A Graph Theory Approach To Human Episodic Memory: Outlining The Spectrotemporal Basis Of Episodic Memory Retrieval

Symposium: S02 - Multi-Frequency Brain Network Dynamics In Human Memory

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A tale of two approaches to memory and neural oscillations

Tolman and cognitive maps

Invasive electrophysiology:

✓Vanderwolf and others characterize type I (movement-related) and type II (immobility) "theta"

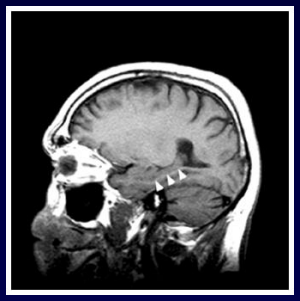
✓ Graystan and others: the search for the behavioral correlates of theta

Human intracranial EEG (iEEG) of hippocampus

What are properties of human hippocampal low frequency oscillations? How do they compare with rats?

Multilobular cortical recordings of low frequency oscillations

How do we represent the spatial and temporal components of episodic memories?



✓fMRI: Activations in medial temporal, parietal, and prefrontal cortex during episodic memory processing

✓Lesions to MTL, and secondarily, prefrontal cortex, impair episodic memory.

Local vs. global low frequency oscillations...theoretical unification?

- Part 1: Characterizing low frequency oscillations in the human and rat hippocampus
- Part 2: Interregional communication via low frequency oscillations and relation to episodic memory

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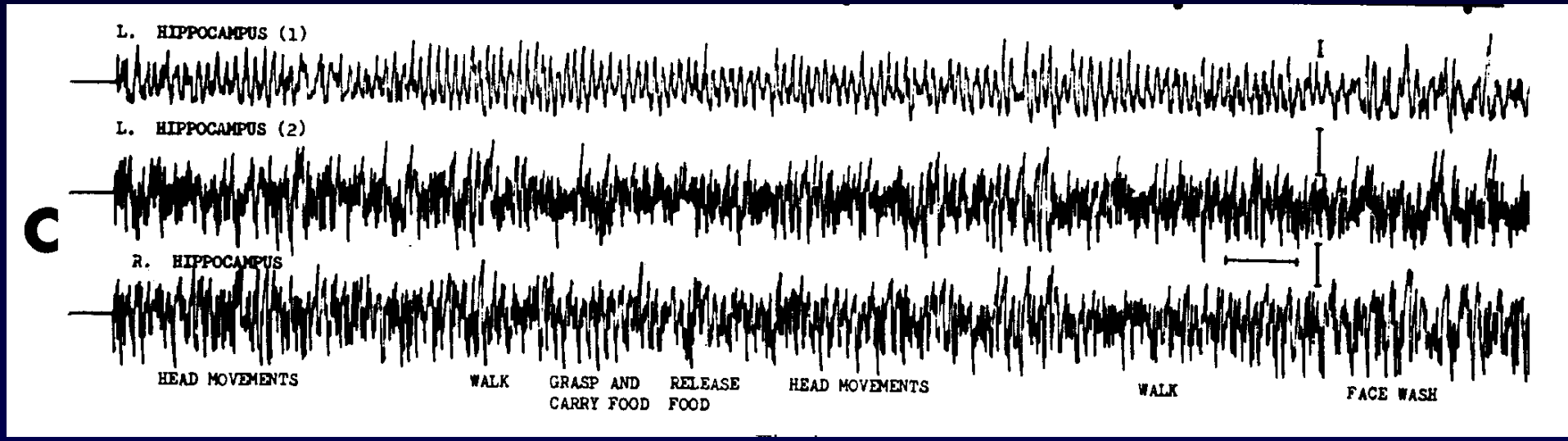
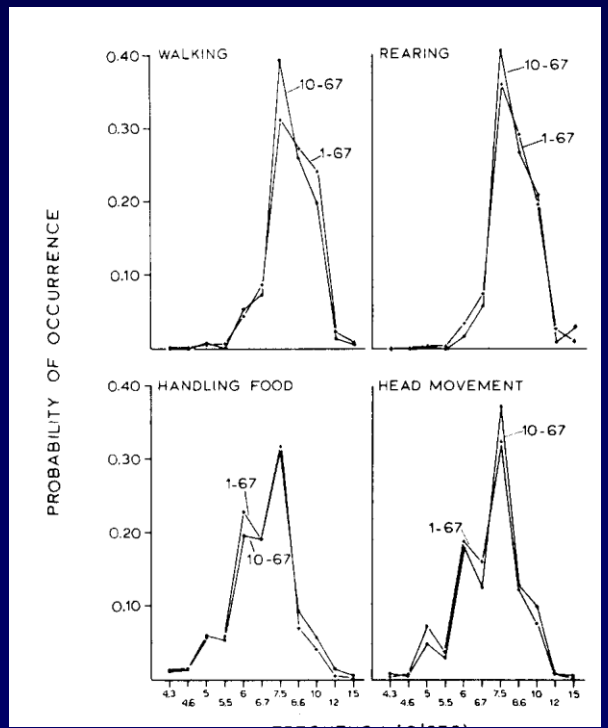
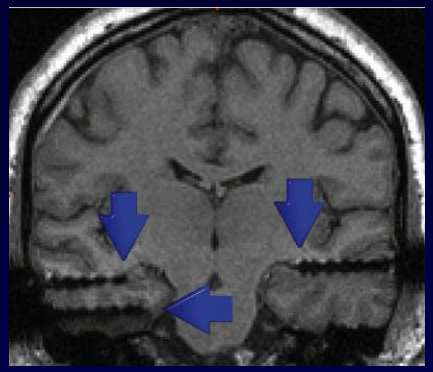
Vanderwolf (1969)





Intracranial EEG recordings from the human brain



- Only possible in patients with pharmacologically intractable epilepsy.
- Single neuron and ensemble (local field potential) recordings possible.

Collaborators: Itzhak Fried, M.D., Ph.D.
Nitin Tandon, M.D.

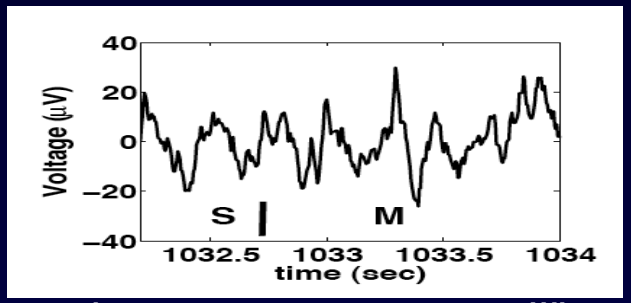
Studying Spatial Cognition in Humans

Virtual engine in PandaEPL and Unity

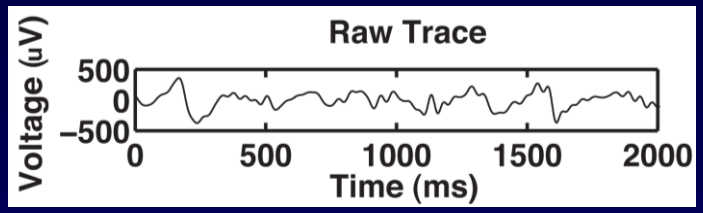
Human hippocampal low frequency oscillations increase with speed

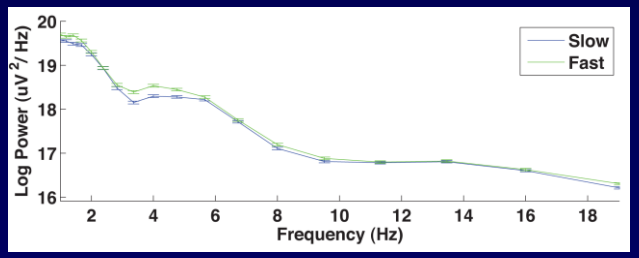
Macroelectrode recordings show θ increases during virtual movement

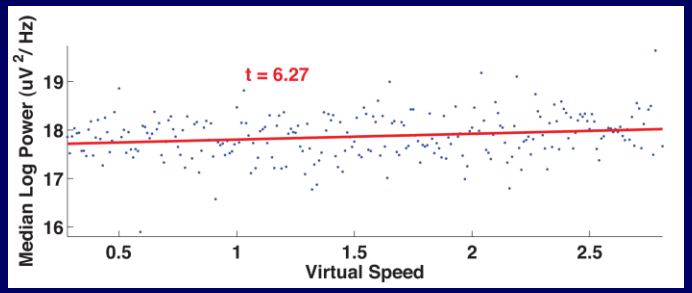
Ekstrom et al., 2005, Hippocampus.



(M= movement, S=still)

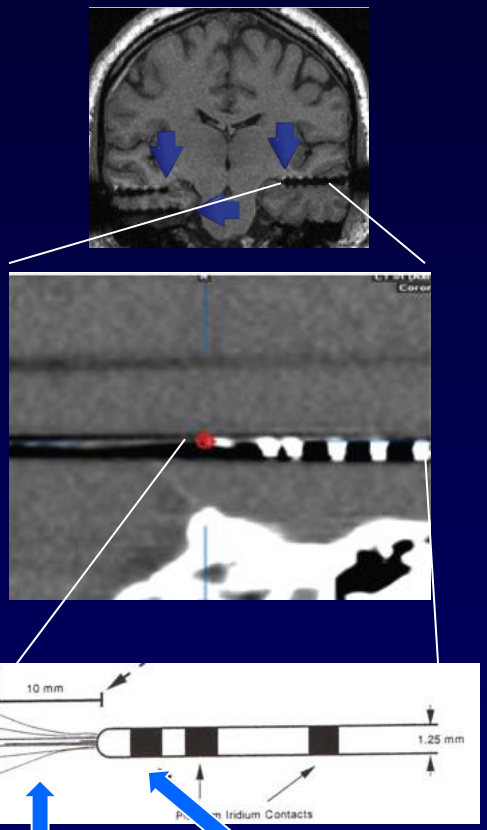






Across group of 317 hippocampal electrodes, significant numbers respond to speed

Watrous et al., 2011, J. Neurophysiology



Microwires (40 um)

Macro contact (~ 1mm)

Interim conclusions

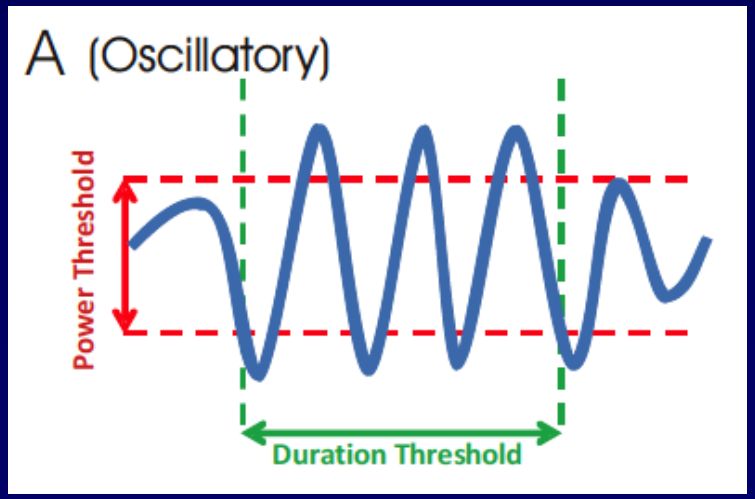
- Low frequency oscillations (1-8Hz) present in human hippocampus and increase in power during movement.

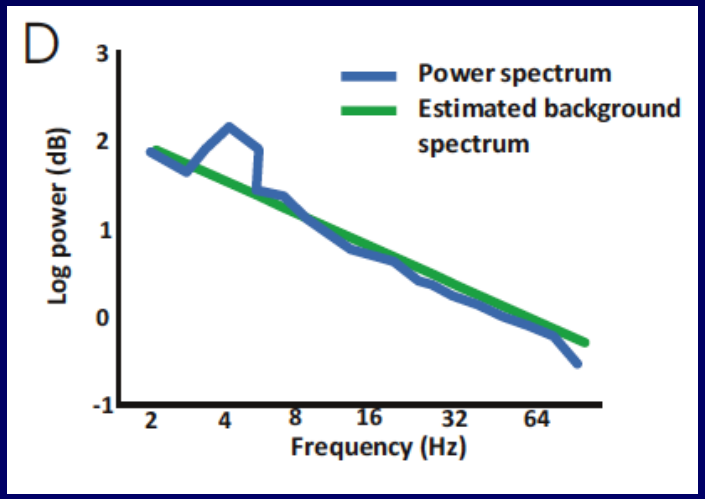
Theta in primates?

- “…little evidence for robust theta-frequency rhythmicity, at least under the behavioral conditions of this study” – Skaggs et., J Neurophys, 2007.
- “Three of three macaques and one of two squirrel monkeys showed clear rhythmic hippocampal EEG activity” – Stewart and Fox, 1991, Brain Res.

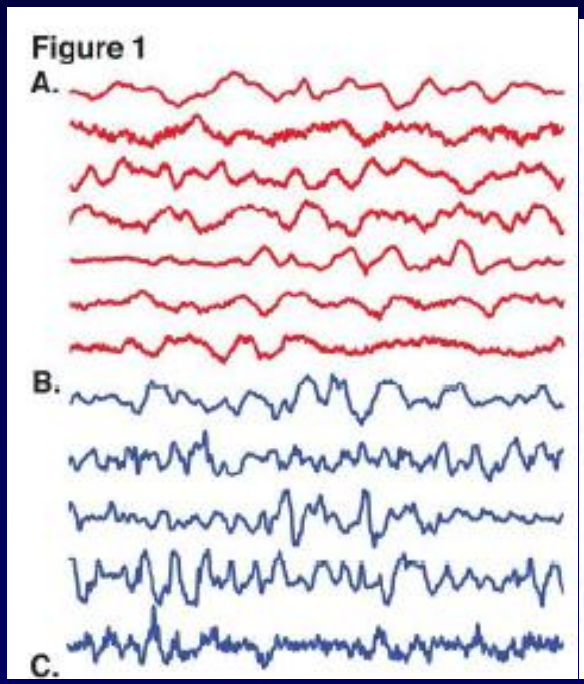
How do human low frequency oscillations compare to rat theta oscillations? Comparative analysis of rat and human theta

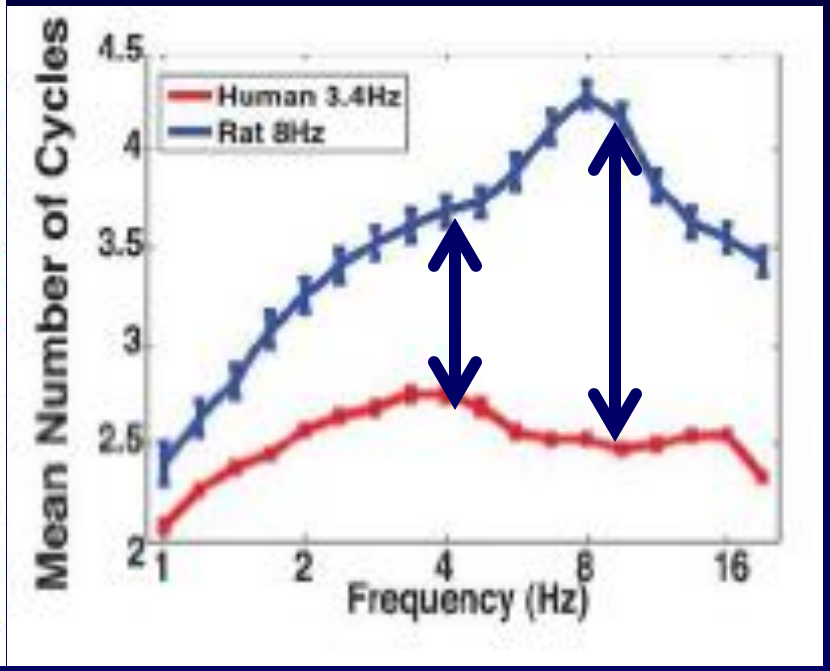
- *Pepisode* (Caplan et al, 2003, J Neuro) detects oscillations above a certain threshold (Pt) for a fixed duration.
- Output is percent of time in oscillatory band.
- Compare recordings from rats running the Barnes maze and humans navigating a virtual environment.





Comparing two recordings, human low frequency oscillations peak at a lower frequency than rats





Average prevalence (%) using 317 microelectrode recordings from humans and 26 microrecordings from rats.

Rat theta peaks at a higher frequency and more continuous than that from humans.

Watrous, Lee, Izadi, Gurkoff, Shahlie, Ekstrom, 2013, *Hippocampus*

Conclusions, part 1

- Hippocampal low frequency oscillations, similar to the rodent, increase in power with increases in speed.
- Human hippocampal low frequency oscillations (recorded intracranially) are less continuous than rodent theta and may peak at a lower frequency band than rats.

- Part 1: Characterizing low frequency oscillations in the human and rat hippocampus.
- Part 2: Interregional communication via low frequency oscillations and relation to episodic memory

Low frequency oscillations as a means of interregional coordination and relation to episodic memory

- Episodic memory more than just spatial context...temporal components also important.
- While hippocampus plays an important role in spatiotemporal representation, other areas also implicated (e.g., parietal, prefrontal cortex).
- How do low frequency oscillations relate to *interregional* processing?
- We can address this issue using multilobular ECOG and graph theory.

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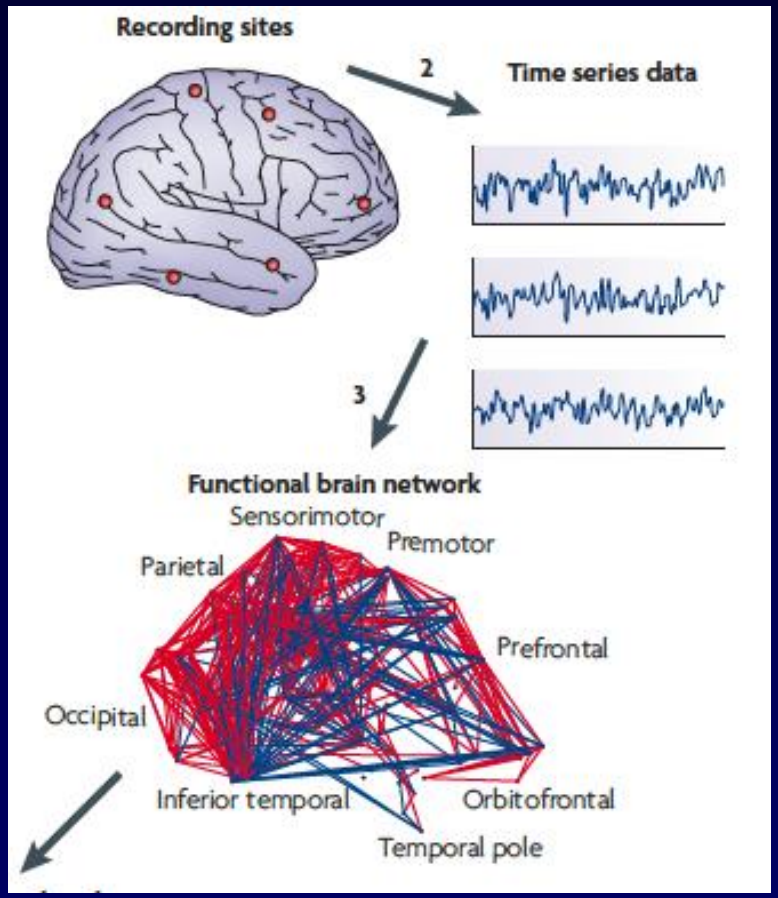
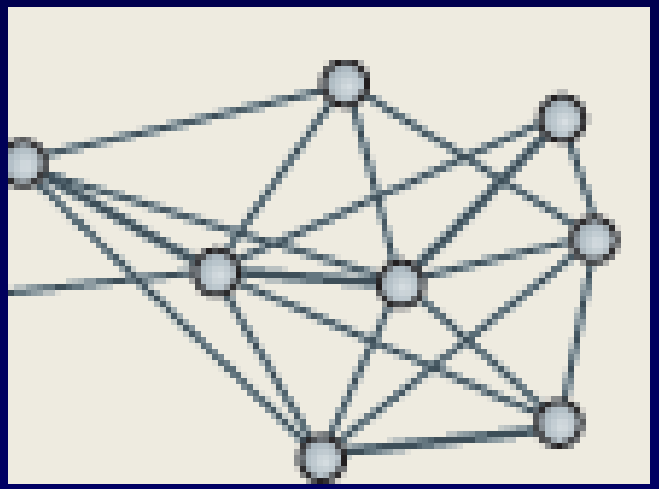
Graph theory approaches to brain data

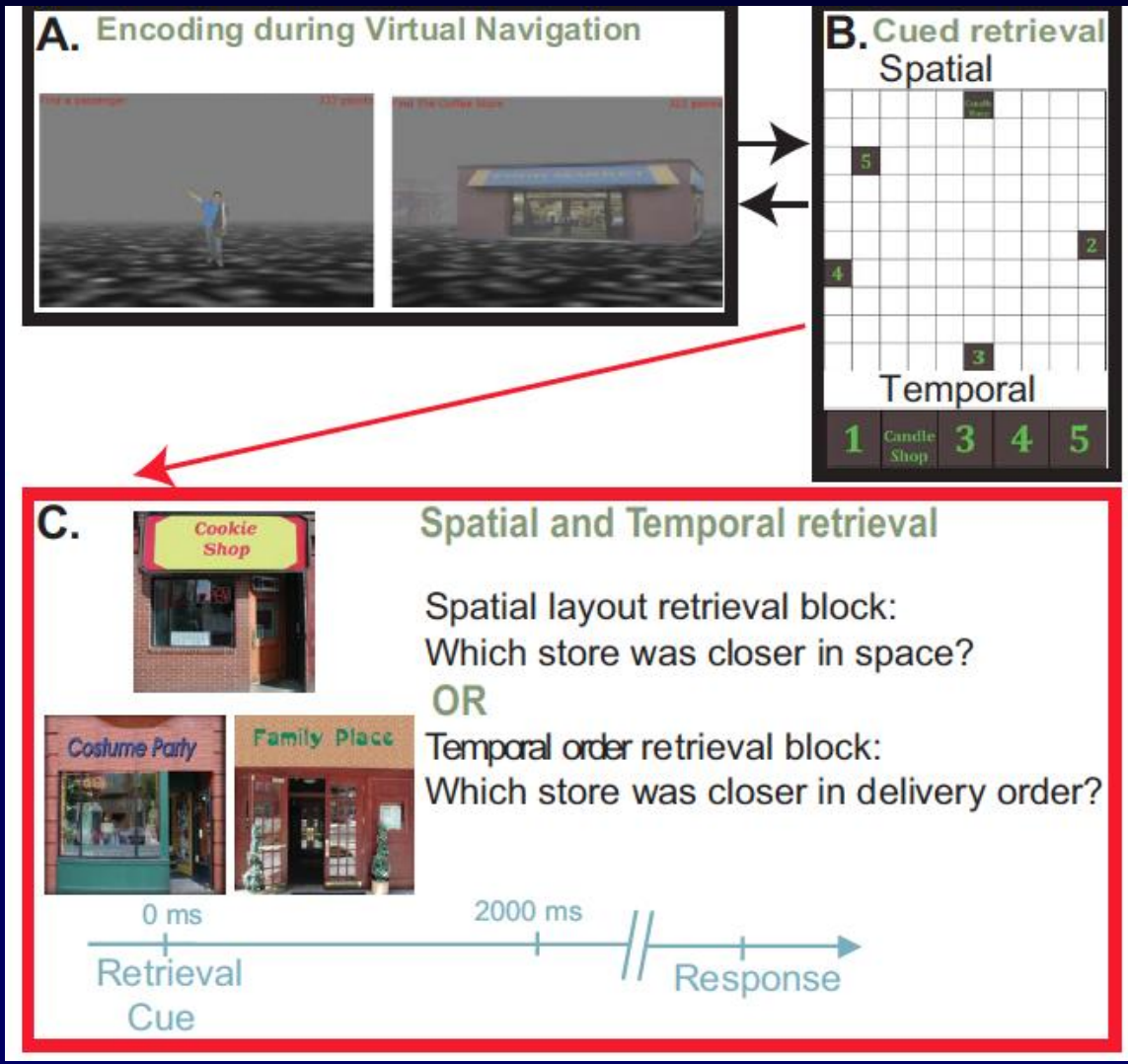


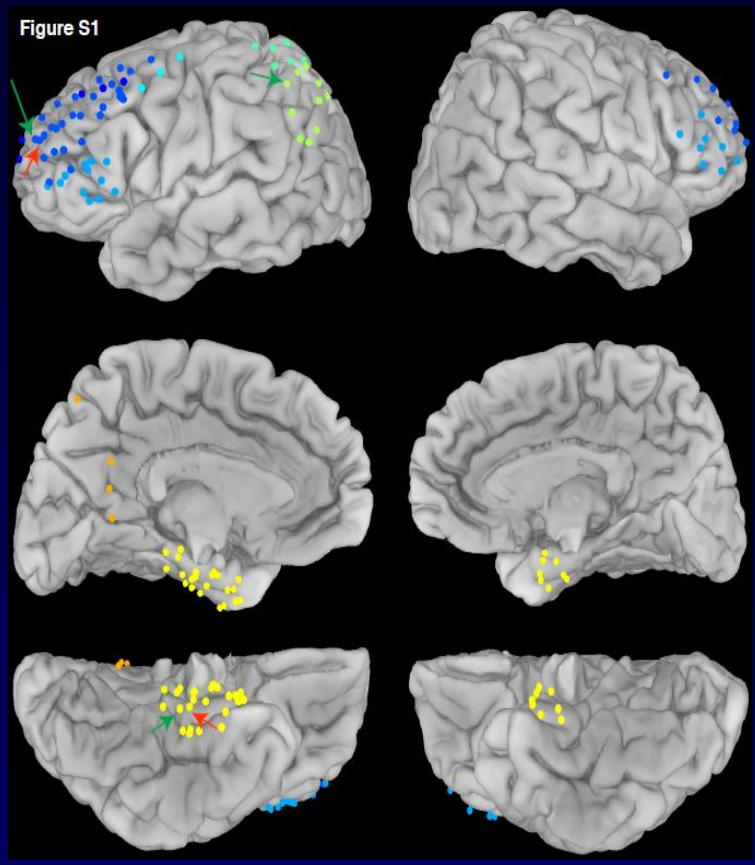
Graph theoretical analysis

Bullmore and Sporns: Considering dynamic connectivity using fMRI and EEG and graph theory may provide insight into interactions at the systems level.



ECoG recordings during retrieval of spatiotemporal memories





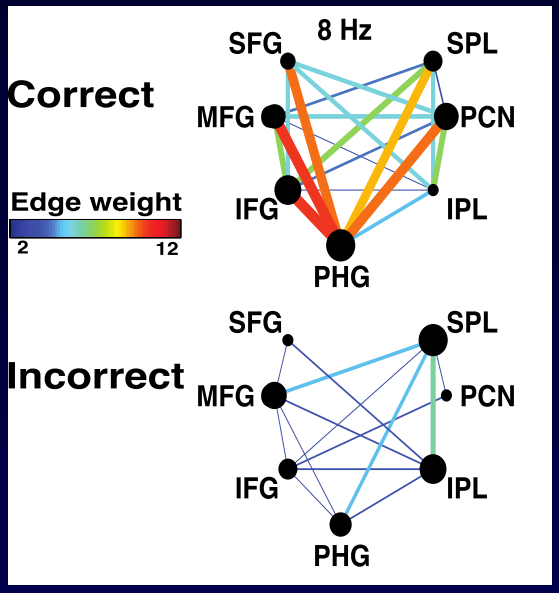
Contrasts of interest:

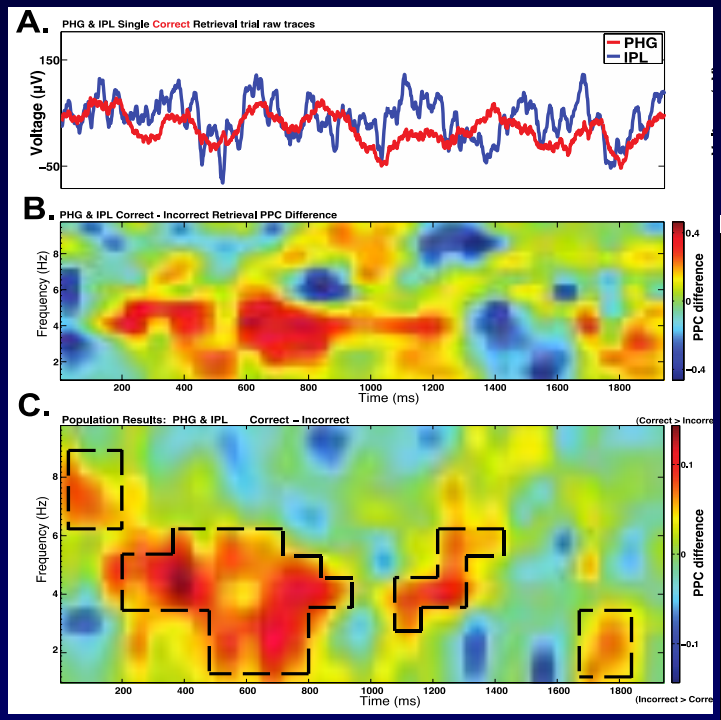
1. Correct vs. Incorrect retrieval
2. Correct spatial vs. correct temporal order retrieval

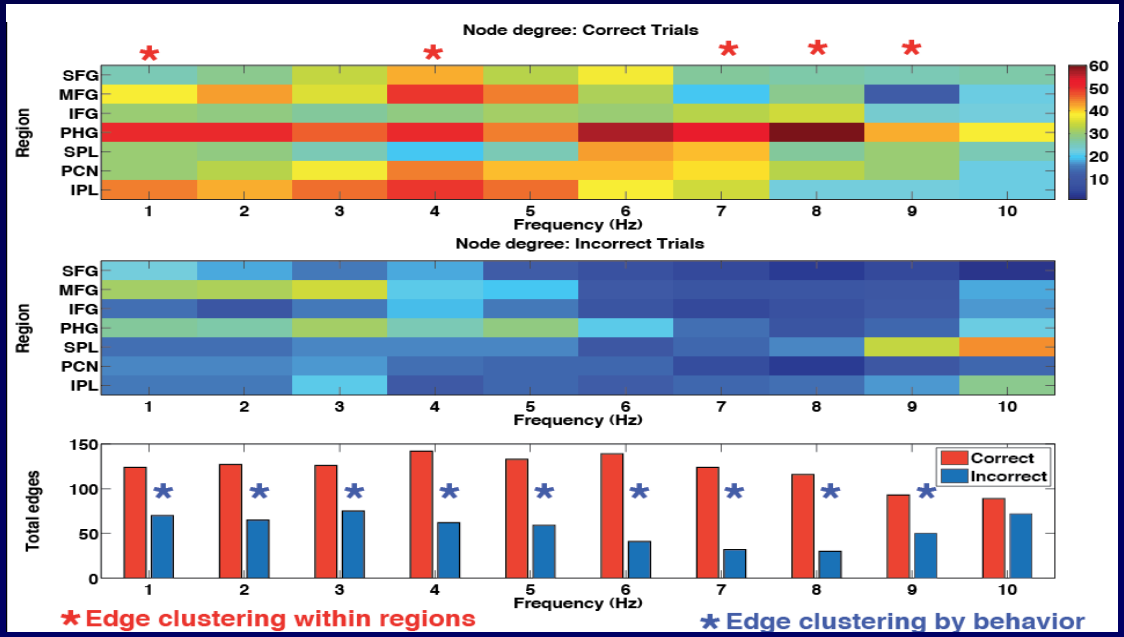
Watrous, Tandon, Conner, Pieters & Ekstrom, 2013, *Nature Neuroscience*

Spatial/Temporal Correct vs. Incorrect Network analysis

Increased PPC between electrodes pairs during for correct > incorrect spatiotemporal retrieval

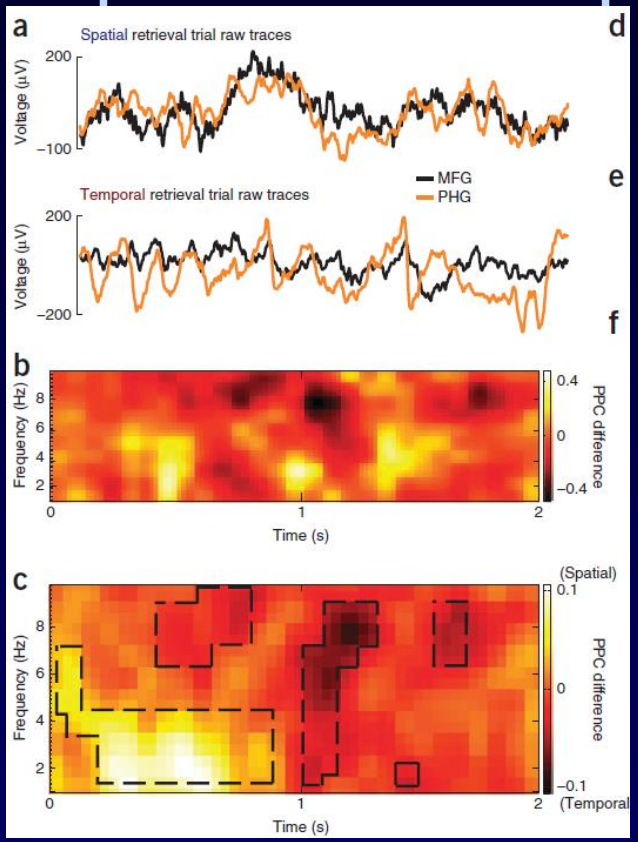




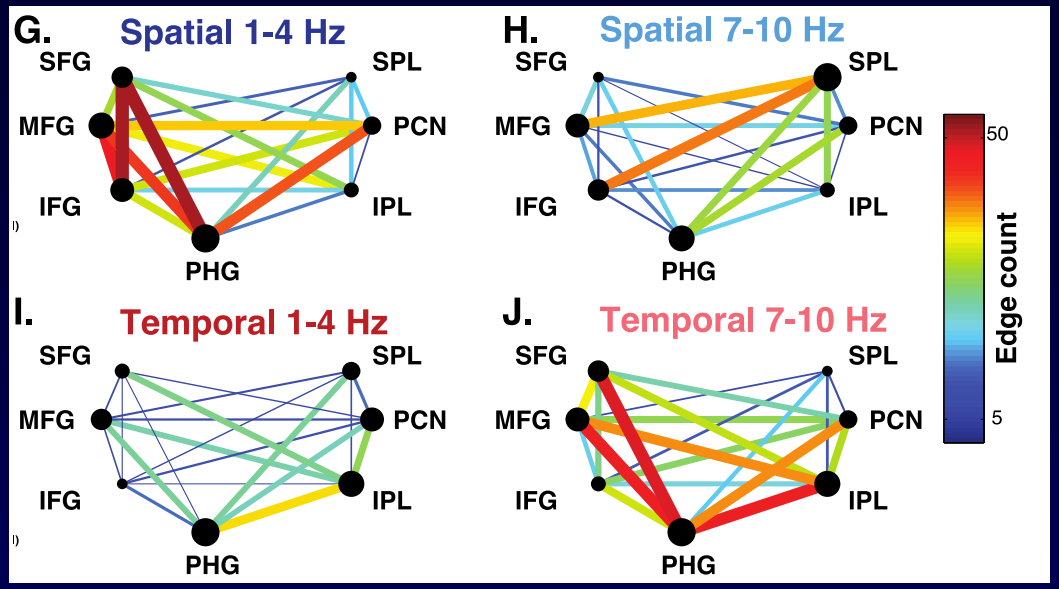


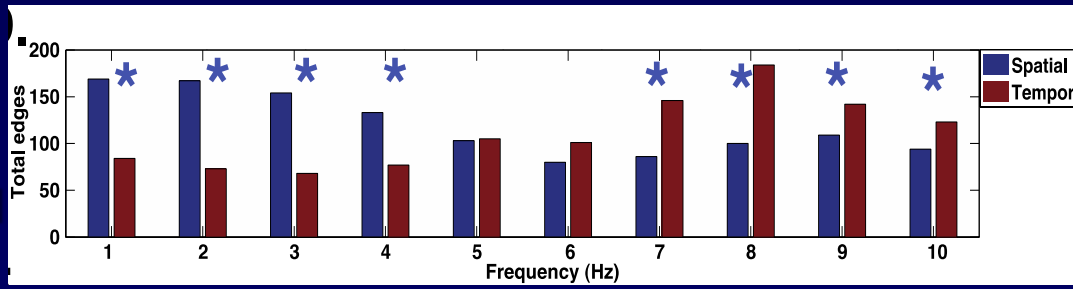
1. Network connectivity increases globally during correct contextual retrieval.
2. PHG acts as a hub for these interactions.

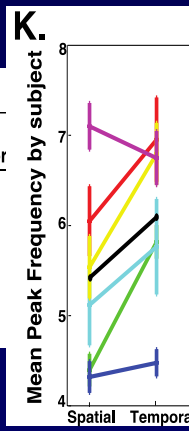
Differences in *frequency* characterize correct spatial vs. temporal context retrieval



Spatial retrieval characterized by lower resonant frequency than temporal order retrieval.

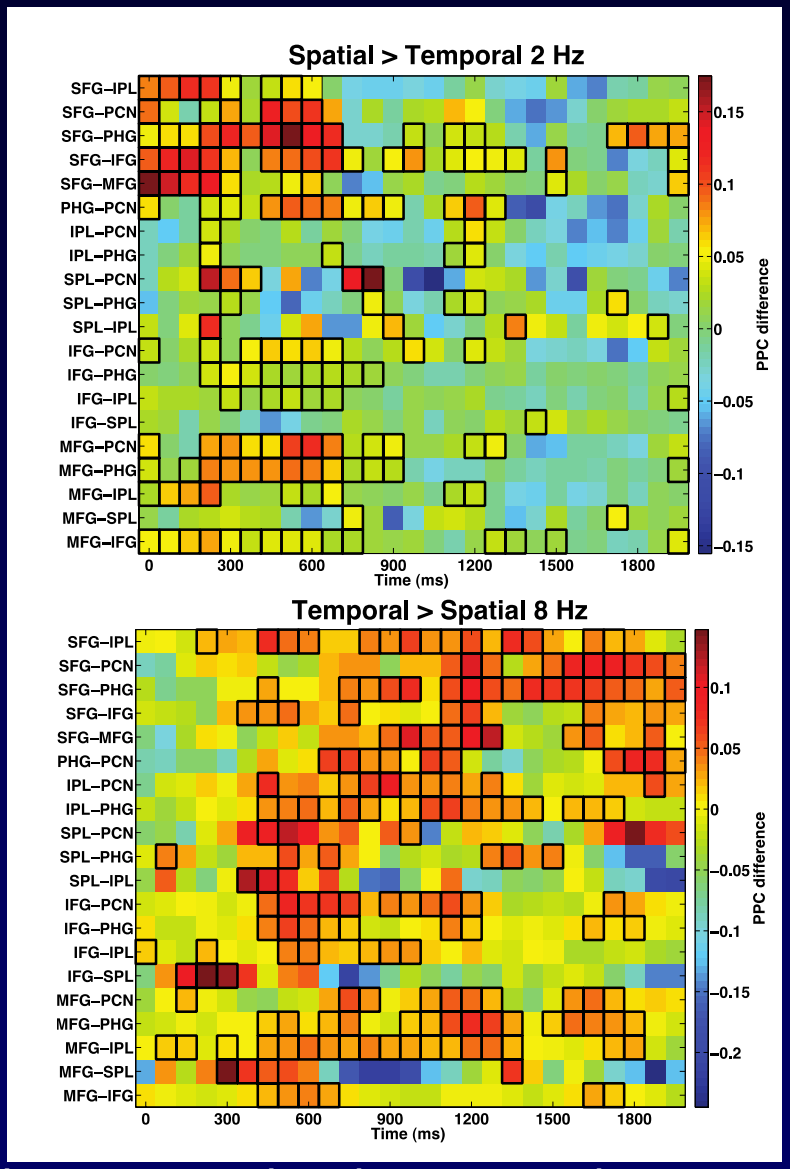


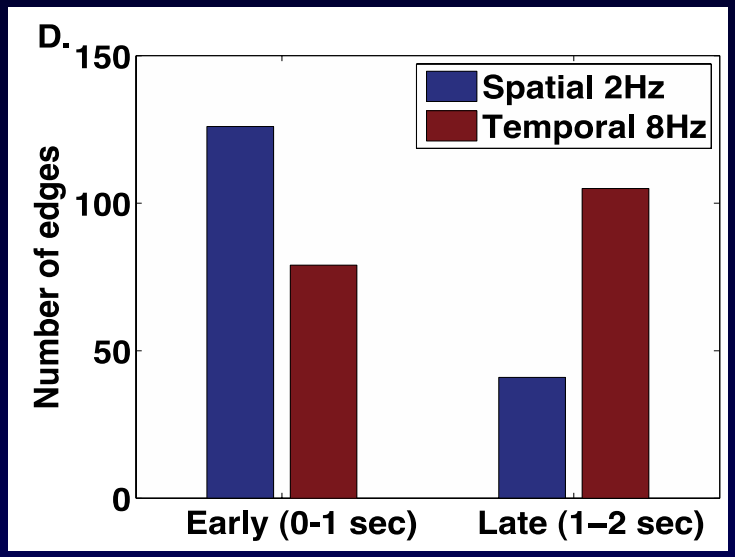


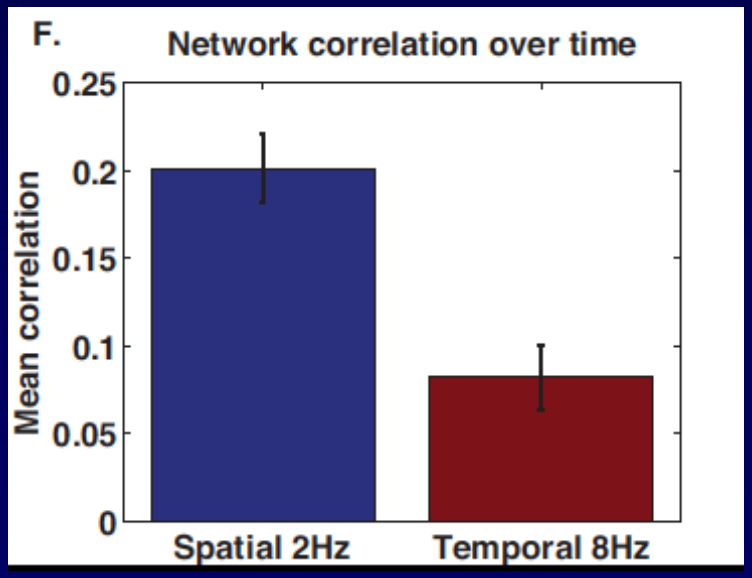


Watrous, Tandon, Conner, Pieters & Ekstrom, 2013, *Nature Neuroscience*

Spatial layout and temporal order retrieval characterized by fundamental differences in network dynamics







Spatial context retrieval, compared to temporal retrieval, results in earlier connectivity across the network and overall greater coherence within the network.

Conclusions, part 2

- Low frequency (~1-10 Hz) coherence increases amongst frontal, parietal, and medial temporal areas during accurate contextual memory retrieval.
- MTL acts as a “hub” for network interactions.
- Accurate spatial and temporal retrieval are dissociated by the spectrotemporal patterns of network coherence

How to explain role of low frequency oscillations in memory? SCERT argues they are a mechanism for coordinating processing from networks to synapses

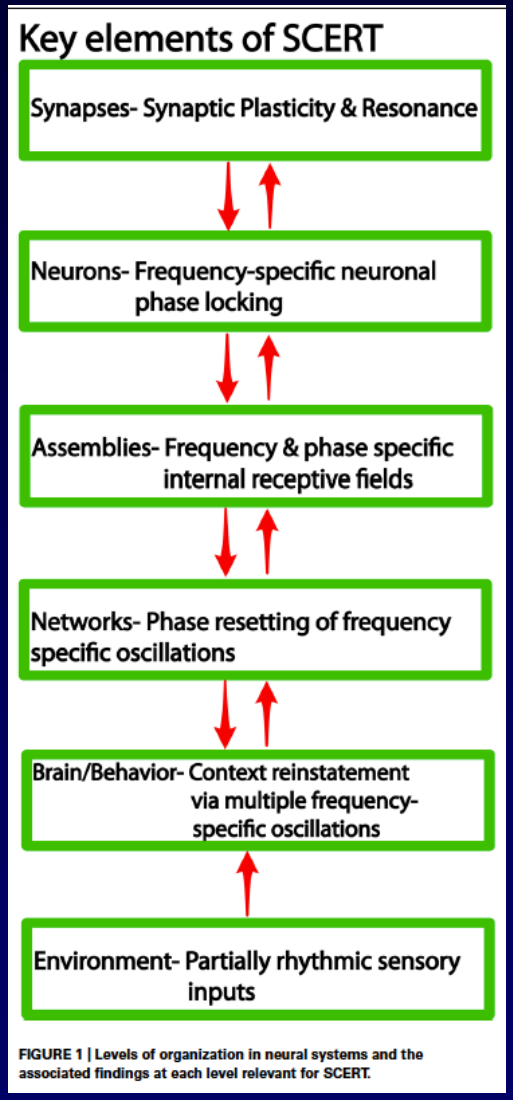


FIGURE 1 | Levels of organization in neural systems and the associated findings at each level relevant for SCERT.

LTP can change dynamics of I_h, which in turn may tune the neuron to respond optimally at that frequency (e.g., Narayanan and Johnston, 2007)

Phase of theta on which spikes occur relates to increased/decreased likelihood of LTP (Huerta & Lisman 1995)

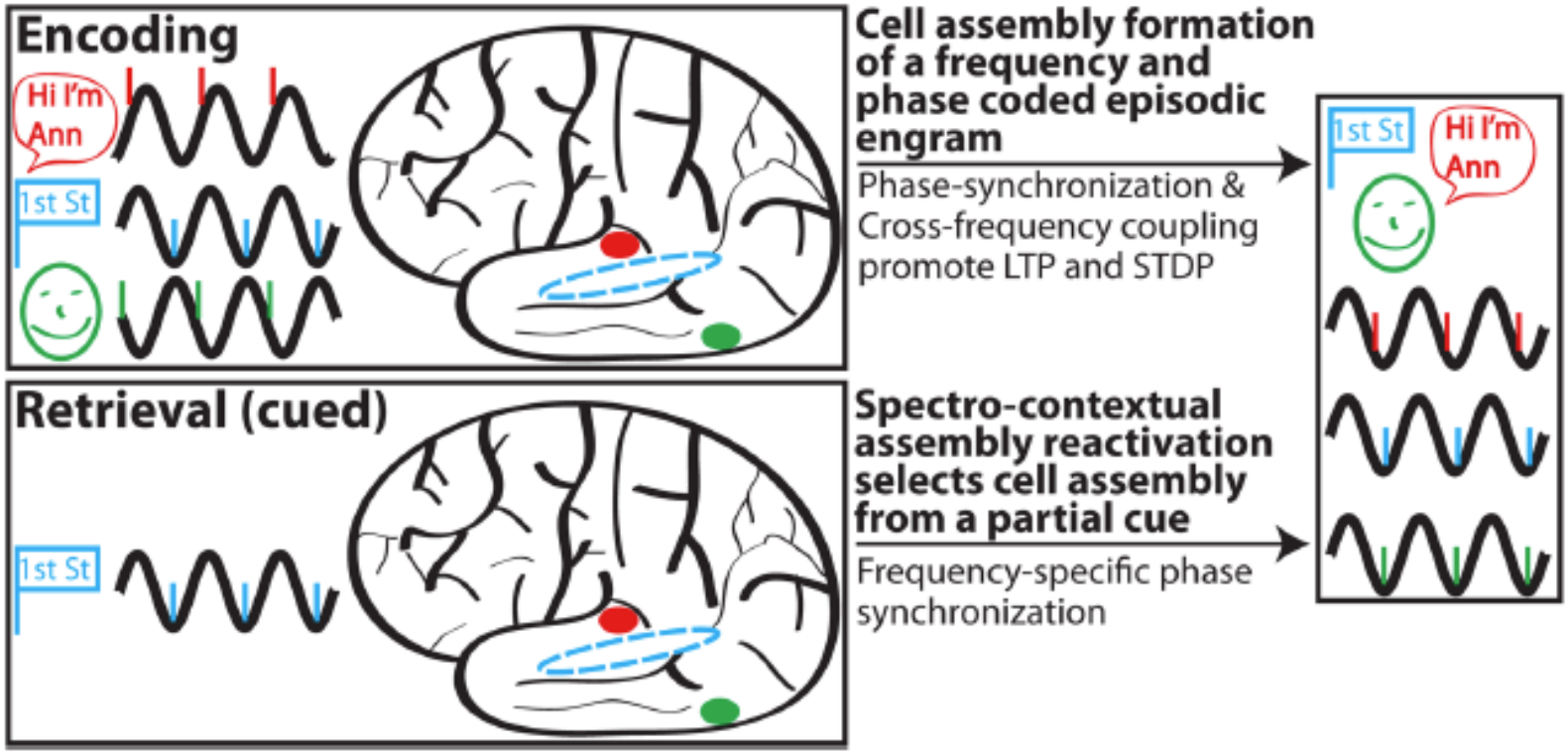
Neurons have preferred LFP-LFP phase coupling to local and distant LFPs (Canolty et al. 2010).

Phase-resetting to memory probes (e.g., Rizzuto et al. 2003)

Different contexts characterized by different frequencies of oscillations within the network (Watrous et al., 2013; Wimber et al. 2012).

Watrous and Ekstrom, 2014, *Frontiers in Human Neuroscience*.

SCERT in action



Watrous and Ekstrom, 2014, *Frontiers in Human Neuroscience*.

Acknowledgements

Key Person:

Andrew Watrous

Spatial Cognition Lab

Collaborators









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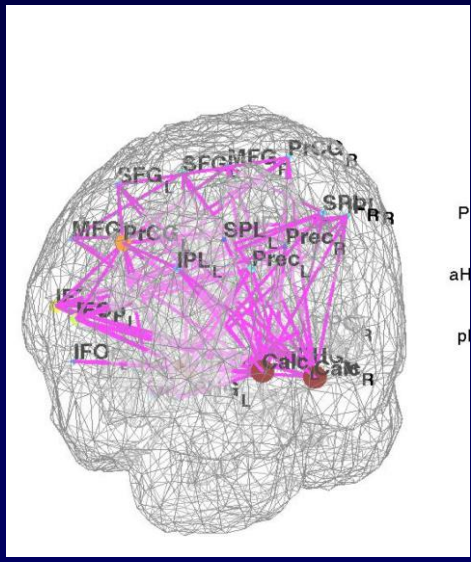
Sloan Foundation

The Hellman Foundation

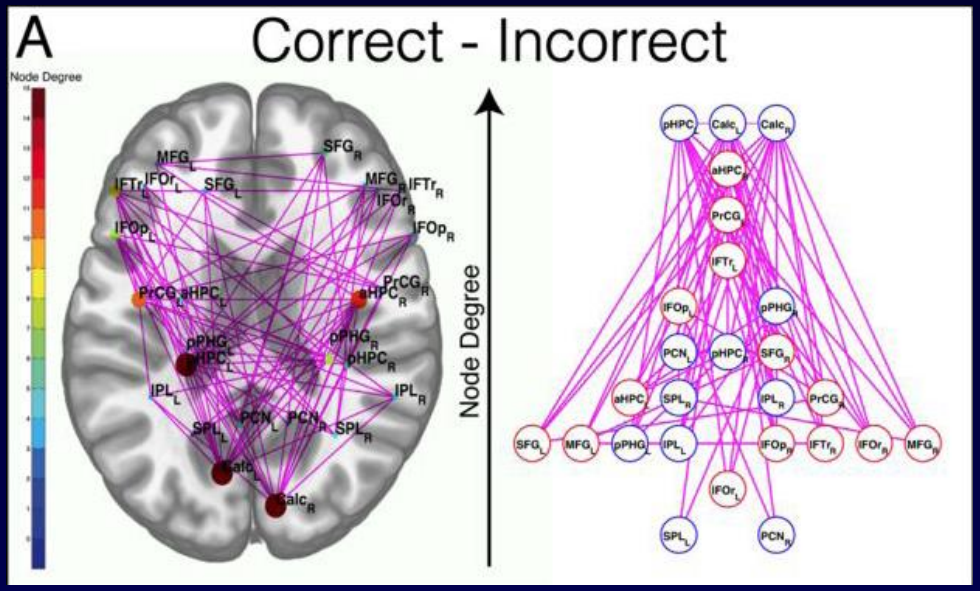
Thank you for your attention!

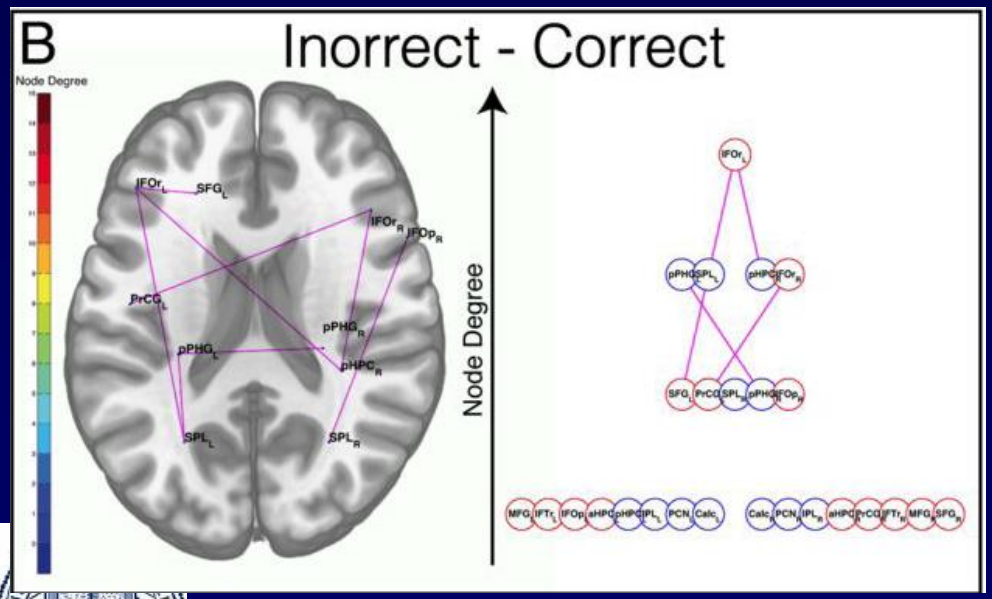
Measuring brain connectivity during spatiotemporal retrieval using fMRI

- Resting state studies: increases in BOLD connectivity correlate with increases in theta coherence (Wang et al., 2012, Neuron)
- Functional connectivity: correlation between the fit of behavioral estimate and hemodynamic response function *between* brain regions.
- Can we replicate basic findings of correct > incorrect using fMRI and more sophisticated graph theory measures?



Correct vs. incorrect networks using fMRI

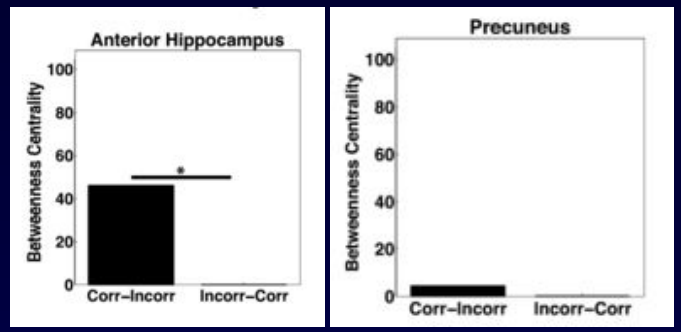




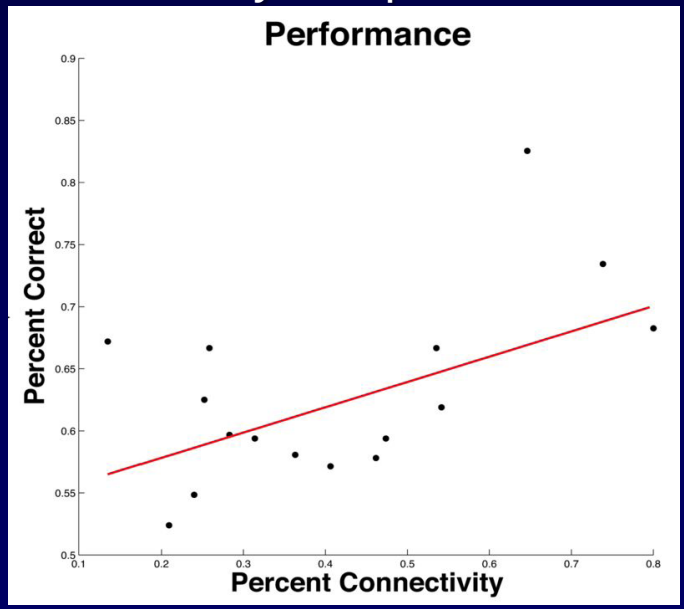
Schedlbauer et. al., *under review*

Relevant hubs

Total # of shortest paths



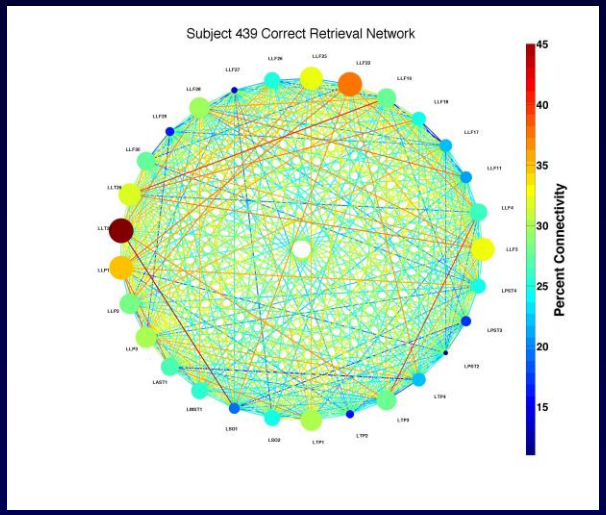
Correlation between total connectivity and performance



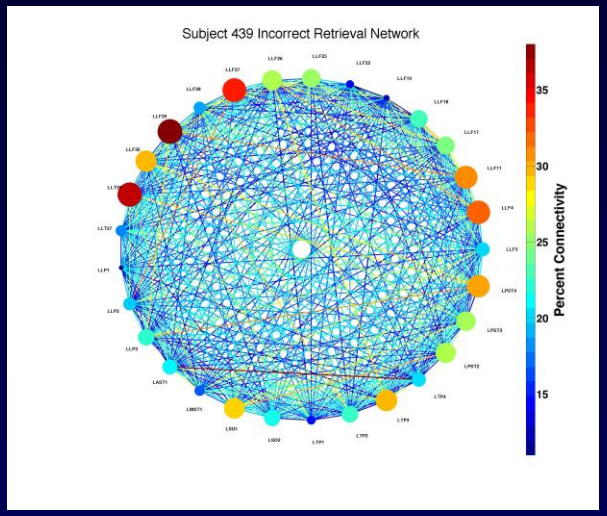
Multivariate regression shows that hippocampus, precuneus, and medial frontal gyrus contribute most variance to this effect

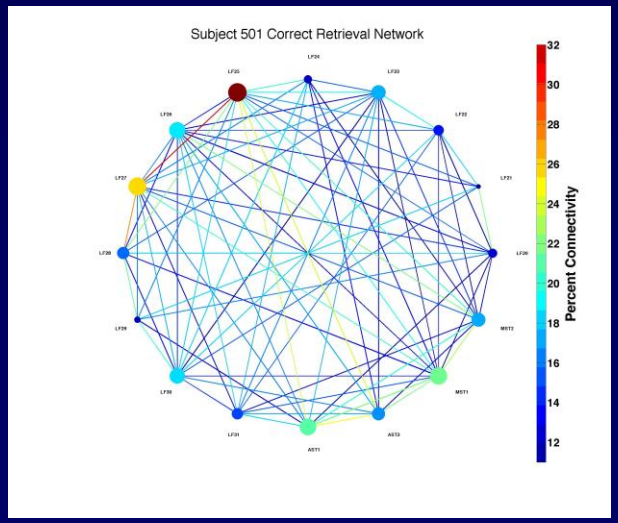
Examples of individual patient networks

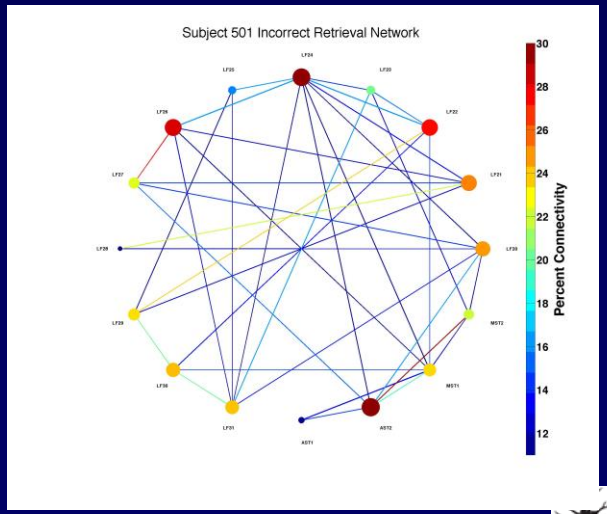
Correct > incorrect



Incorrect > correct

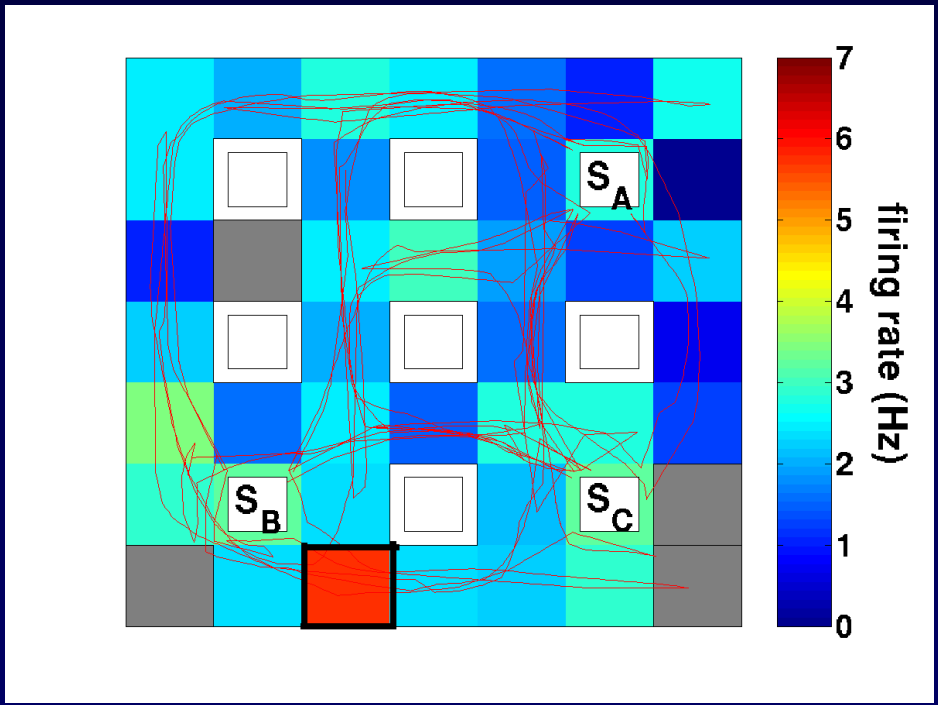


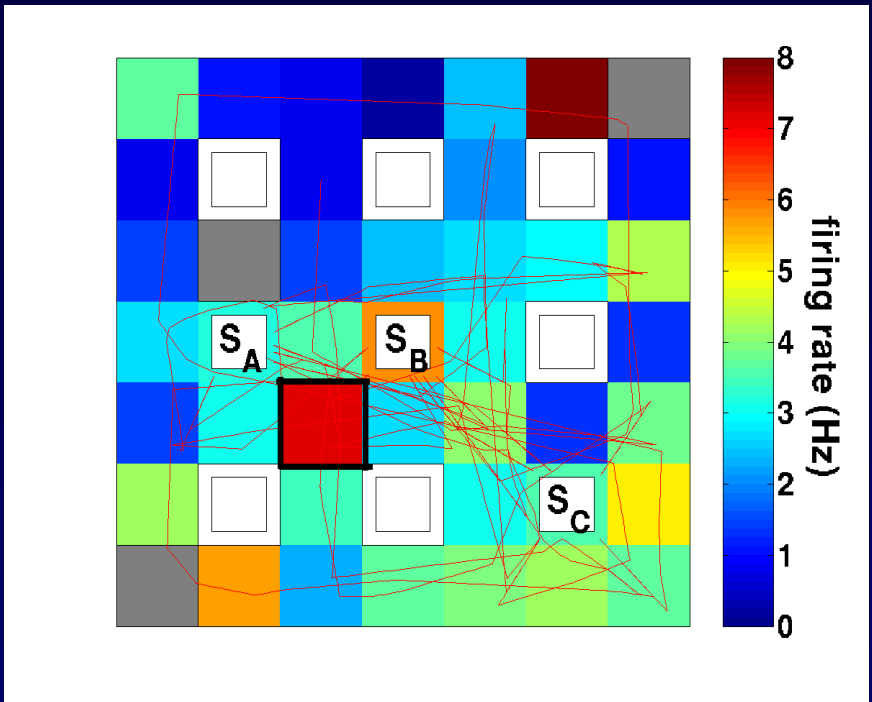




Watrous et al. *in prep*

Other Examples of Place Cells



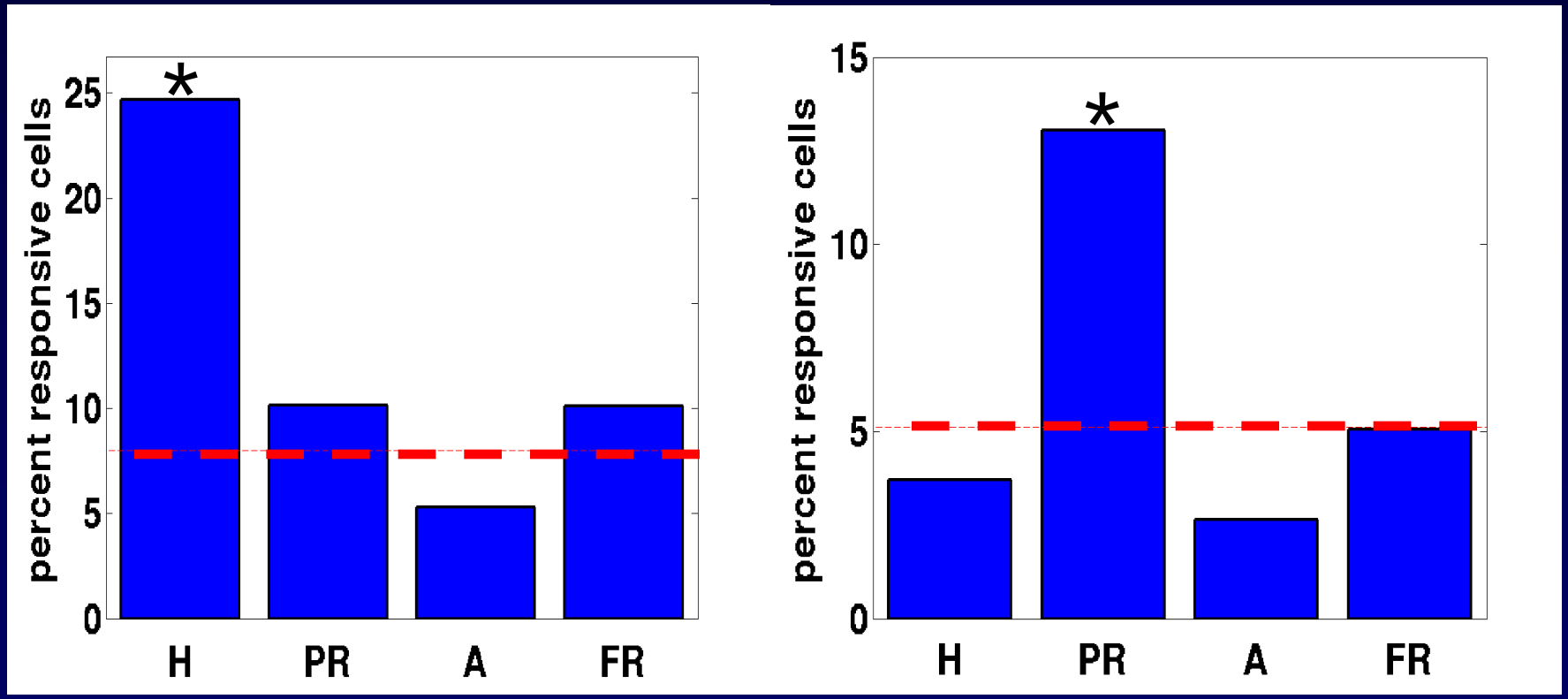


Gray indicates areas occupied for < 1 sec.

Anatomical Distribution of Place and View Responsive Neurons

Place

View



Red dotted line indicates bootstrapped type I error rate

ström, Kahana, Caplan, Fields, Isham, Newman, and Fried, 2003, *Nature*

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