Principles of Cognition:
The Hippocampus in Memory & Navigation

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Conditioning (Pavlov)

Emotional Memory

Habituation (Kandel)

Autobiographical (Conway)

Genetics (Dudai/Quinn)

Eye-witness Testimony (Loftus)

Hippocampal role in long-term memory and navigation

UCL

MEMORY

Object, Context Memory vs Episodic Memory

Recognition vs Recall

Implicit vs Explicit

Jennifer Aniston Cells, Amnesia

Standard Consolidation Theory vs Multiple Trace Theory

NAVIGATION

Mazes and Free exploration vs Route and Map Learning

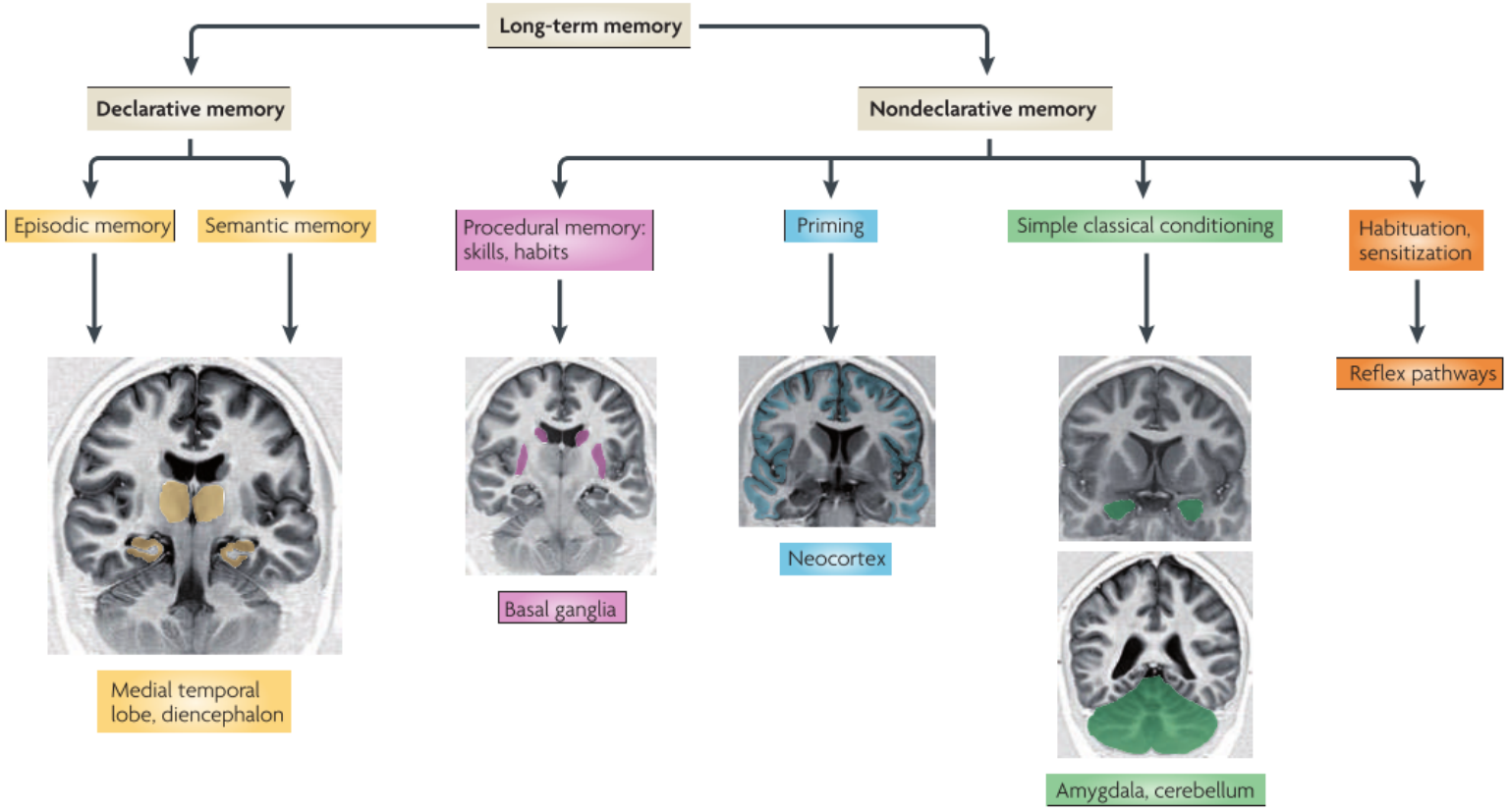
Actual Movement vs Static or Imagined Navigation

Place,Grid,Boundary Cells

Euclidian Space/Cognitive Map vs Topological Map

Frameworks in Memory

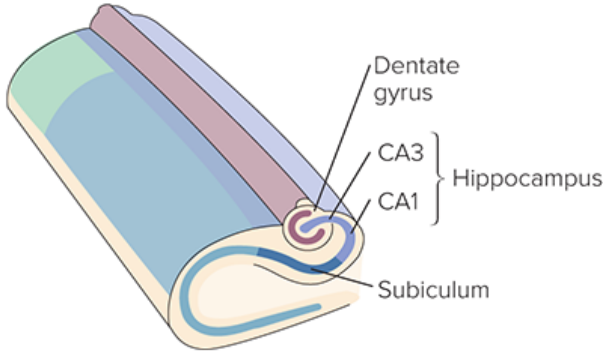
- Explicit vs Implicit
- Semantic vs Episodic
- Recall/Recollection vs Recognition/Familiarity

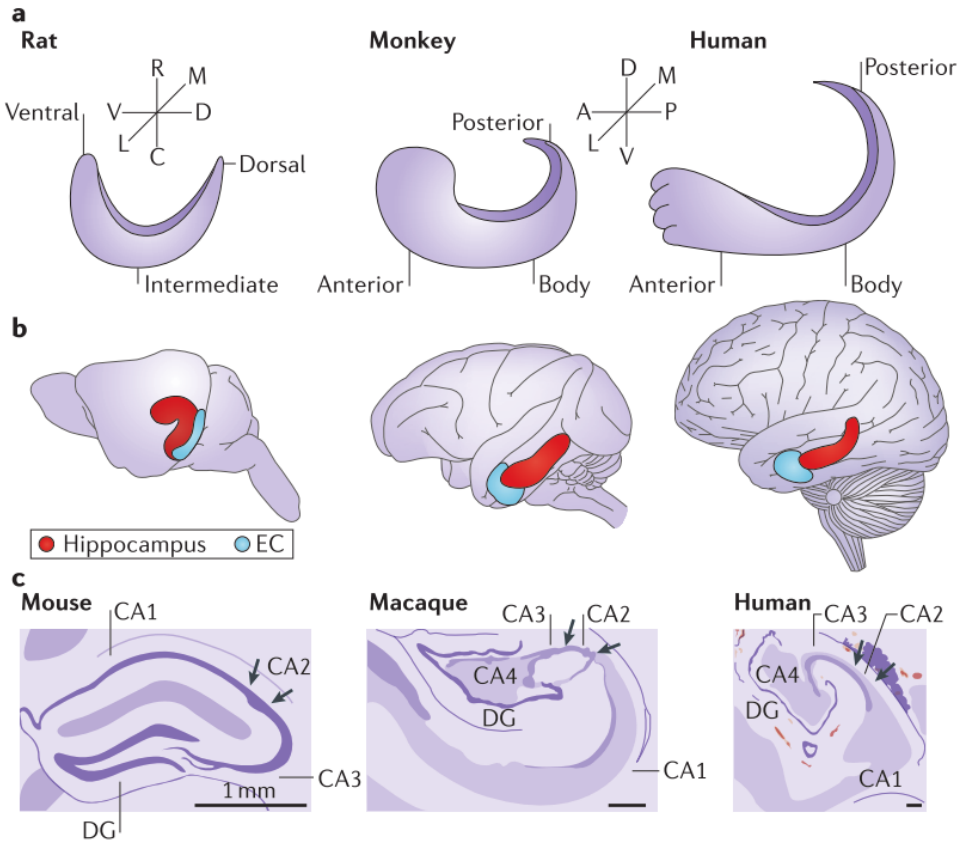


Henke, K. (2010). A model for memory systems based on processing modes rather than consciousness. *Nature Reviews Neuroscience*, *11*(7), 523–532.

Anatomy: Same but Different

- Evolutionarily rodents and humans closer than bats to either (Jacobs 2003)
- yet place-cells, grid cells and direction coding replicated across species (monkey: Buffalo lab; bat: Ulmanovsky lab; bird: Bingman)
- Homology CA1 high, but CA4 only in primates
- Linguistic input into left HC in humans (Knecht, 2004) - no rodent analogy to date (though see Aronov 2017)
- Vision: primates/bats good, rodents bad

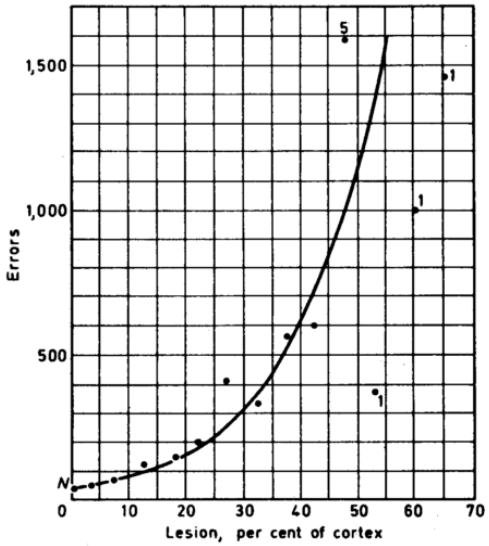


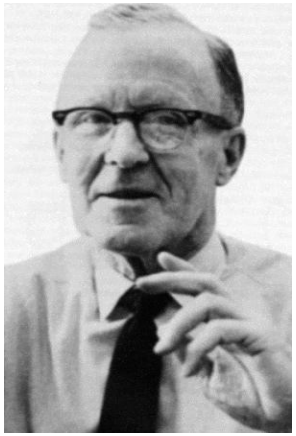


Strange, B. a, Witter, M. P., Lein, E. S., & Moser, E. I. (2014). *Nature Reviews Neuroscience*, *15*(10), 655–669.

The Engram: Mass Action & Hebbian Synapses

Karl Lashley



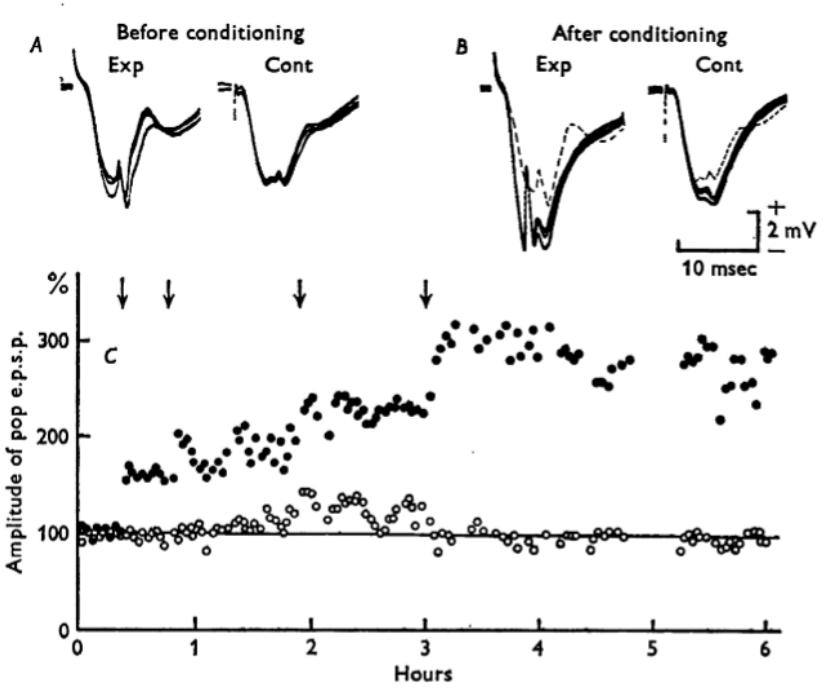


Donald Hebb

- Hebb's Rule: "Cells that fire together wire together" (1949)
- Synaptic plasticity through modification of connections based on simultaneous activity
- Long-term potentiation (discovered by Bliss & Lomo 1973)

SUMMARY

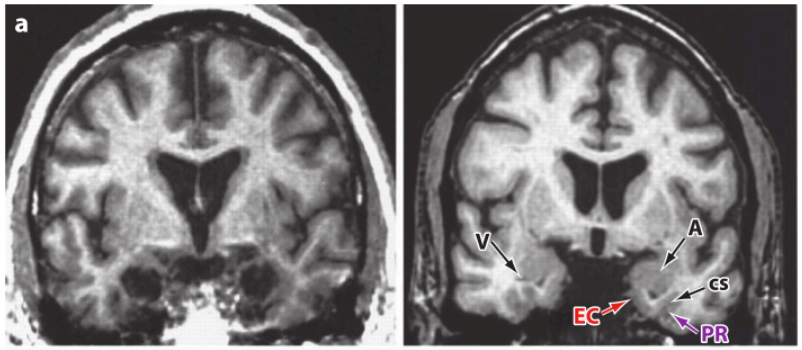
This series of experiments has yielded a good bit of information about what and where the memory trace is not. It has discovered nothing directly of the real nature of the engram. I sometimes feel, in reviewing the evidence on the localization of the memory trace, that the necessary conclusion is that learning just is not possible. It is difficult to conceive of a mechanism which can



H.M., Episodic Memory & The Hippocampus

Wilder Penfield

Brenda Milner

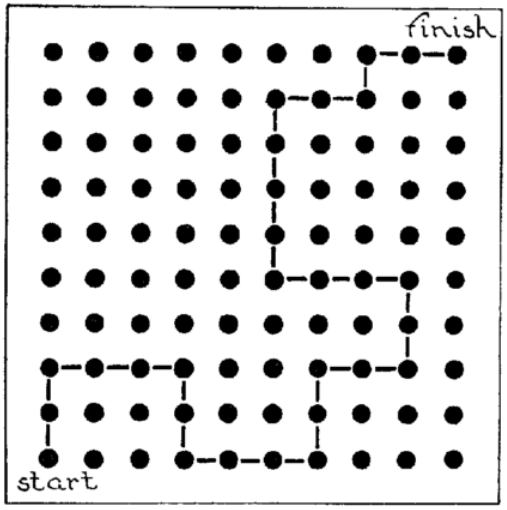


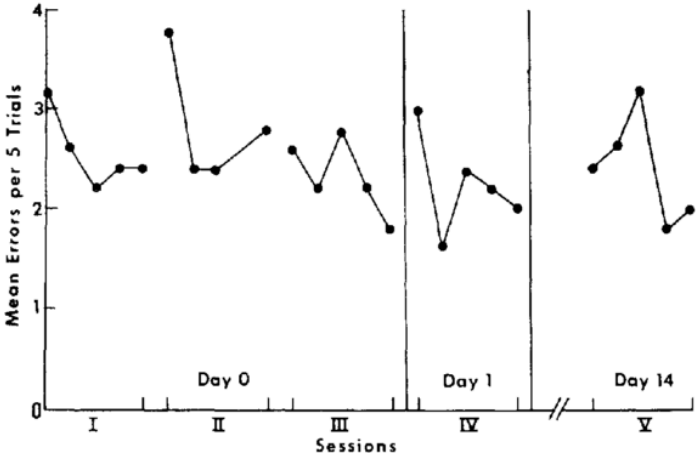
CLASSIFICATION OF CASES

Cases	Age at Time of Follow-up (yr.)	Sex	Diagnosis	Operation	Bi- or Uni-lateral	Approximate Extent of Removal along Medial Temporal Lobes (cm.)	Time between Operation and Testing (mth.)	Wechsler Scale	
								Intelligence Quotient	Memory Quotient
Group I: Severe Memory Defect									
Case 1, H. M.	29	M	Epilepsy	Medial temporal	B	8	20	112	67
Case 2, D. C.	47	M	Paranoid schizophrenia	Medial temporal and orbital undercutting	B	5·5	21	122	70
Case 3, M. B.	55	F	Manic-depressive psychosis	Medial temporal	B	8	28	78	60
Group II: Moderate Memory Defect									
Case 4, A. Z.	35	F	Paranoid schizophrenia	Medial temporal	B	5	40	96	84
Case 5, M. R.	40	F	Paranoid schizophrenia	Medial temporal and orbital undercutting	B	5	39	123	81
Case 6, A. R.	38	F	Hebephrenic schizophrenia	Medial temporal and orbital undercutting	B	4·5	47	Incomplete	
Case 7, C. G.	44	F	Schizophrenia	Medial temporal	B	5·5	41	Incomplete	
Case 8, A. L.	31	M	Schizophrenia	Medial temporal	B	6	38	Incomplete	
Group III: No Memory Defect									
Case 9, I. S.	54	F	Paranoid schizophrenia	Uncectomy	B	4	53	122	125
Case 10, E. G.	55	F	Incisural herniation	Inferior temporal lobectomy	U-Rt.	9	16	93	90

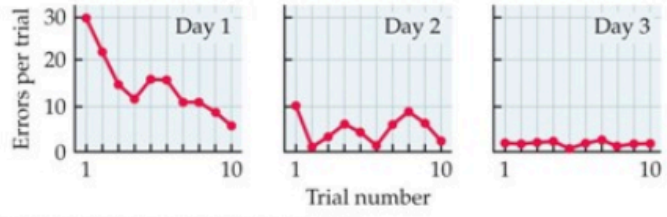
Scoville, W. & Milner, B. Loss of recent memory after bilateral hippocampal lesions. *J. Neurol. Neurosurg.* … (1957).

Explicit vs Implicit Memory



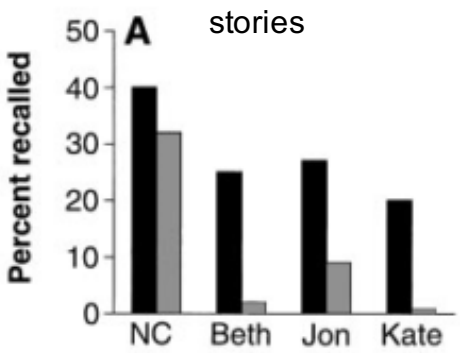


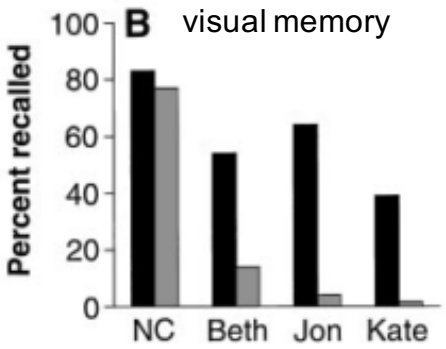
(B) Performance of H.M. on mirror-tracing task

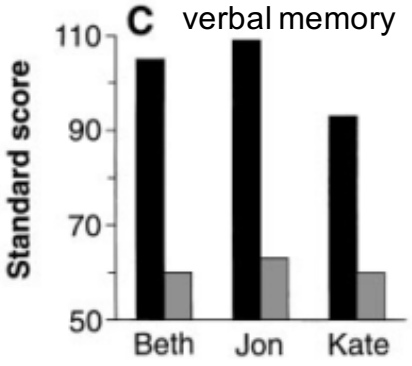


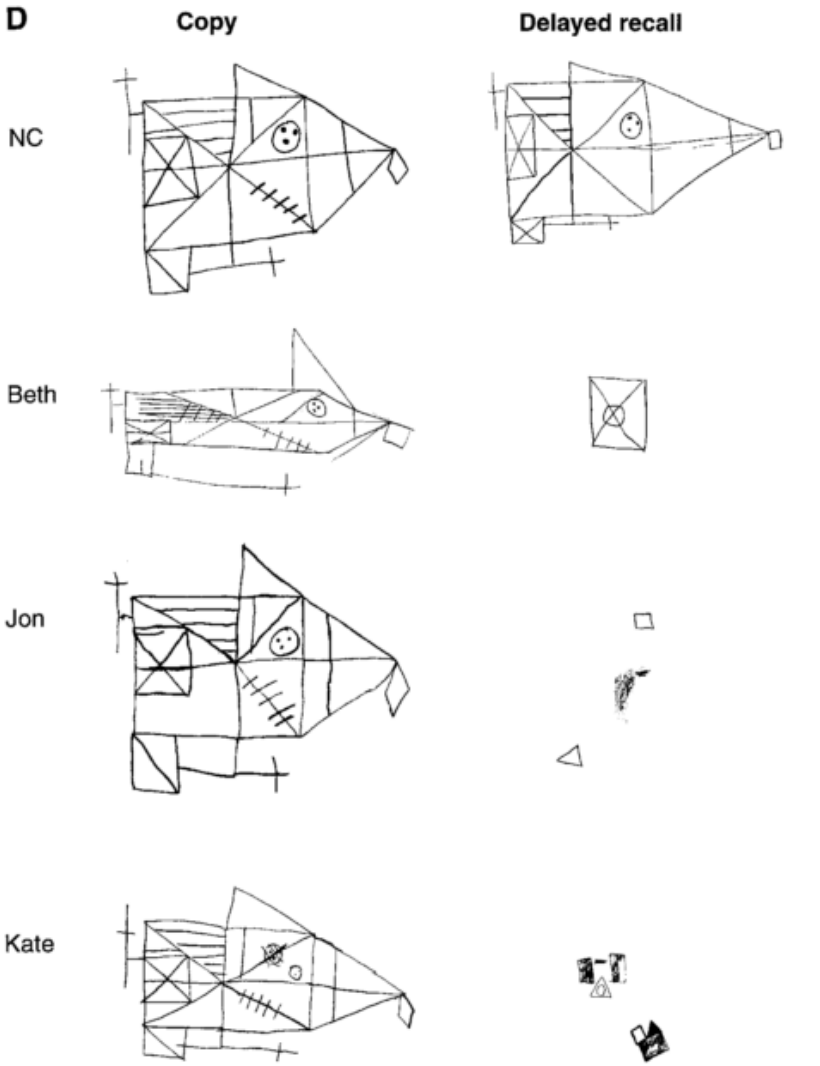
Milner, B., Corkin, S. & Teuber, H.-L. *Neuropsychologia* **6,** 215–234 (1968).

Developmental Amnesia





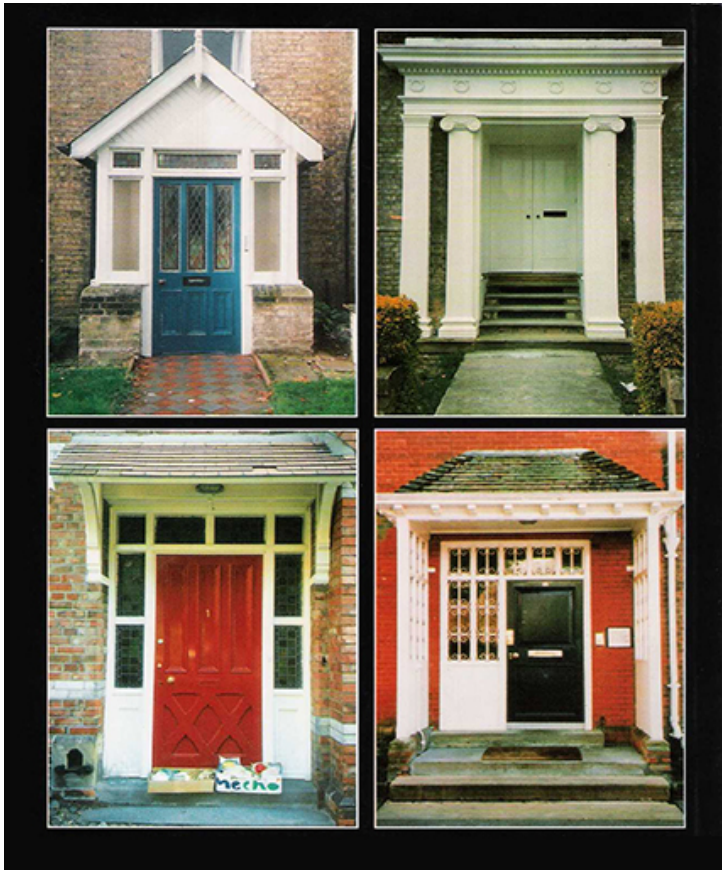


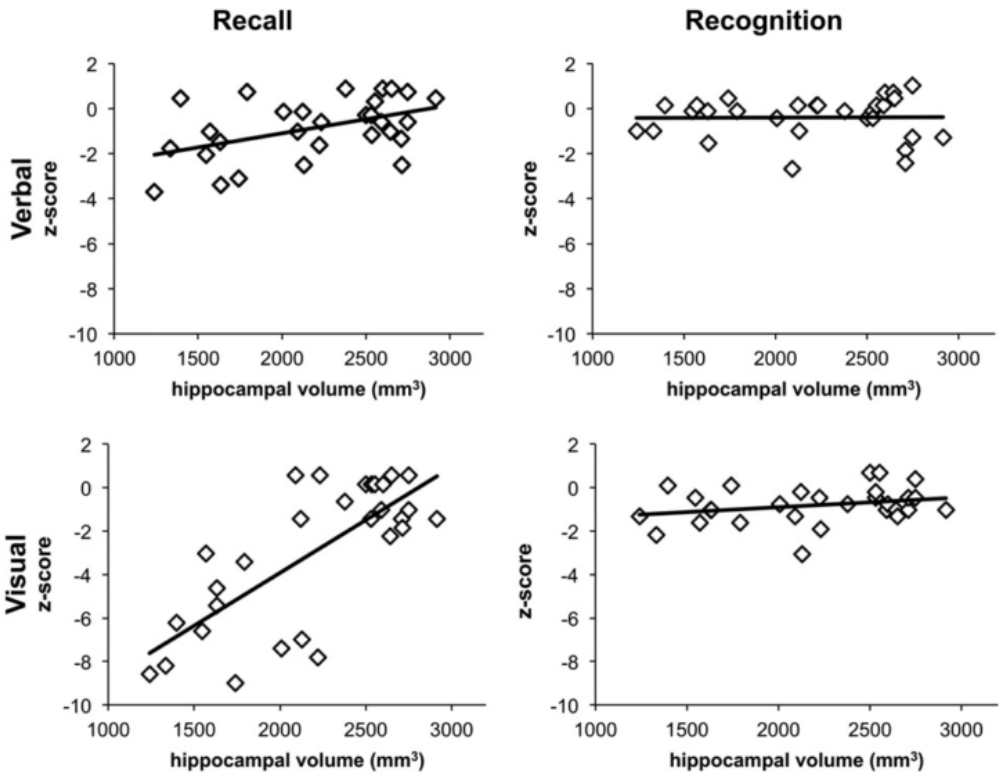


Vargha-Khadem, F. *et al. Science (80-.).* **277,** 376–380 (1997).

Spiers, H. J., Burgess, N., Hartley, T., Vargha-Khadem, F. & O'Keefe, J. *Hippocampus* **11,** 715–25 (2001).

Developmental Amnesia: Recall vs Recognition





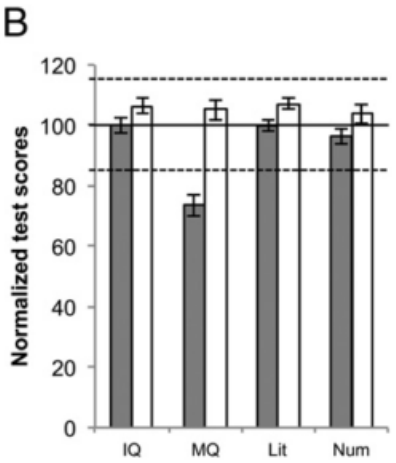
Patai, E. Z., Gadian, D. G., Cooper, J. M., Dzieciol, A. M., Mishkin, M., & Vargha-Khadem, F. (2015*Proceedings of the National Academy of Sciences* , *112*(41), 12830–12833.

Developmental Amnesia: Semantic vs Episodic Memory

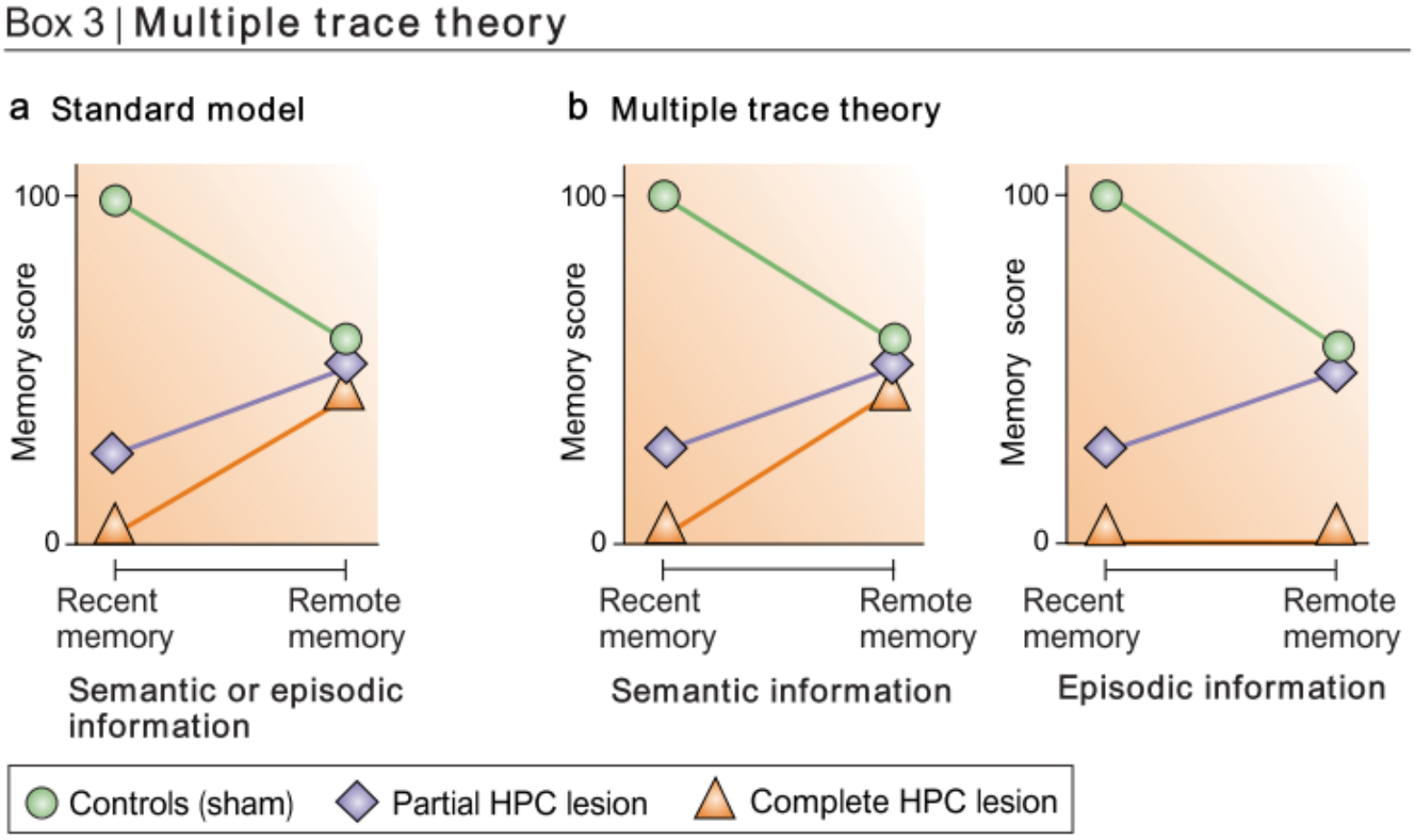
- High IQ, good working memory
- Normal schooling – fact memory intact (despite hippocampal lesion at early age!)
    - Fast mapping? (Sharon et al, 2011, PNAS)
- Impaired at visual and verbal recall
- Impaired topographical and associative memory
- **Tulving: episodic memory**

Tulving, E. (2002). Episodic memory: from mind to brain. *Annual Review of Psychology*, *53*, 1–25.

    - Recollective experience of the past
    - Postulated to be hippocampal dependent (always)
    - Independent of semantic memory



Consolidation Models



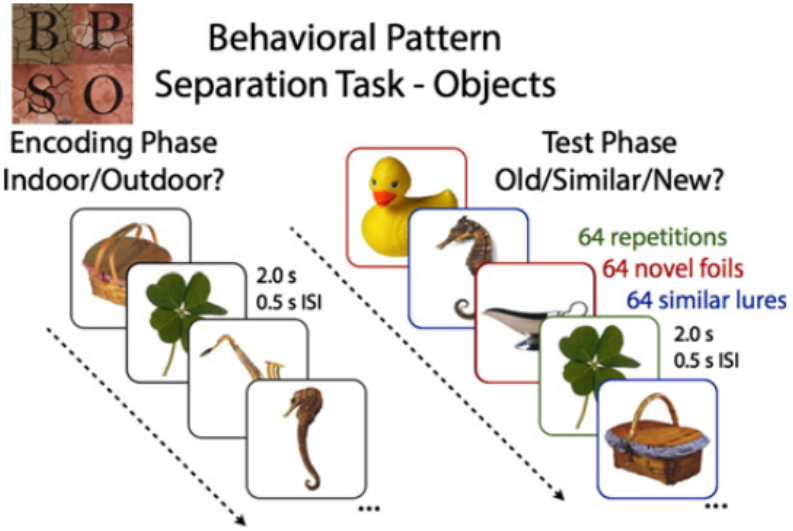
Squire LR (1992) Memory and the Hippocampus : A Synthesis From Findings With Rats , Monkeys , and Humans. Psychol Rev 99(2):195–231.

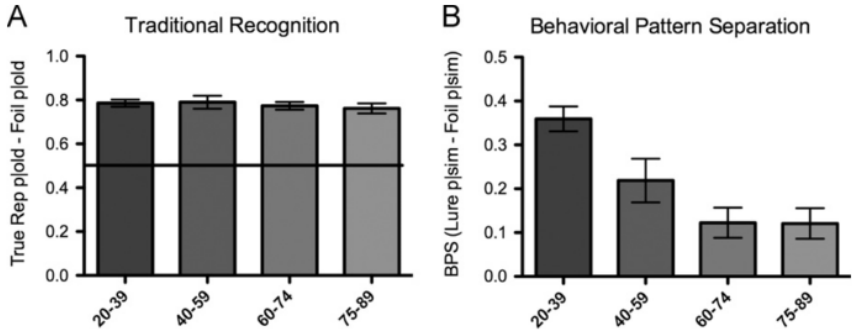
Squire LR, Zola-Morgan S (1998) Episodic Memory , Semantic Memory , and Amnesia. Hippocampus 8:205–211.

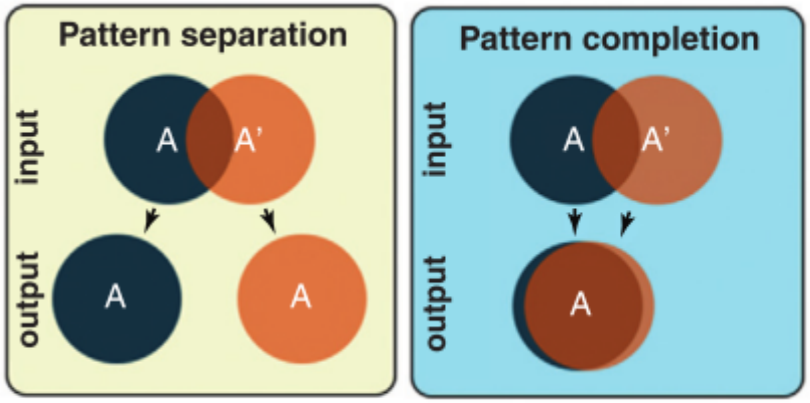
Winocur G, Moscovitch M (2011) Memory Transformation and Systems Consolidation. J Int Neuropsychol Soc 17(5):766–780.

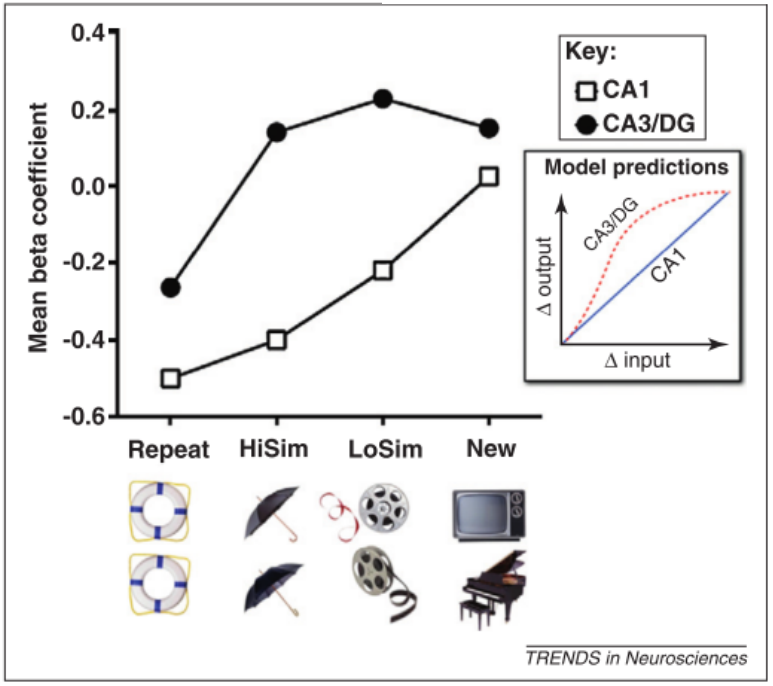
Nadel L, Moscovitch M (1997) Memory consolidation and the hippocampal complex. Curr Opin Neurobiol 7:217–227.

Recognition Memory – intact but is it?





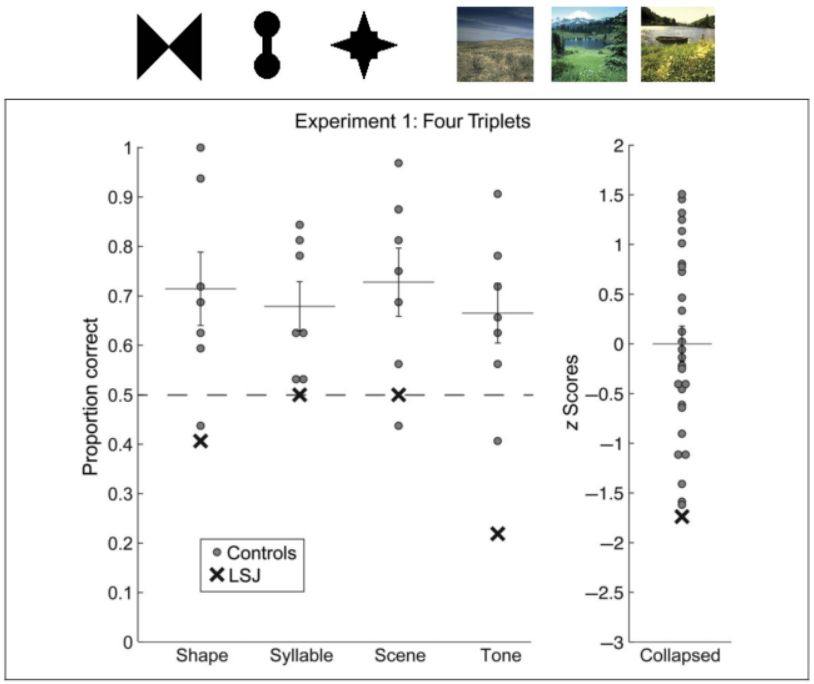




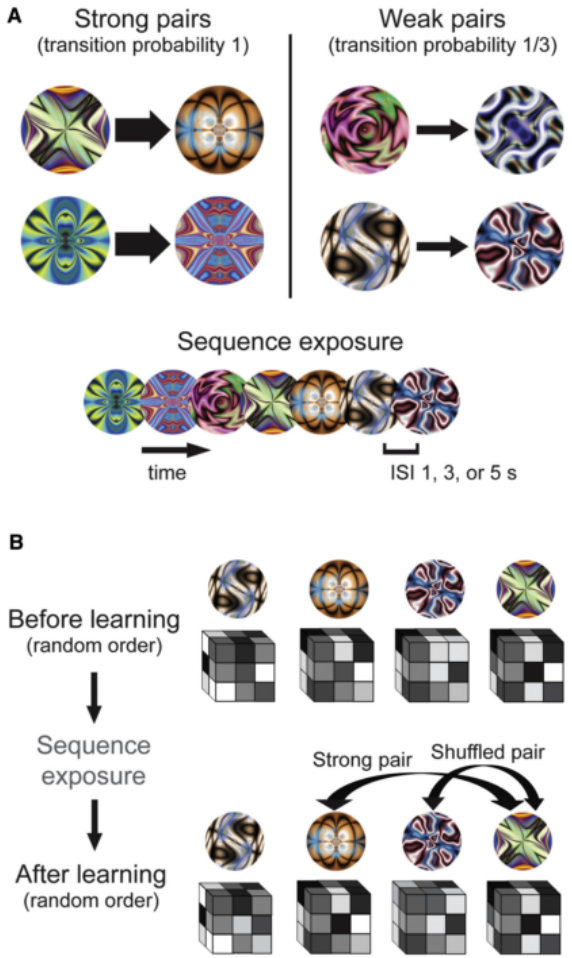
Stark, S. M., Yassa, M. a, Lacy, J. W., & Stark, C. E. L. (2013*Neuropsychologia*, 1–8.
Yassa, M. a, & Stark, C. E. L. (2011). *Trends in Neurosciences*, *34*(10), 515–25.

Statistical Learning

If hippocampus only needed for explicit memories (episodic and/or semantic) and implicit memory intact, then why are patients impaired at statistical learning?



Familiarity for individual items intact, just not the sequence

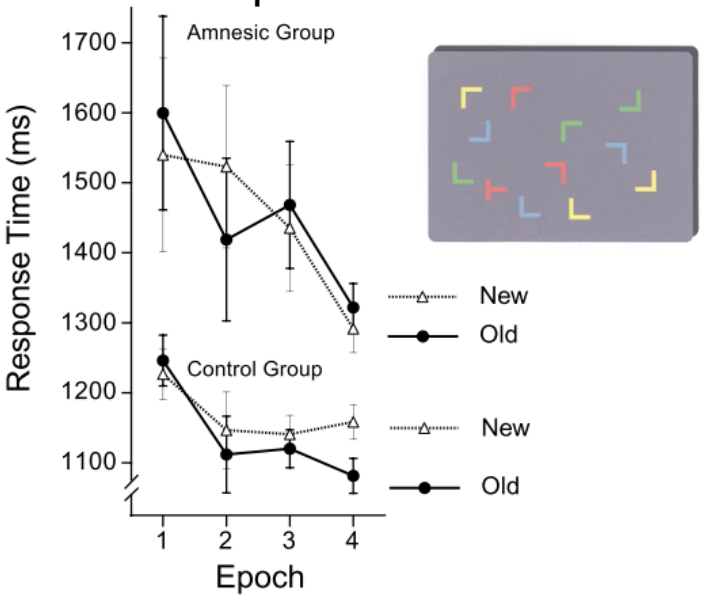


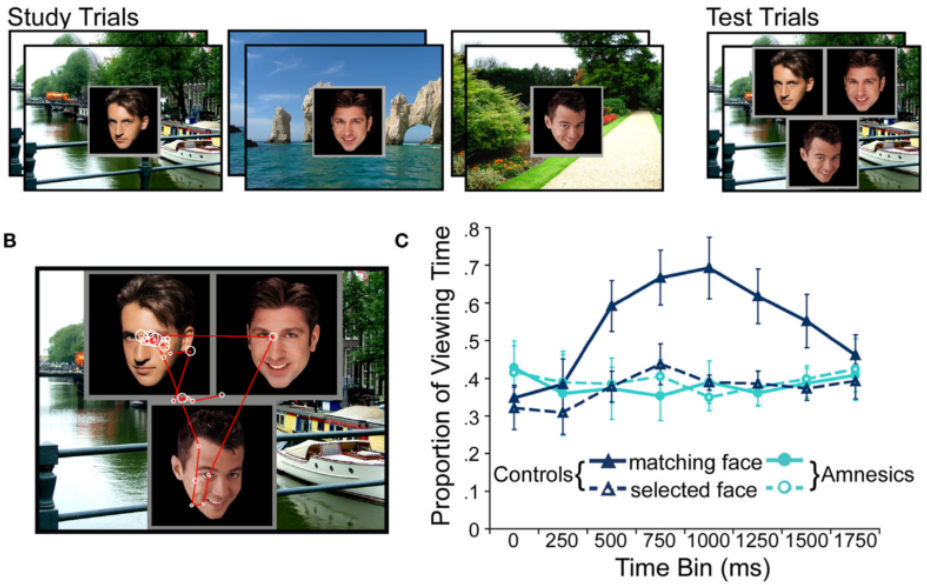
Patterns in the hippocampus more similar for strongly associated pairs

Schapiro, A. C., Emma Gregory, B. L. M. M., & Turk-Browne, N. B. (2014). *Journal of Cognitive Neuroscience*, *26*(8), 1736–1747.
Schapiro, A. C., Kustner, L. V., & Turk-Browne, N. B. (2012). *Current Biology*, *22*(17), 1622–1627.

More implicit stuff dependent on the hippocampus…

Amnesic patients do not show learning in repeated contexts



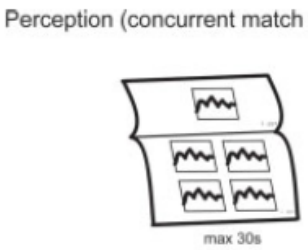


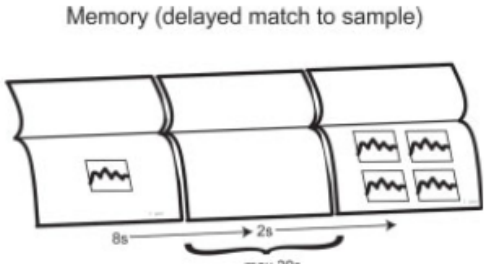
This result illustrates hippocampal recruitment, even when explicit memory has failed.

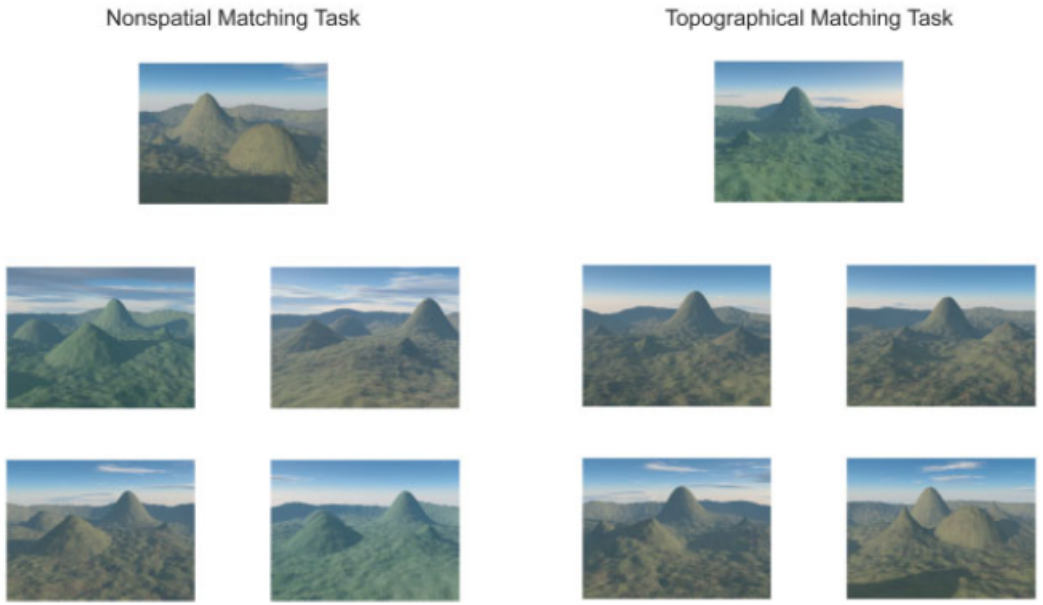
Incorrect Trials: High Viewing > Low Viewing

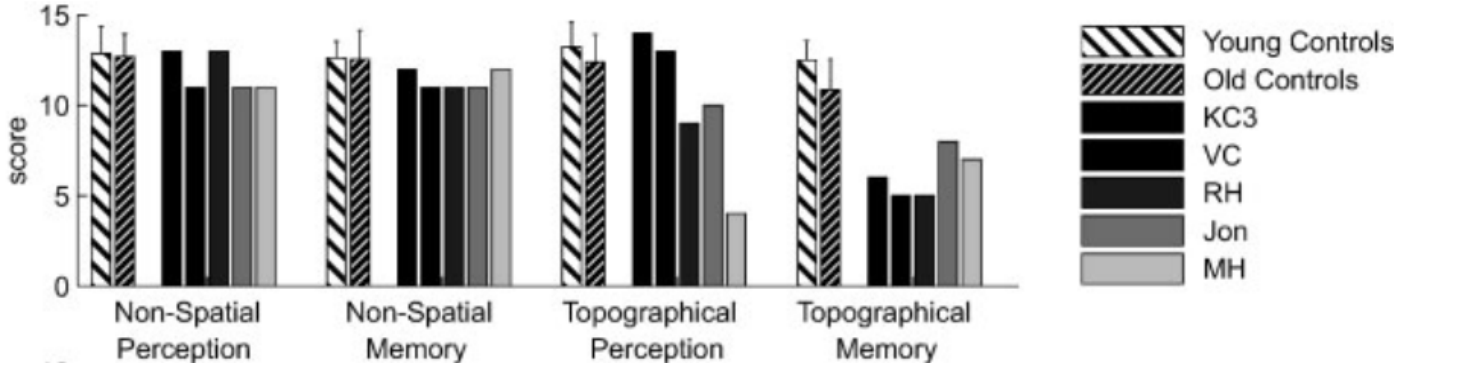
Chun, M. M., & Phelps, E. (1999). *Nature Neuroscience*, *2*(9), 844–7.
Review: Hannulaet al. (2010). *Frontiers in Human Neuroscience*,

“Perception” in the Hippocampus









Hartley, T., Bird, C. M., Chan, D., Cipolotti, L., Husain, M., Vargha-Khadem, F., & Burgess, N. (2007). *Hippocampus*, *17*(1), 34–48.
Lee, A. C. H., Yeung, L.-K., & Barense, M. D. (2012). The hippocampus and visual perception. *Frontiers in Human Neuroscience*, *6*(April), 1–17.

Frameworks in Memory
UPDATED

- **Explicit vs Implicit** – depends how you test it
- **Semantic vs Episodic** – can't reliably test in animals by definition
- **Recall/Recollection vs Recognition/Familiarity** – depends on stimuli

HIPPOCMAPUS AS A ***RELATIONAL*** *PROCESSOR*

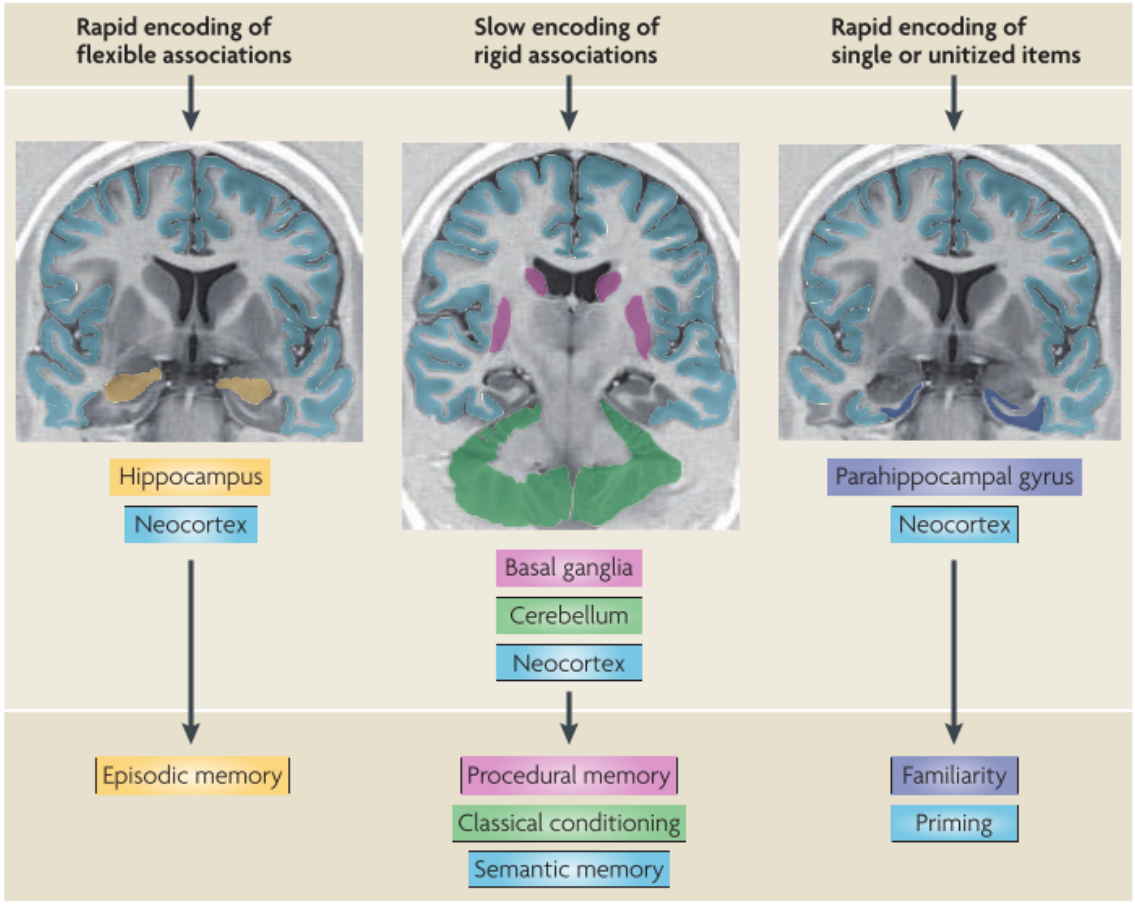
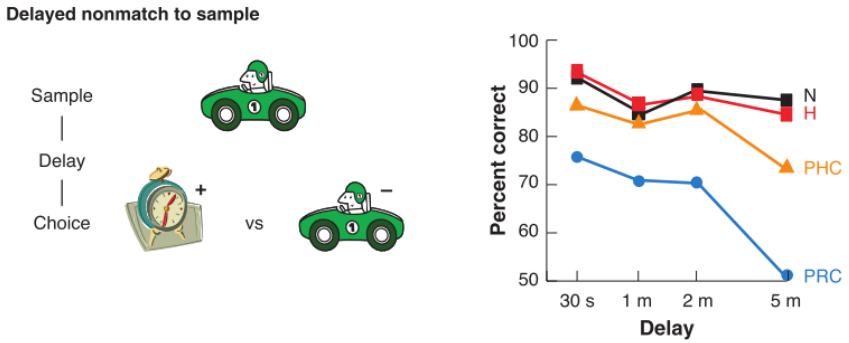
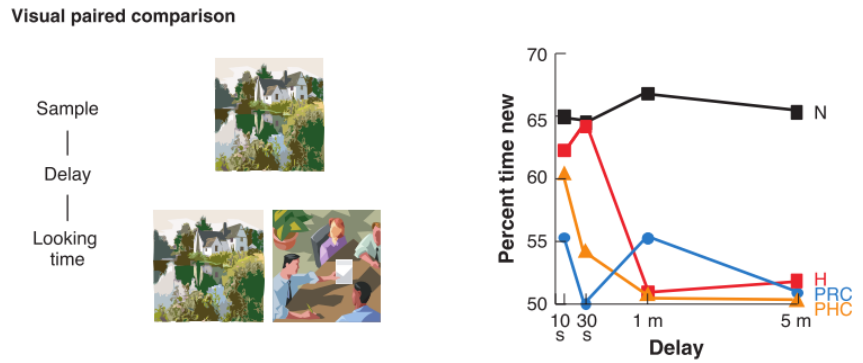


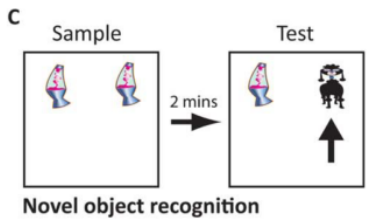
Figure 3 | **A processing-based division among memory systems.** The model distinguishes three basic processing modes that differ with respect to three variables: rapid versus slow encoding; associative versus single item encoding; and flexible and compositional versus rigid and unitized representation. The three processing modes select for specialized brain systems, which in turn generate qualitatively distinct memories that can be classified in traditional terms. Consciousness of encoding and retrieval does not select for memory systems and hence does not feature in this model.

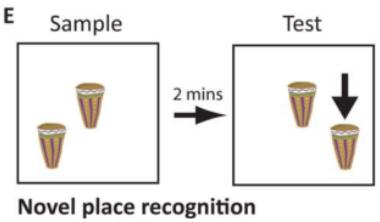
Henke, K. (2010). A model for memory systems based on processing modes rather than consciousness. *Nature Reviews Neuroscience*, *11*(7), 523–532.

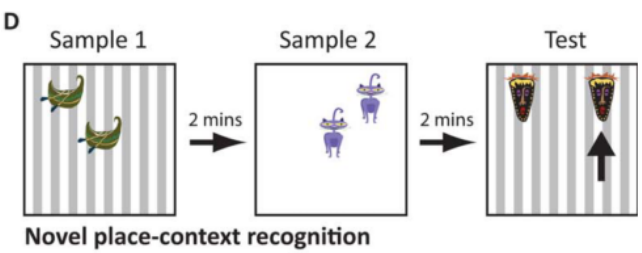
Hippocampus as Relational Processor

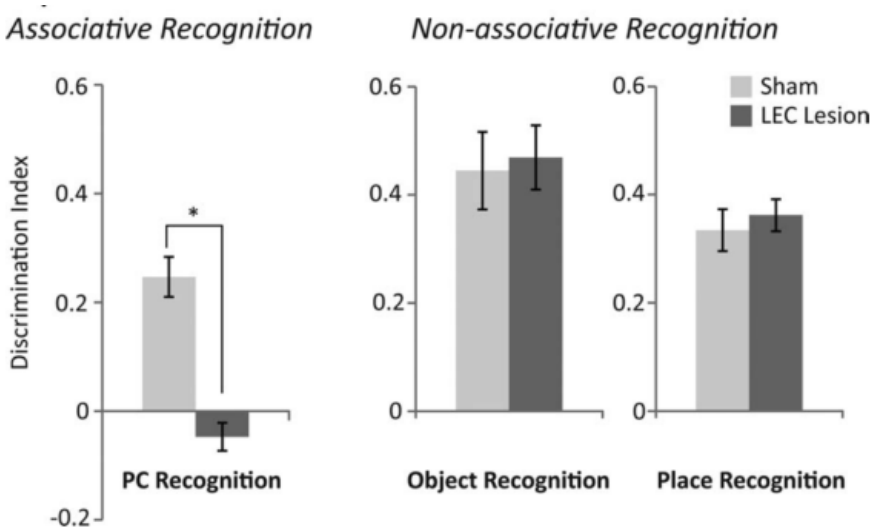






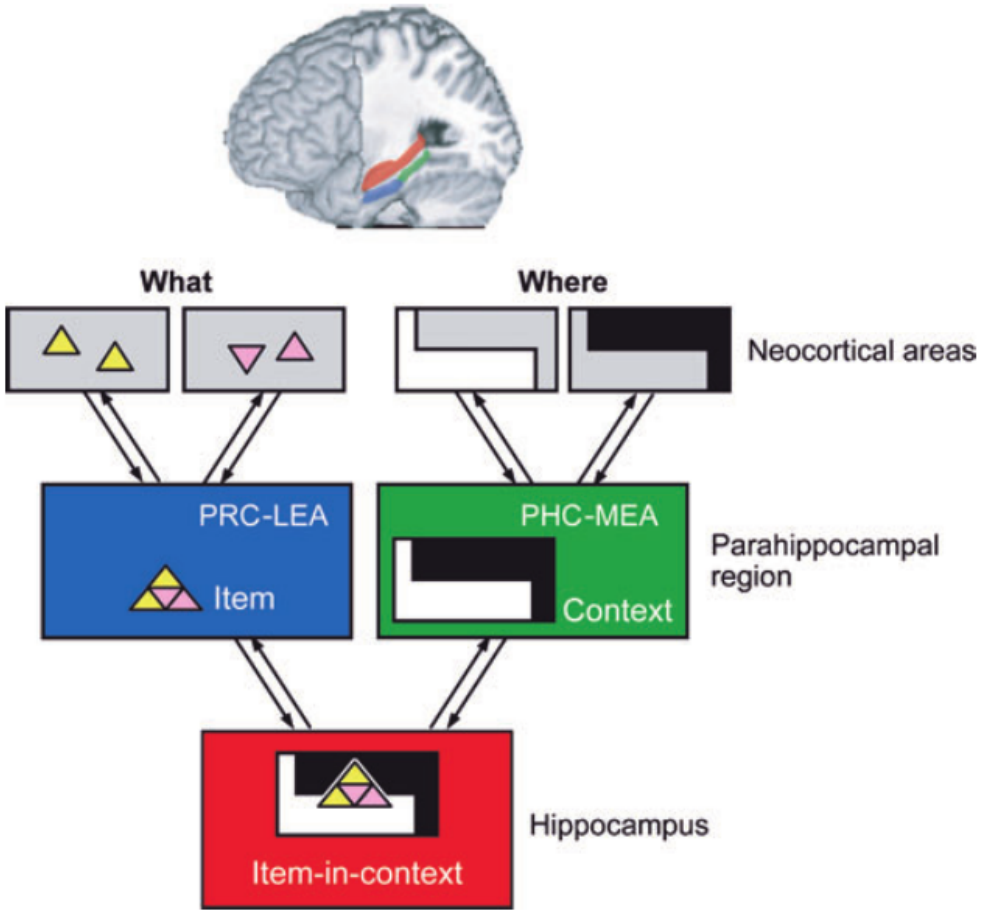






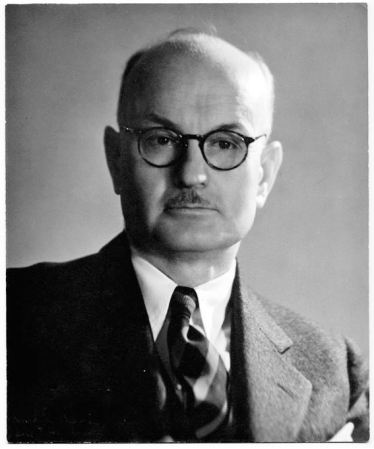
Nemanic, S., Alvarado, M. C., & Bachevalier, J. (2004). *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *24*(8), 2013–26.
Wilson, D. I. G., Watanabe, S., Milner, H., & Ainge, J. A. (2013 *Hippocampus*, *23*(12), 1280–1290.

Hippocampus as Relational Processor

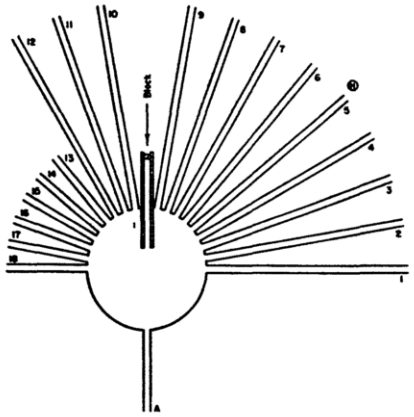


Eichenbaum, H., Yonelinas, A. P., & Ranganath, C. (2007). The medial temporal lobe and recognition memory. *Annual Review of Neuroscience*, *30*, 123–52.

The Cognitive Map



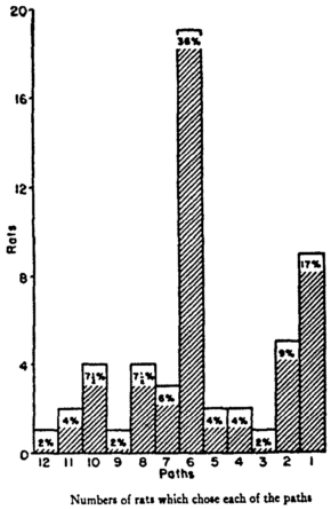
Edward Tolman



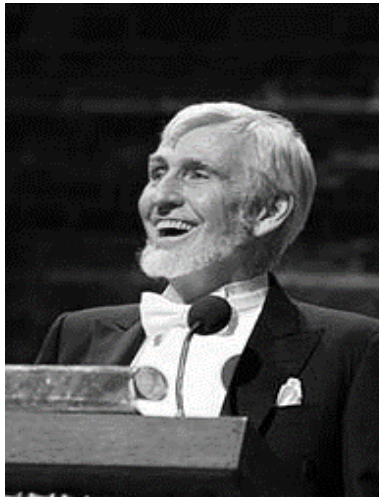
Apparatus used in the test trial

FIG. 16

(From E. C. Tolman, B. F. Ritchie and D. Kalish, Studies in spatial learning. I. Orientation and short-cut. *J. exp. Psychol.*, 1946, **36**, p. 17.)



Numbers of rats which chose each of the paths



John O'Keefe

- Representation of space
- Flexible
- Global and local elements encoded

Tolman, E. C. (1948). Cognitive maps in rats and men. *Psychological Review*, *55*(4), 189–208.
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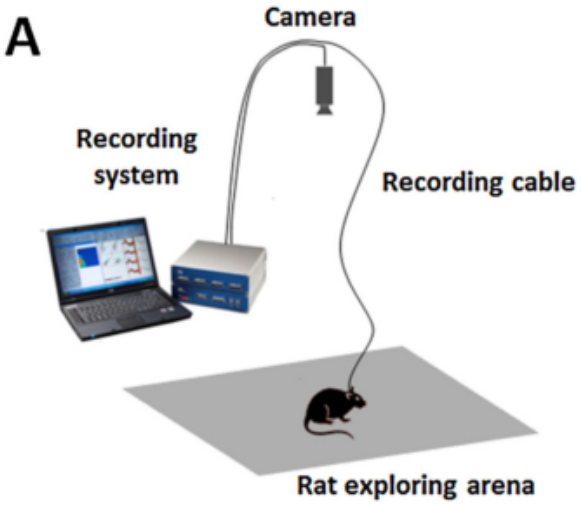
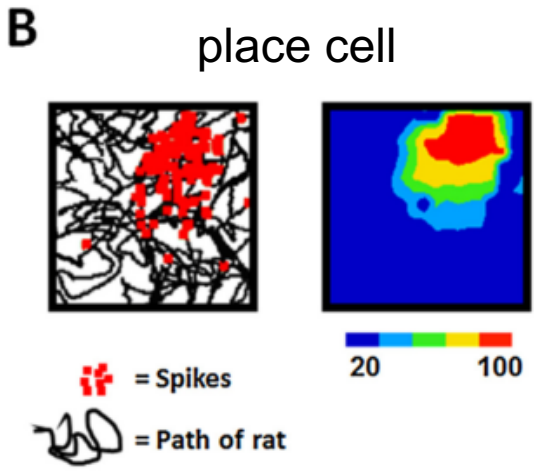
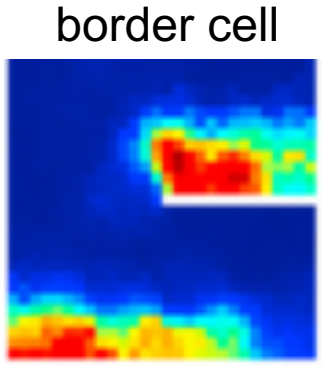
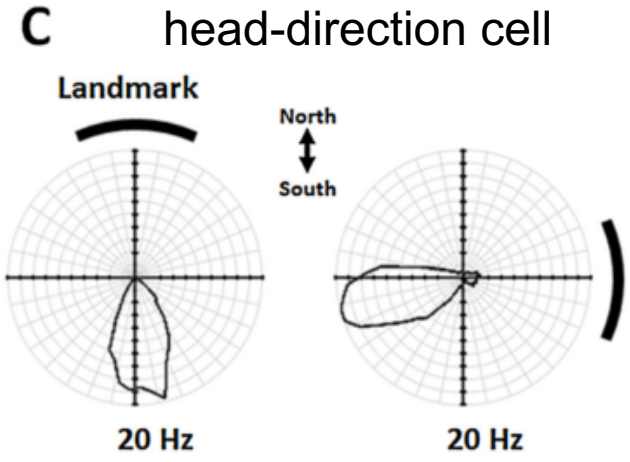
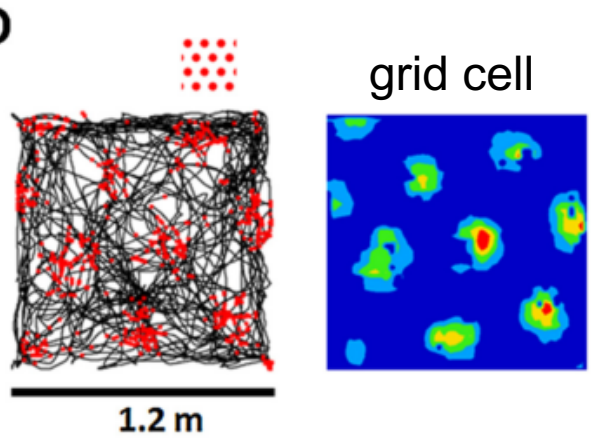
Cells that form The Cognitive Map











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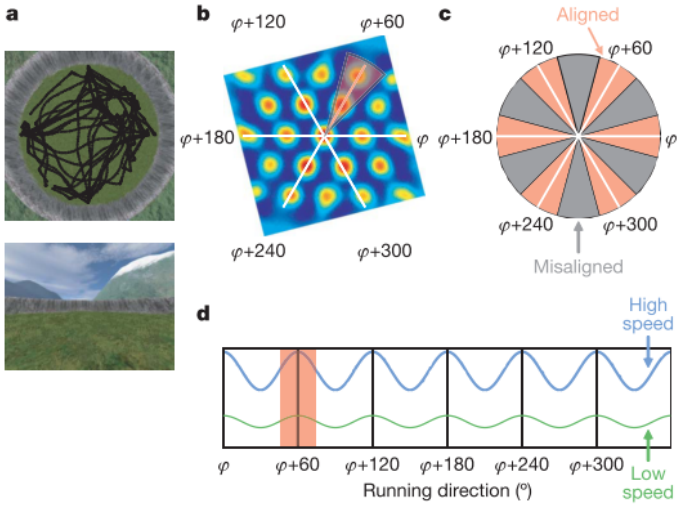
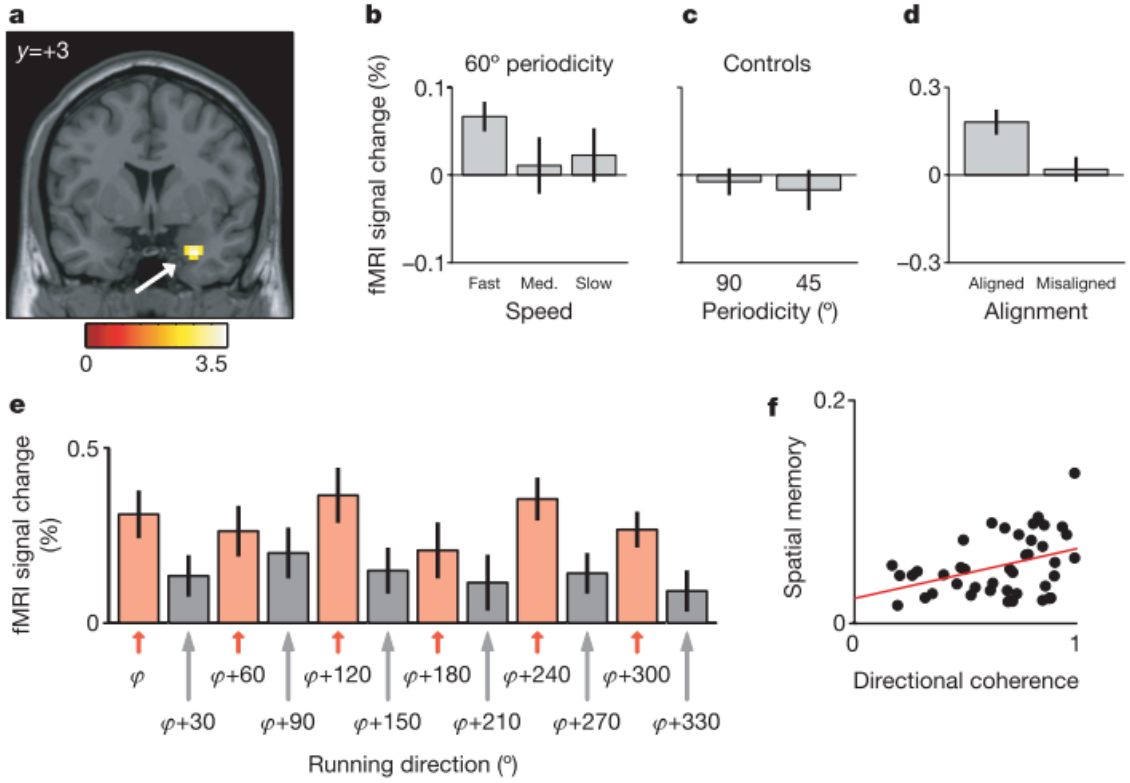
The Cognitive Map in Humans





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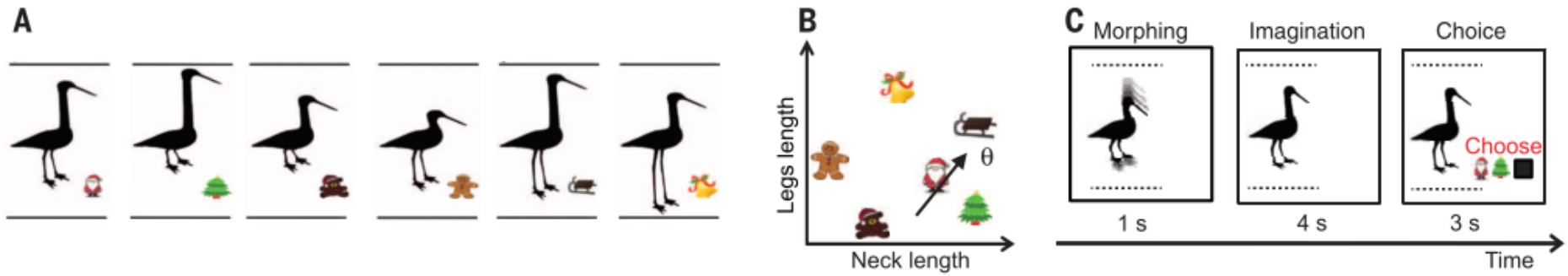
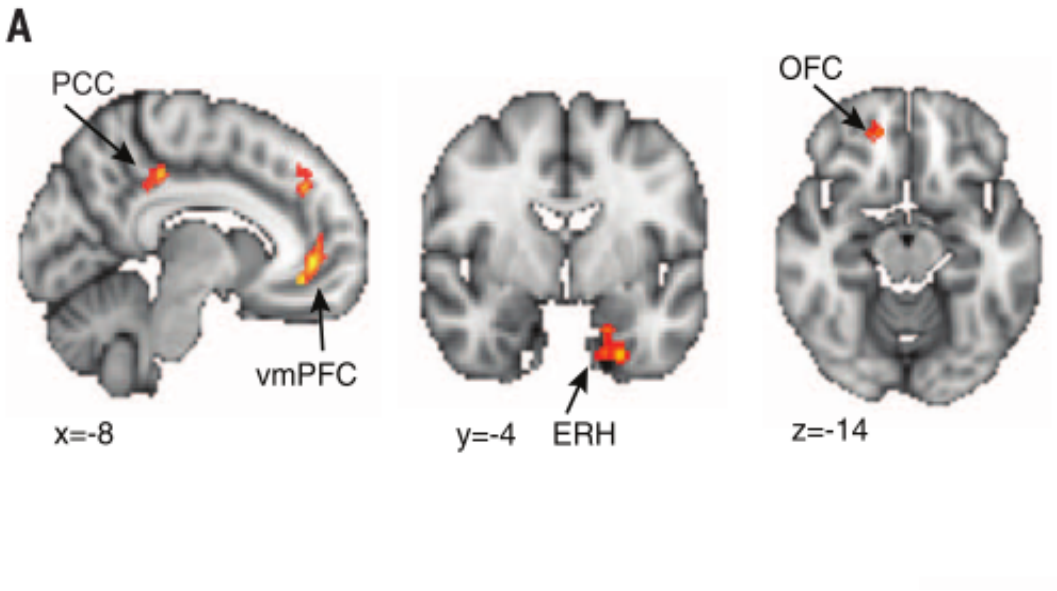
Nadasdy, Z., Nguyen, P., Török, Á., Shen, J., Briggs, D., & Modur, P. (2017). Context-dependent spatially periodic activity in the human entorhinal cortex. *PNAS*.

The Cognitive Map in Humans: Beyond Physical Space





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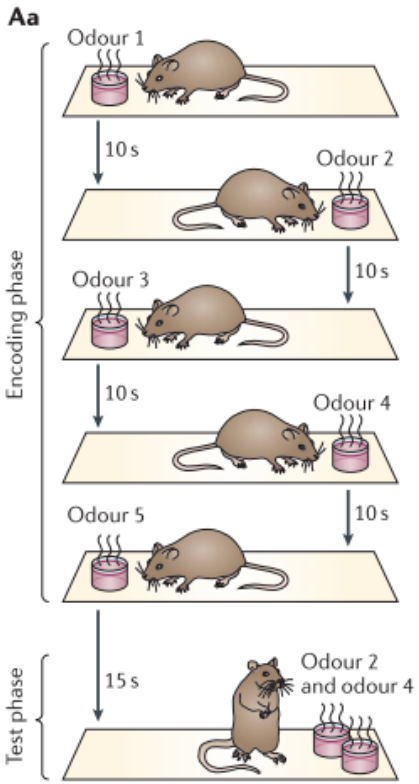
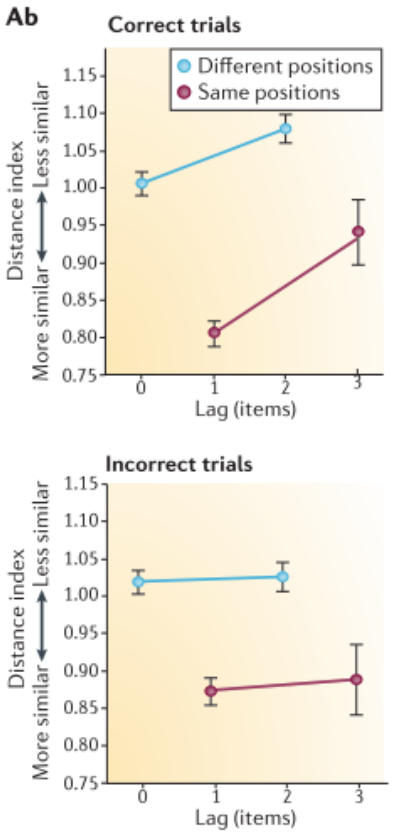
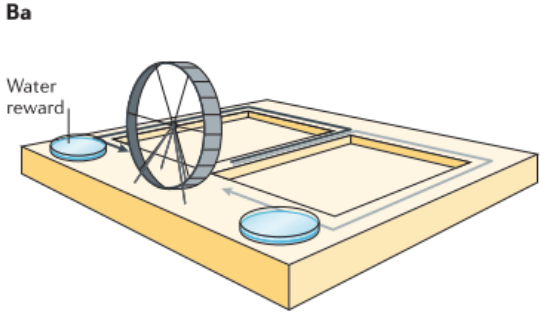
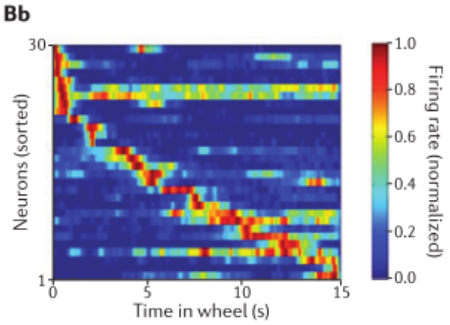
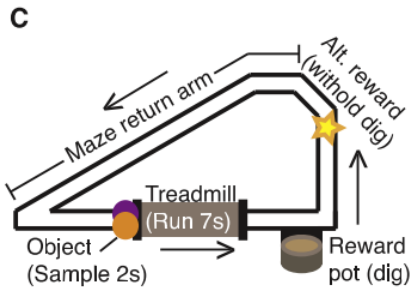
Or Time Cells?

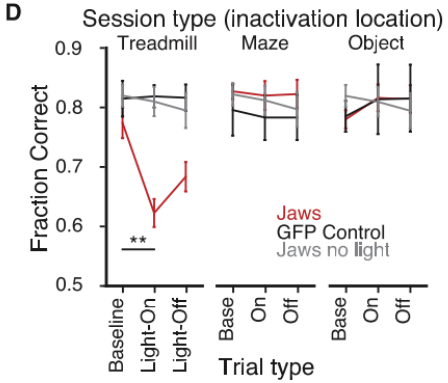












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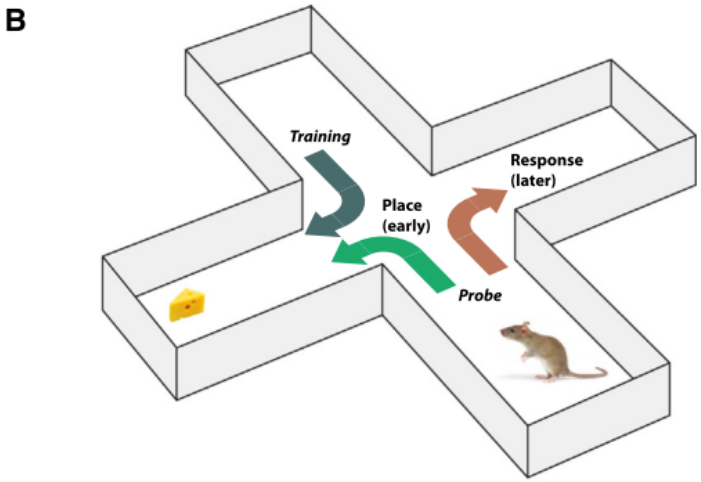
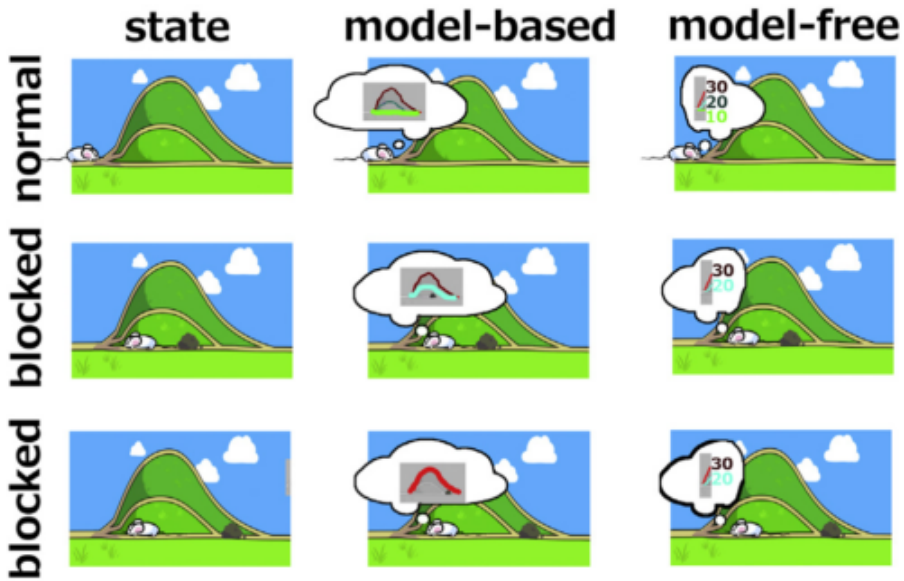
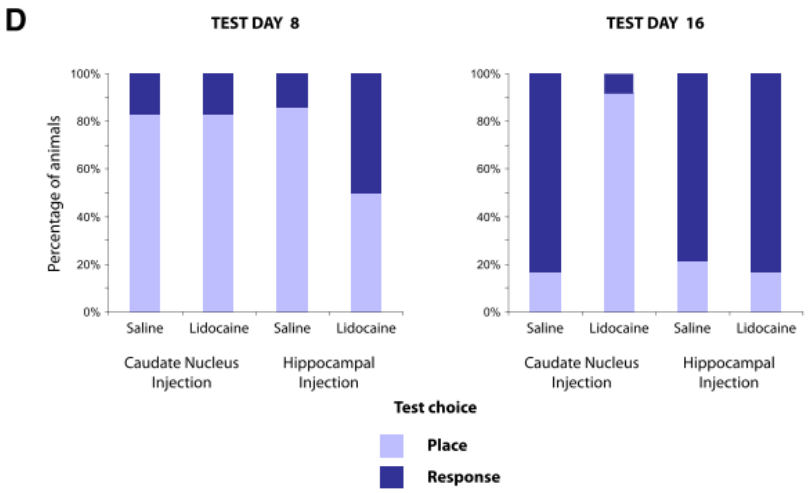
Hippocampus vs Striatum







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Is the Hippocampus doing Memory or Navigation?

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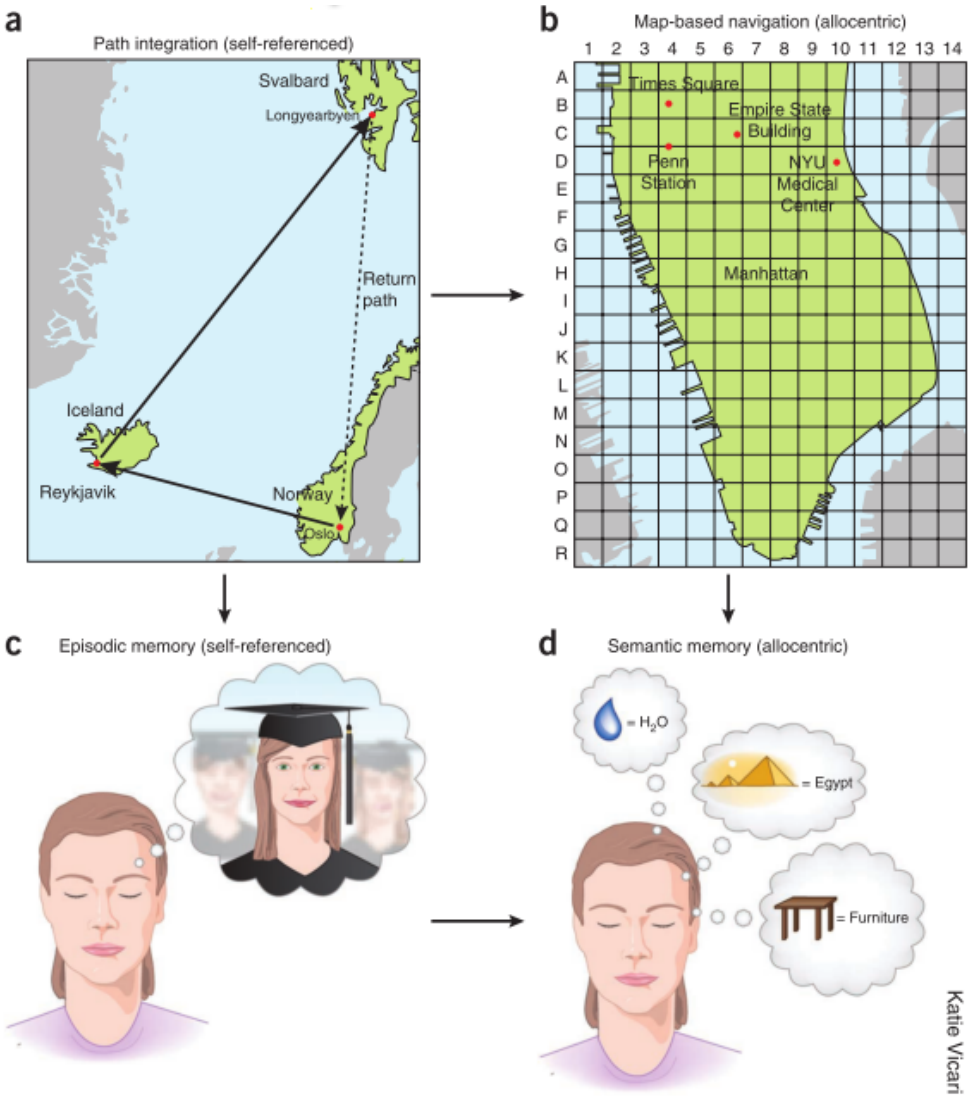
Is Navigation Supporting Memory?



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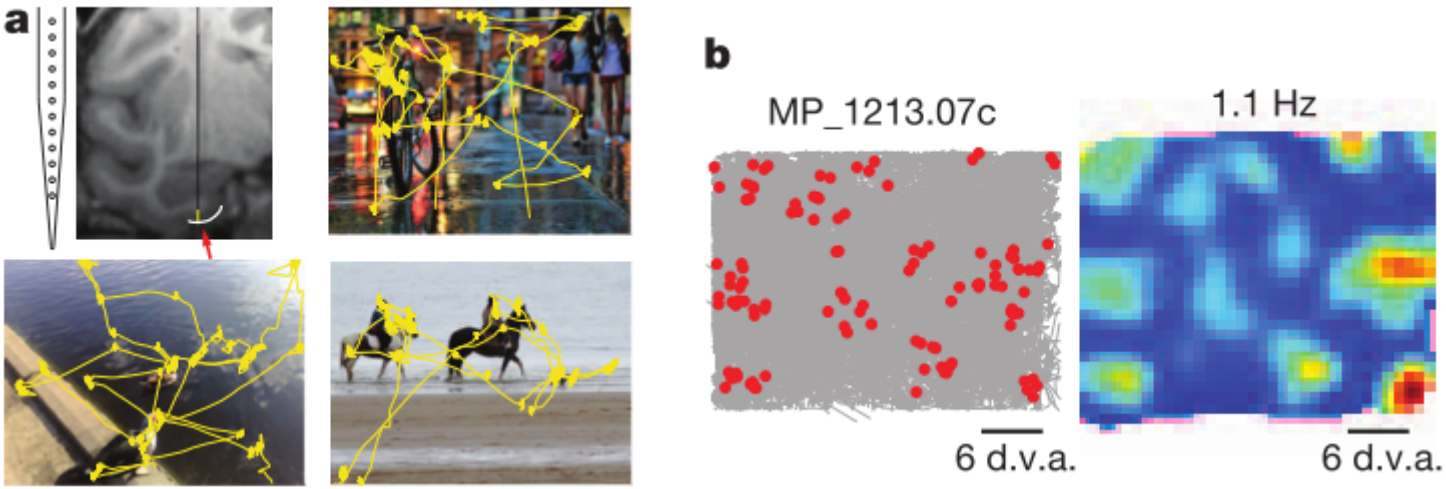
Is Navigation Supporting Memory?

"As active exploration is a prerequisite for the computation of distances and calibration of landmark relationships, we submit that movement is the primary source of the brain's ability to remember past experiences and plan future actions."

But what about saccades? Do sponges have no memory?



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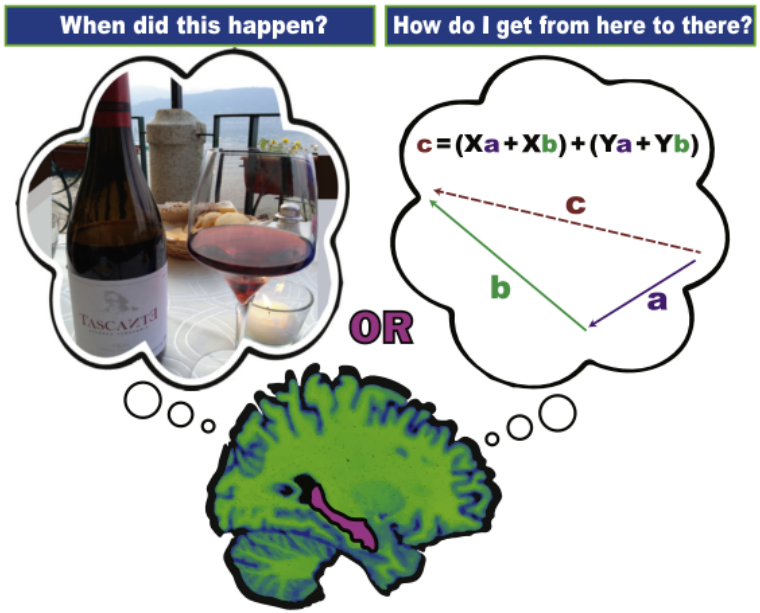
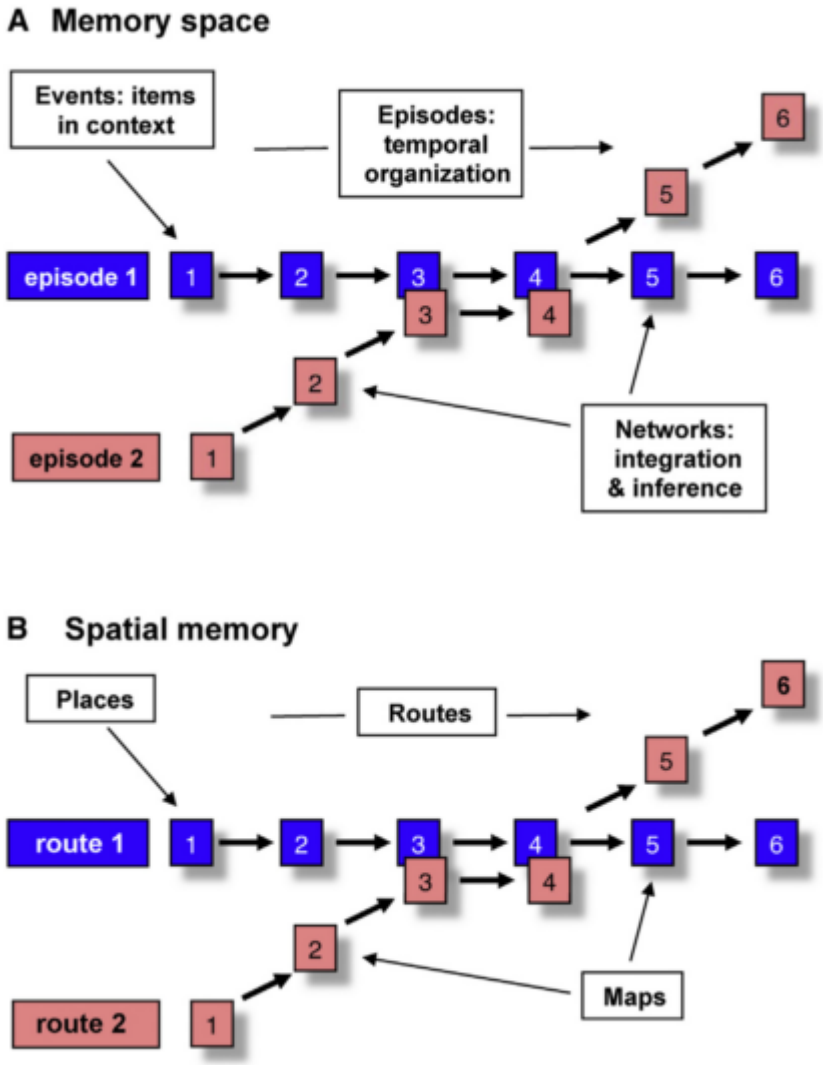
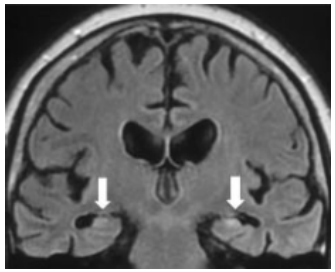
Is Navigation Supporting Memory?

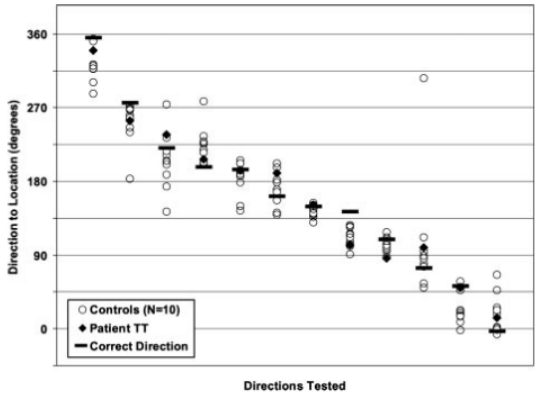




Eichenbaum, H., & Cohen, N. J. (2014). Can We Reconcile the Declarative Memory and Spatial Navigation Views on Hippocampal Function? *Neuron*, *83*(4), 764–770.

Hippocampal role in long-term memory and navigation





Intact: Navigation on major roads
Impaired: Small roads & non-salient landmarks

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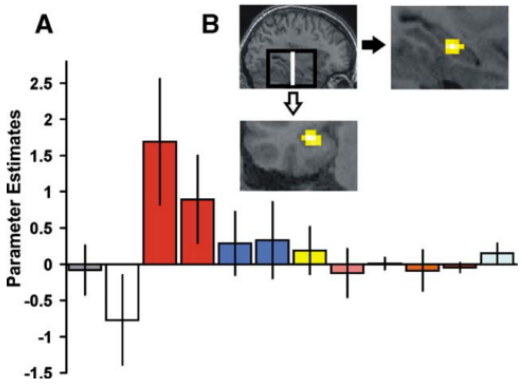
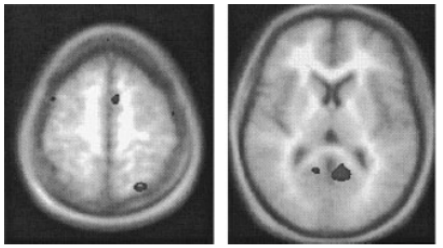
Maguire, E. A., Nannery, R. & Spiers, H. J. Brain (2006).
Rosenbaum, R. S. et al. Nat Neurosci (2000).



Left hippocampus active at the start of the trial when a new goal is given or updated mid-route

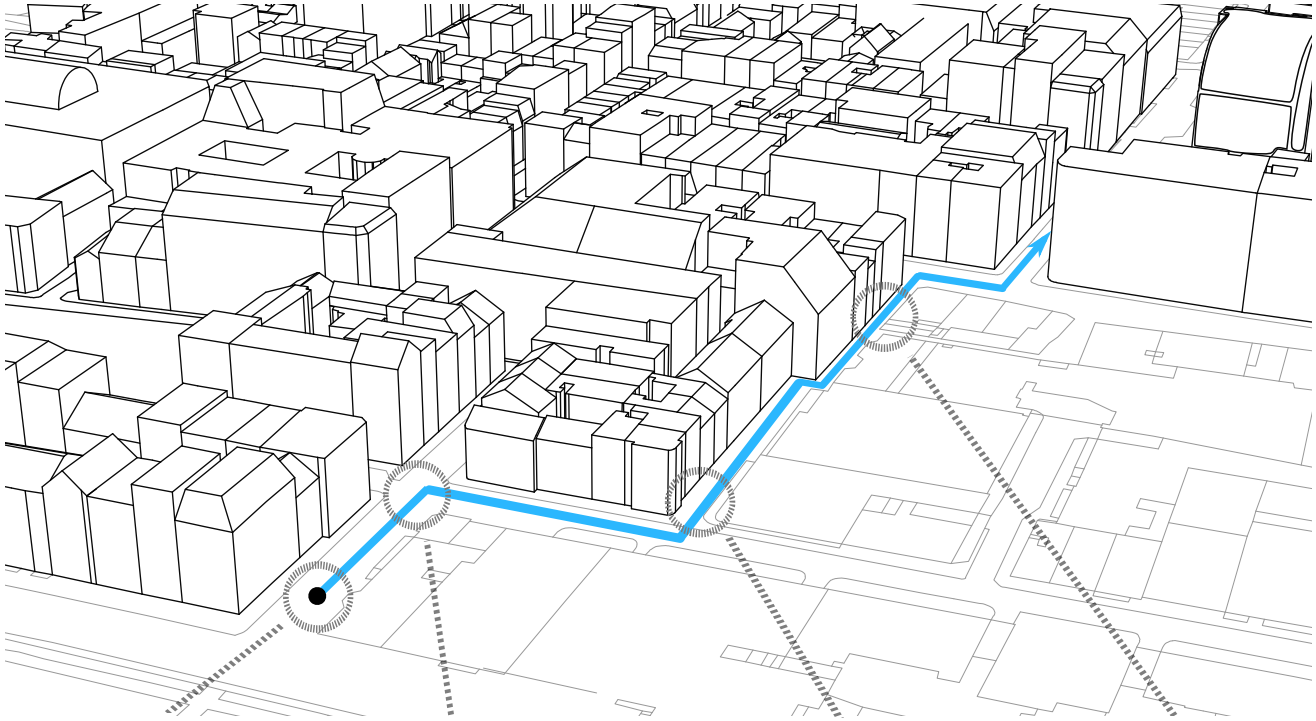
Spiers, H. J. & Maguire, E. A. Neuroimage 31, 1826 1840 (2006).



No hippocampal activity found in navigating remote locations

Rosenbaum, R. S., Ziegler, M., Winocur, G., Grady, C. L. & Moscovitch, M. Hippocampus (2004).

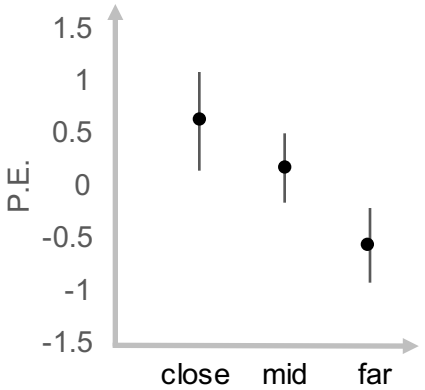
Distance coding in the hippocampus

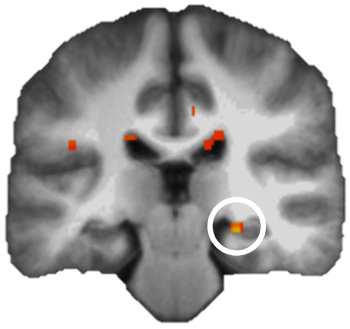


New Goal	Decision Point	New Street Entry	Travel
			
Entorhinal Euclidian	Hippocampus Path Distance & Goal Direction	Hippocampus # of Connected Streets	Hippocampus Path Distance

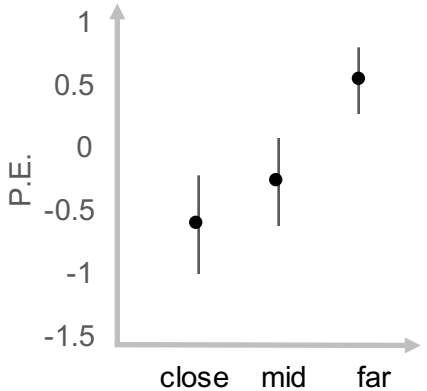
Howard, L. R. et al. Curr. Biol. (2014).; Javadi, A.-H. et al. Nat. Commun. (2017).; Spiers, H. J. & Barry, C. Curr. Opin. Behav. Sci.(2015).

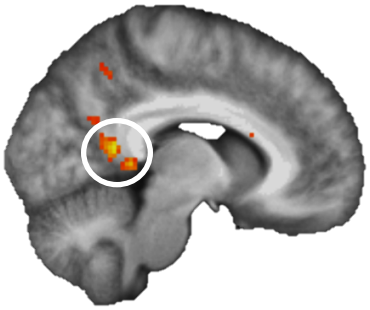
Place among other studies…



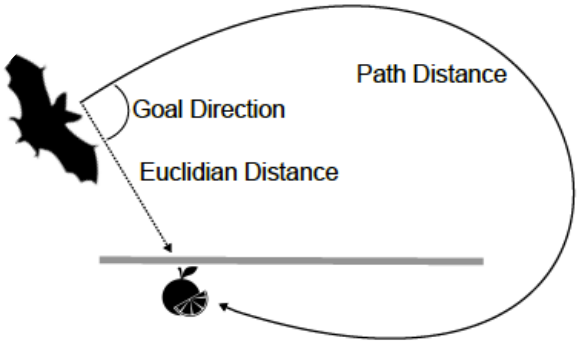


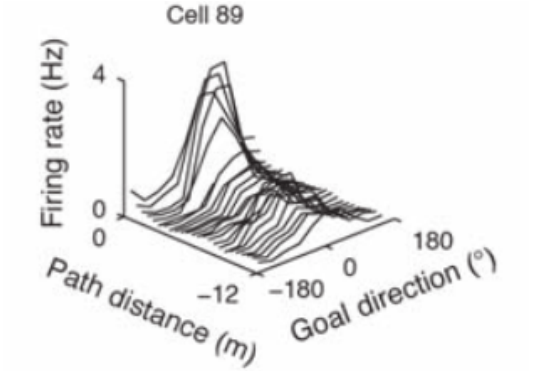
posterior hippocampus
RECENT

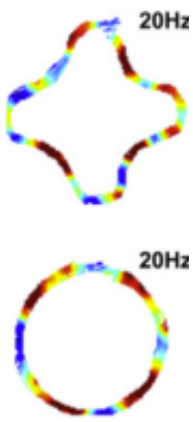


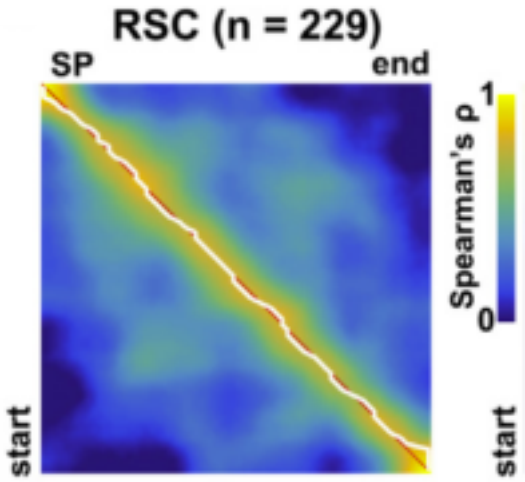


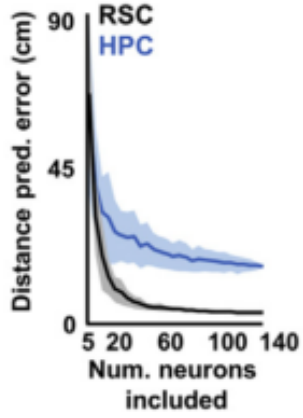
retrosplenial cortex
FAMILIAR











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