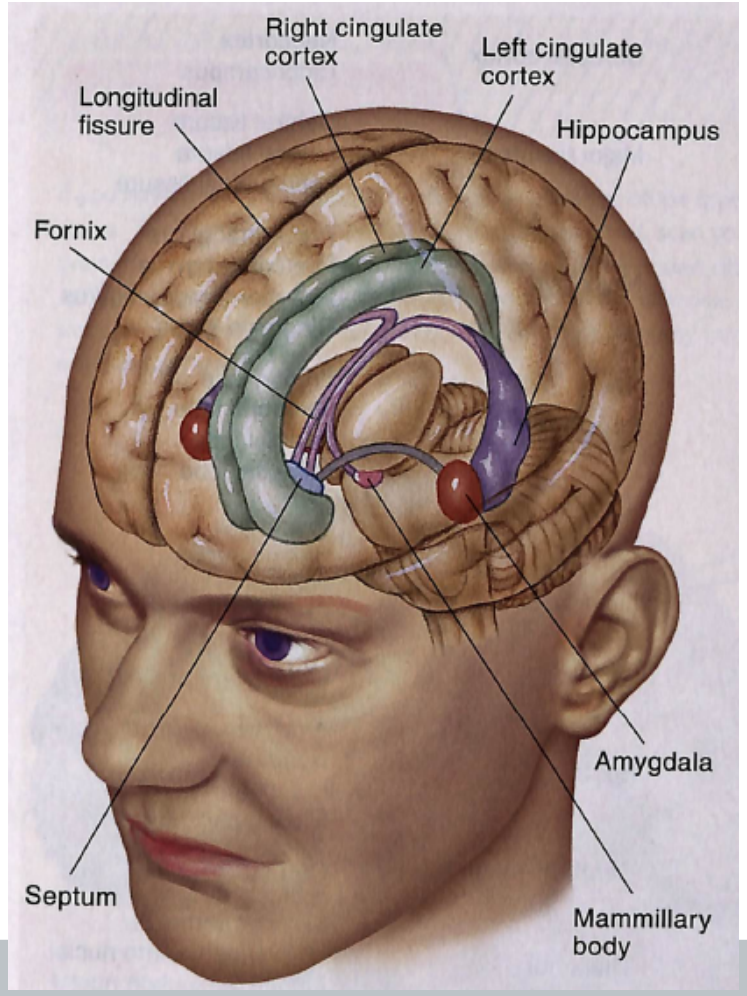
2) Procedural task: now, food was in arms with light. Rats had to learn to visit the arms with light and received food every time they went there.



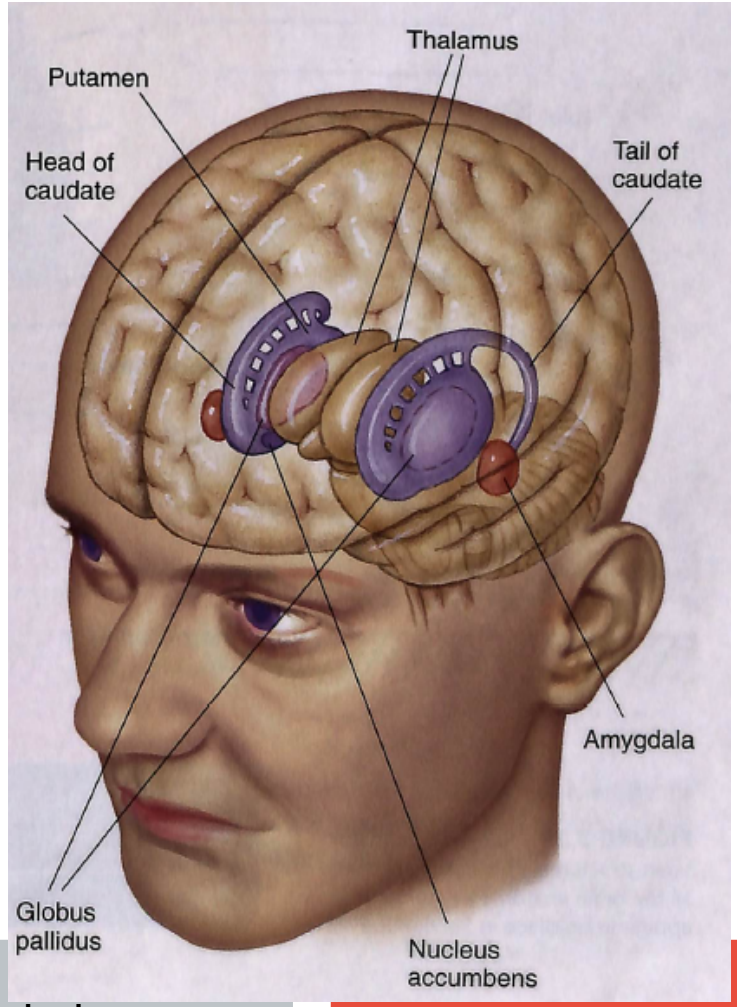
Rats could not do this task when the basal ganglia (striatum) was damaged.

Hippocampus and Basal Ganglia

Limbic system with hippocampus and fornix (output of hippocampus): spatial memory/declarative memory.



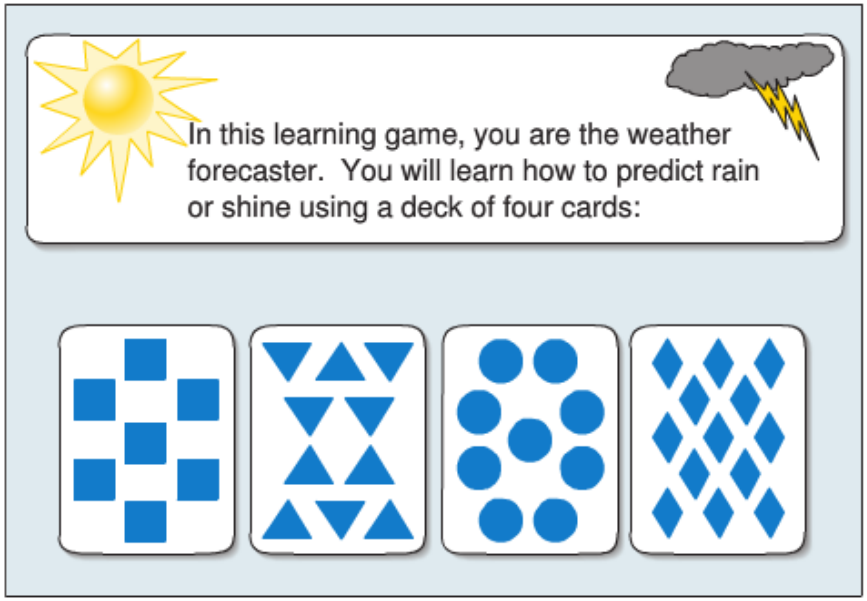
Basal ganglia with striatum (Putamen and Caudate nucleus): procedural memory.



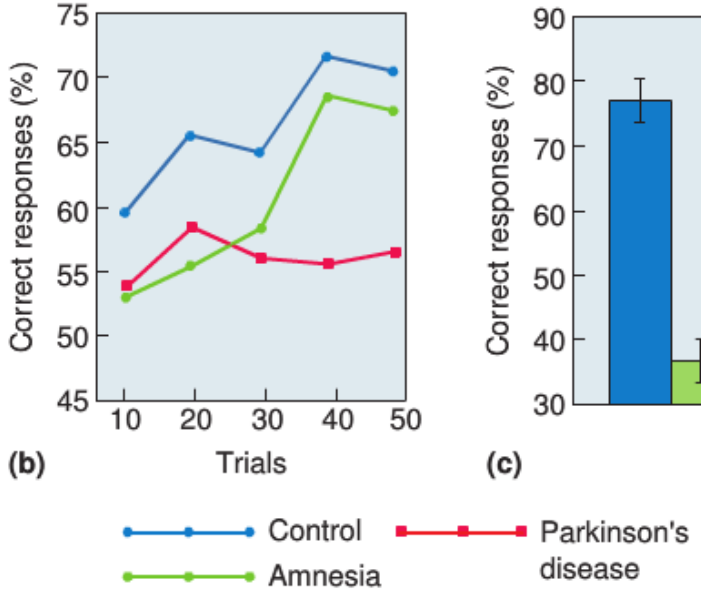
Basal Ganglia: Procedural Memory?

The basal ganglia are also affected in Parkinson's disease patients: dopaminergic neurons in the substantia nigra degenerate.

The Parkinson's disease patients show deficits (a,b) in a procedural learning task ("weather forecast"). In this task, a set of cues was probabilistically related to an outcome (rain/sunshine) and learning occurs without awareness of the rules.
In contrast, in a declarative memory test (a questionnaire about the cues, layout of computer screen, etc.) the Parkinson's disease patients performed like normal controls.



(a)

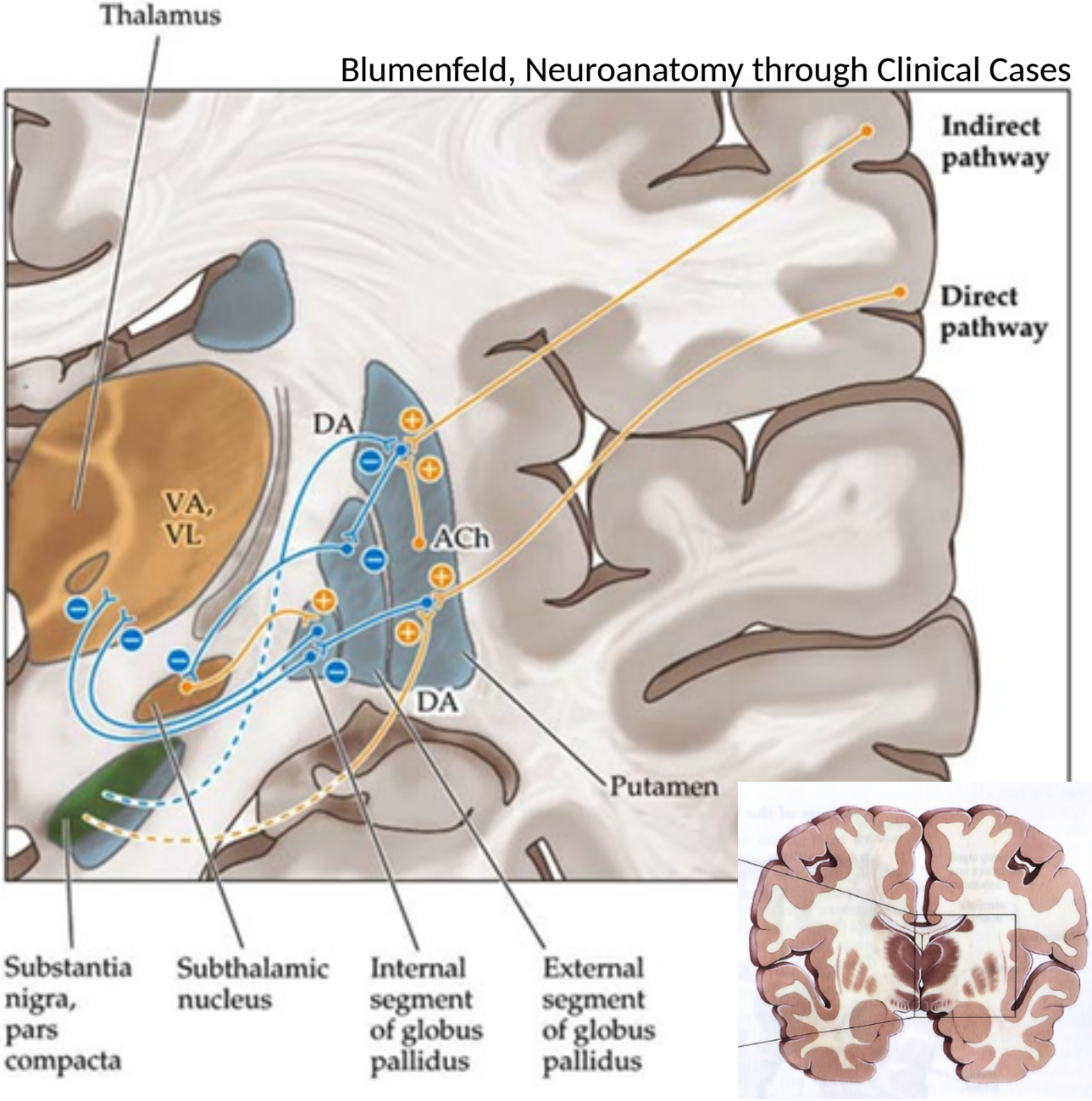


Parkinson's Disease (Basal Ganglia)

Symptoms:
- slow movement (bradykinesia)
- rigidity (increased muscle tone)
- resting tremor (hand/jaw).
- difficulty to initiate movement (akinesia)

Cause: Cell death in substantia nigra

Blumenfeld, Neuroanatomy through Clinical Cases

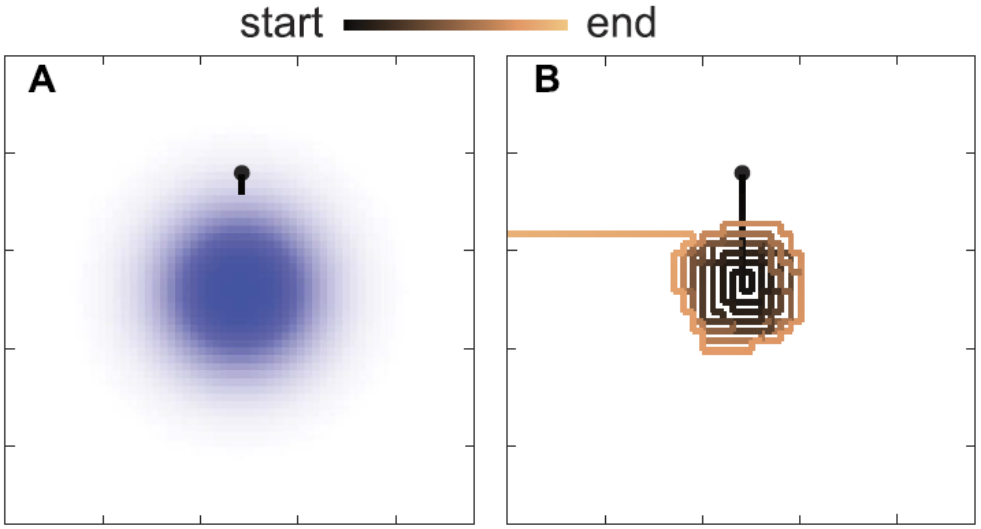


Curiosity / Exploration

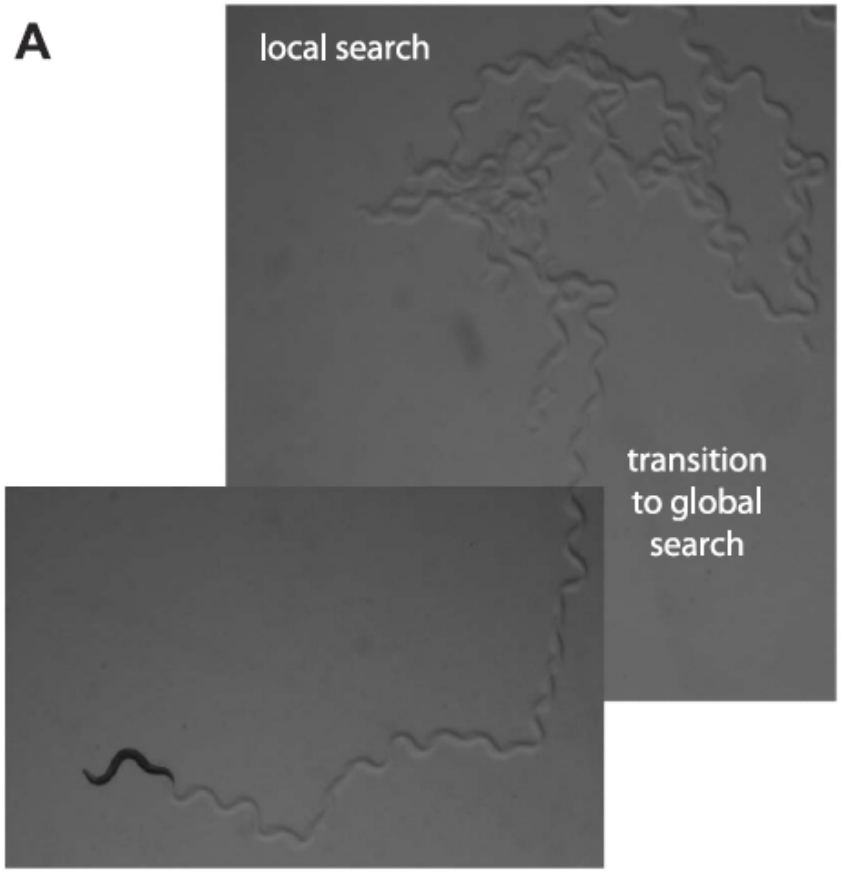
Some landscapes make you want to explore them… What is behind the next island?

Maybe this is exploratory behavior is an evolutionary adaptation to maximize the probability of our survival?

Curiosity / Exploration

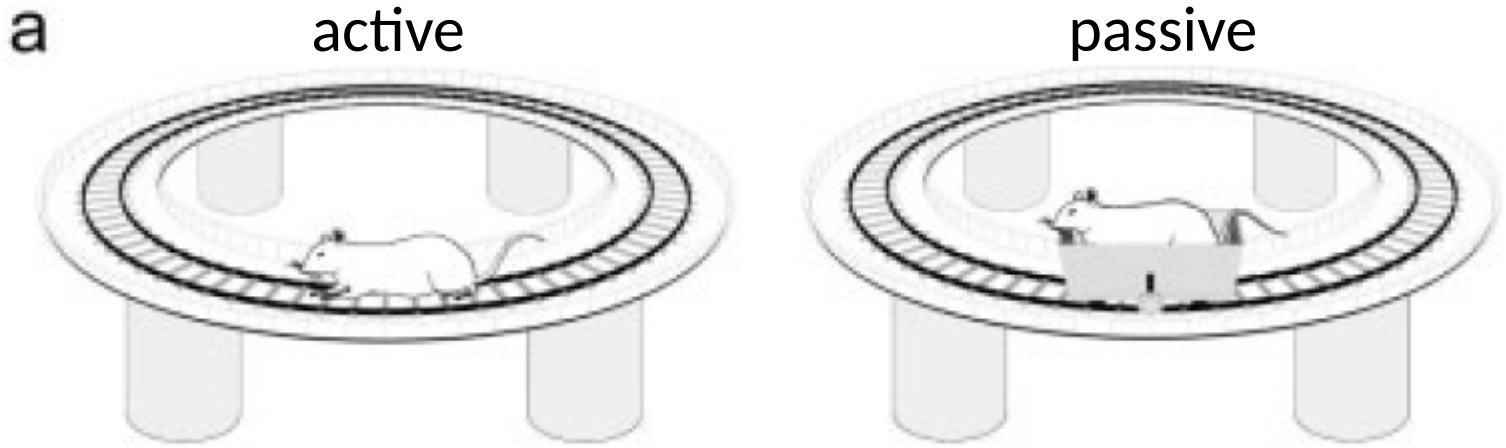


Blue: area of suspected food



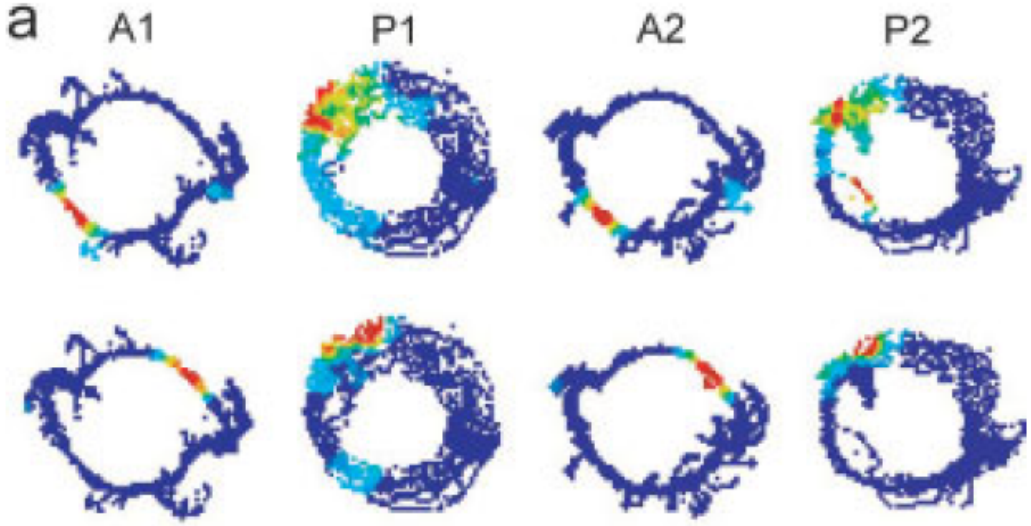
A simple organism like Caenorhabditis elegans (worm) switches from local search behavior (circling an area where food is suspected) to a global search (going straight for a while) to maximize the probability to find food (Calhoun et al., eLife, 2014).

Curiosity / Exploration



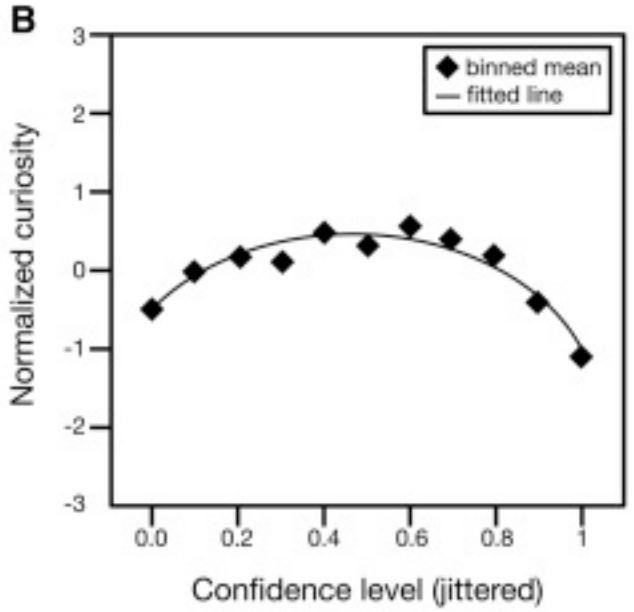
In this experiment (Song et al., Hipppocampus, 2005), the place fields of hippocampal place cells depended on active or passive exploration of a railroad area.

The cells showed stable place fields within a context (e.g., active ▭ active), but a "remapping" between contexts (e.g., active ▭ passive).



Curiosity / Exploration

Exploration entails the active search for missing information. Accordingly, we are most curious for information we are moderately confident to know of (Kang et al., Psychological Science, 2009). Thus, we are less curious about trivial information or something we know nothing about.



Sample questions:

	What instrument was invented to sound like a human singing? Violin	What is the name of the galaxy that Earth is a part of? Milky Way

Curiosity / Exploration in Education

- Students should search and find missing information themselves -> active exploration.
- A meaningful task is needed: for example, explain a concept to other students, or build some prototype.
- Material should be of medium difficulty, not completely unknown, not too trivial.

Summary: Spatial Memory / Navigation

Spatial Memory and Navigation

- Place and grid cells in hippocampus and entorhinal cortex provide a neural basis of spatial navigation and memory.

- The difference of studies on rat and human (H.M.) hippocampus could be resolved by taking into account the more detailed organization of the hippocampus.

- Procedural memory involves basal ganglia circuits, independent of the hippocampal system.