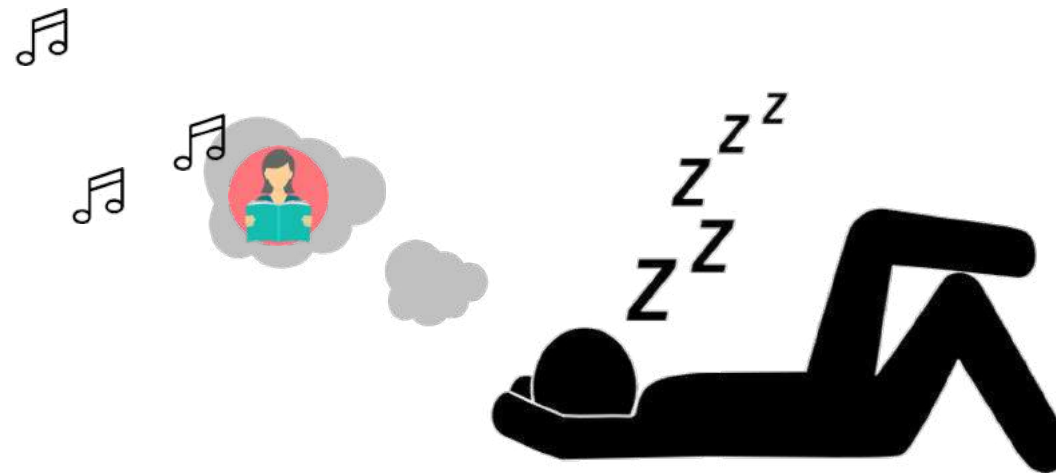
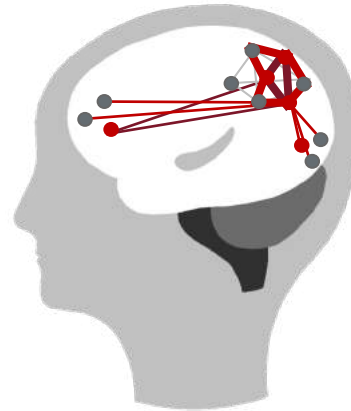

Human Sleep and Memory Consolidation





Advantage: We can ask our participants about their subjective experience!

Disadvantage: Methodological constraints

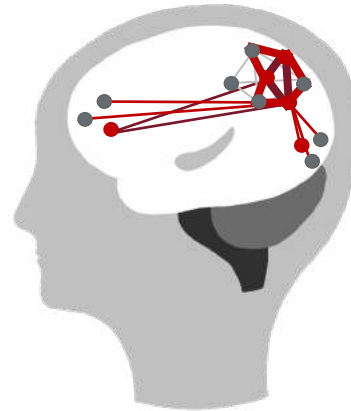


How do we store memories?

Perception

Neuronal activity
Memory storage in neural substrate
→ „The engram“ (Semon, 1904)

Memory



Location of the engram?

Karl Lashley: In search of the engram, 1950

No definite result on location of the engram in the cortex.

Distributed representation?

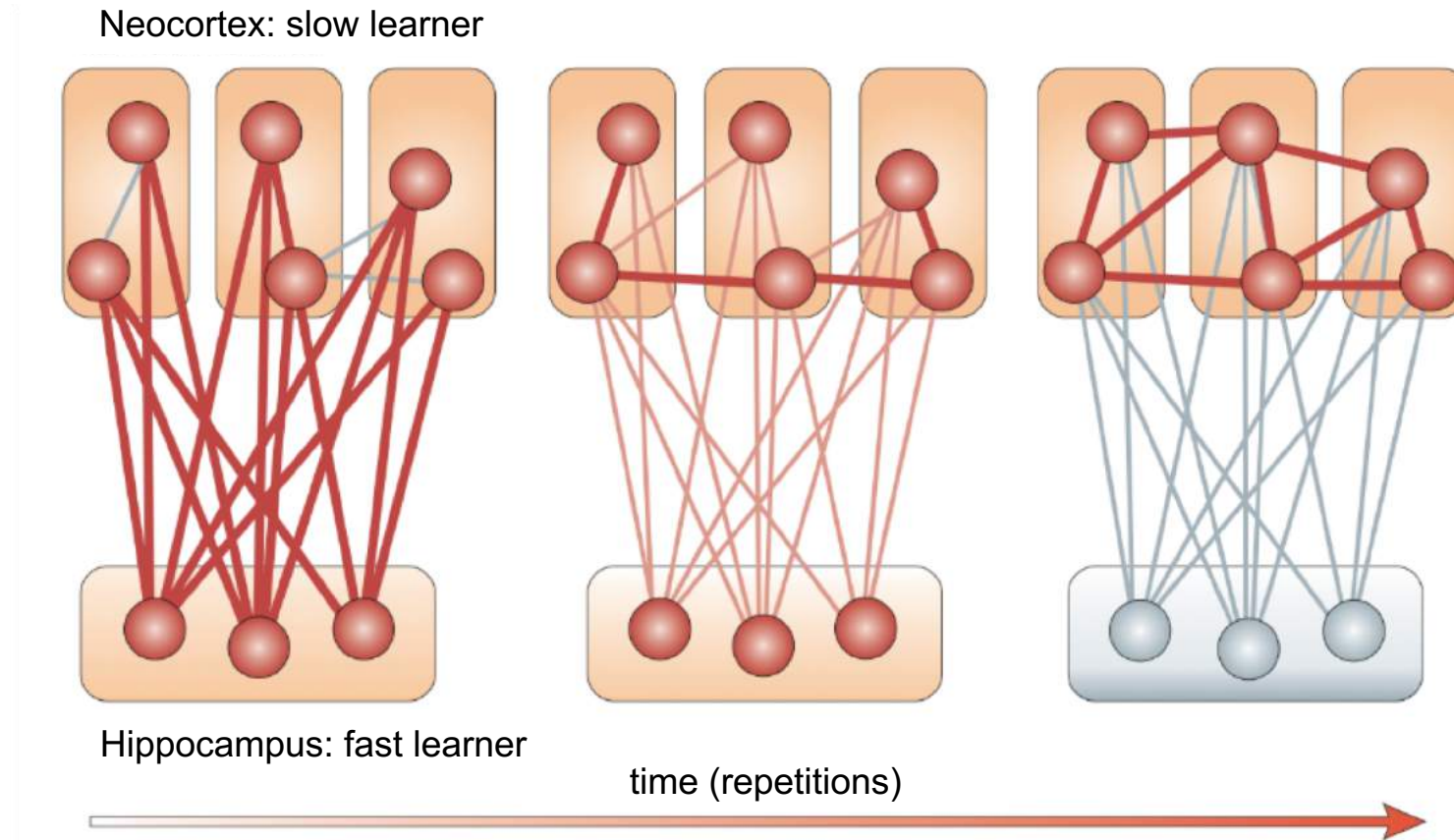
Scoville & Milner 1957: Patient H.M.

Massive memory deficits after removal of the hippocampus.

Older memories and semantic memory remained intact.

Does the engram change location over time?

The standard model of memory consolidation





What is the role of sleep in this?

It is [43] a curious fact, of which the reason is not obvious, that the interval of a single night will greatly increase the strength of the memory, whether this be due to the fact that it has rested from the labour, the fatigue of which constituted the obstacle to success, or whether it be that the power of recollection, which is the most important element of memory, undergoes a process of ripening and maturing during the time which intervenes. Whatever the cause, things which could not be recalled on the spot are easily co-ordinated the next day, and time itself, which is generally accounted one of the causes of forgetfulness, actually serves to strengthen the memory. On the other hand, the abnormally rapid [44] memory fails as a rule to last and takes its leave as though, its immediate task accomplished, it had no further duties to perform. And indeed there is nothing surprising in the fact that things which have been implanted in the memory for some time should have a greater tendency to stay there.

Quintillian, 100 AD

Sleep benefits memory retention

MINOR STUDIES FROM THE PSYCHOLOGICAL LABORATORY
OF CORNELL UNIVERSITY

Communicated by E. B. TITCHENER

LXXII. OBLIVISCENCE DURING SLEEP AND WAKING

By JOHN G. JENKINS and KARL M. DALLENBACH

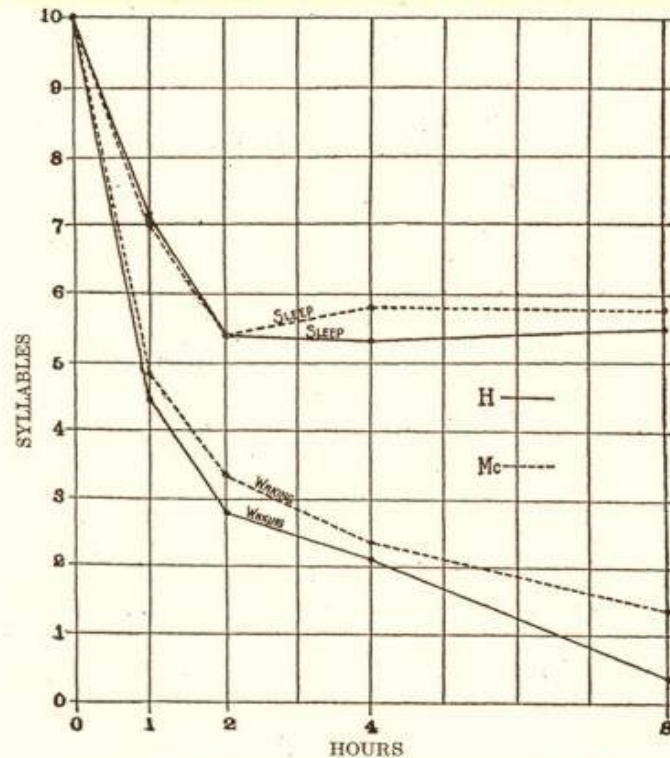
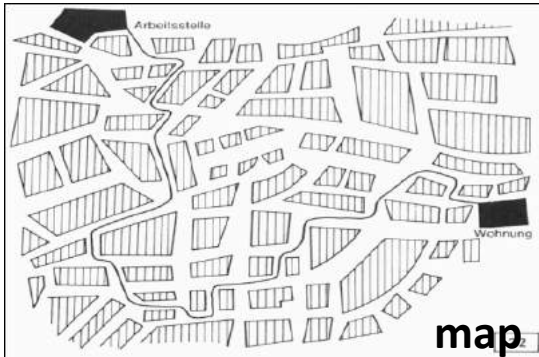


FIG. I. Average Number of Syllables Reproduced by each O after the Various Time-Intervals of Sleep and Waking

(based on
Ebbinghaus' forgetting
curves, 1885)

Is this effect active or passive?

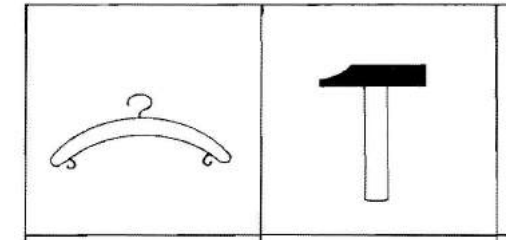
Meditation as a state of reduced interference



phone numbers

1. Swimming pool....220
2. City hall.....200
3. School.....777
4. Pharmacy.....191
5. Museum.....300

objects



LGT-3, Bäumlér



active wake

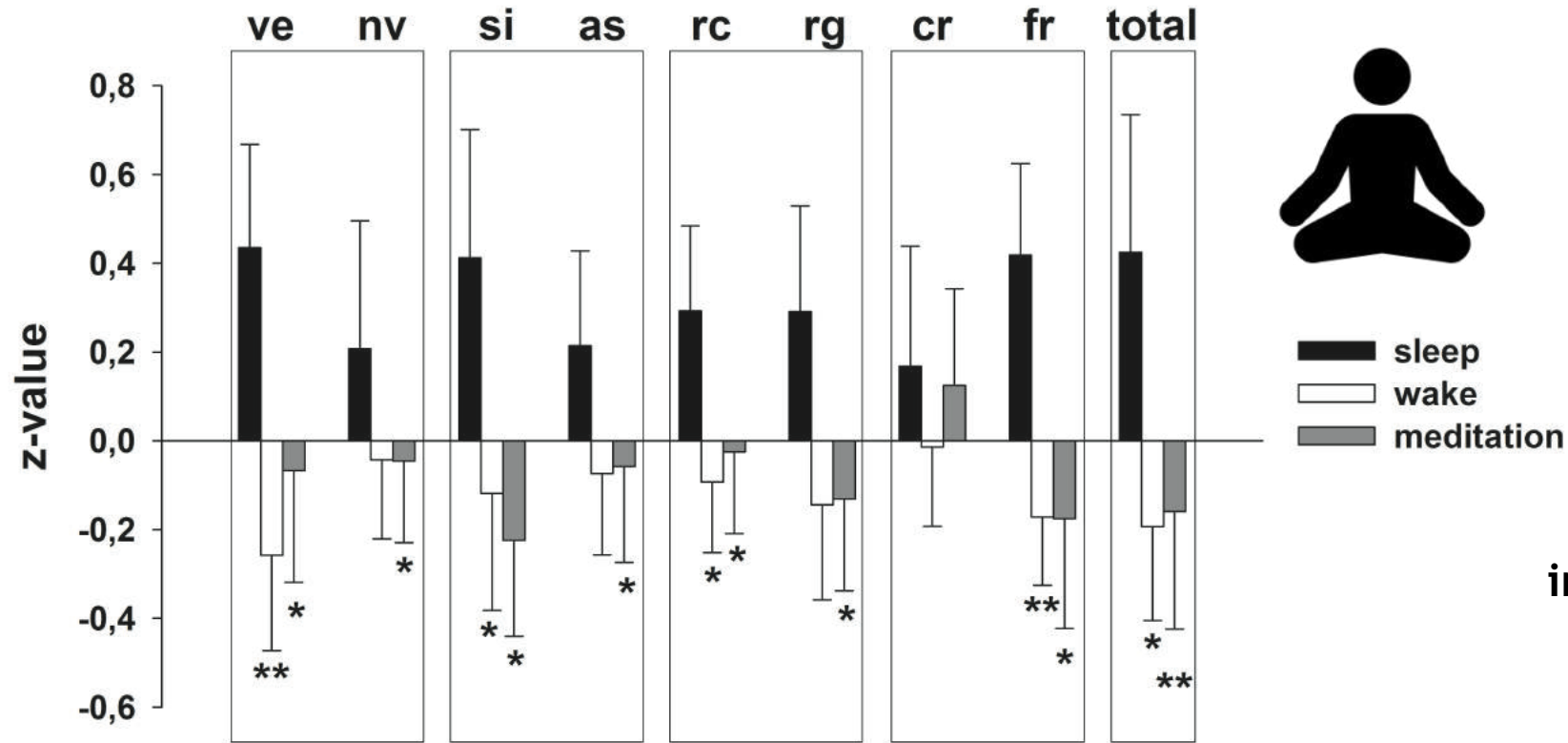


sleep



meditation

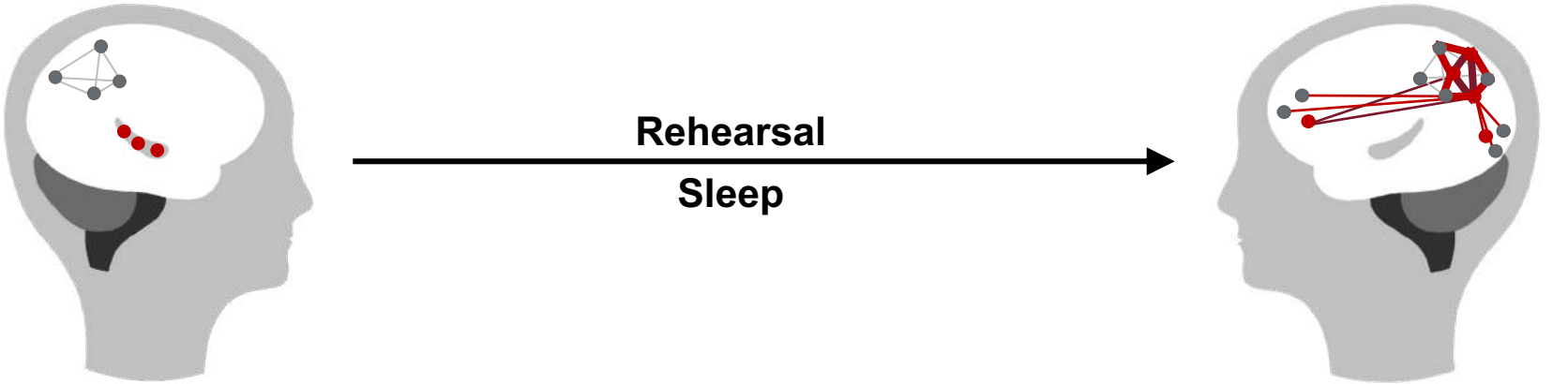
Meditation as a state of reduced interference



ve = verbal, nv= nonverbal; si = single item, as = associated item;
rc = recall, rg = recognition; cr = cued recall, fr = free recall

A simple reduction of interference does not have the same beneficial effect on declarative memory consolidation as sleep.

Mechanisms of systems memory consolidation



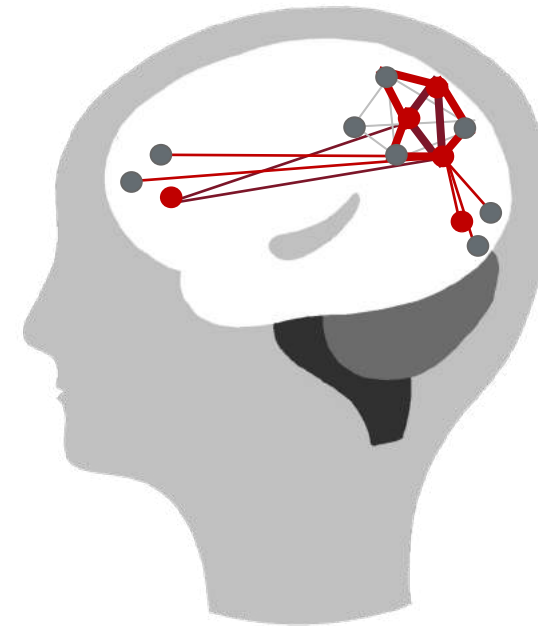
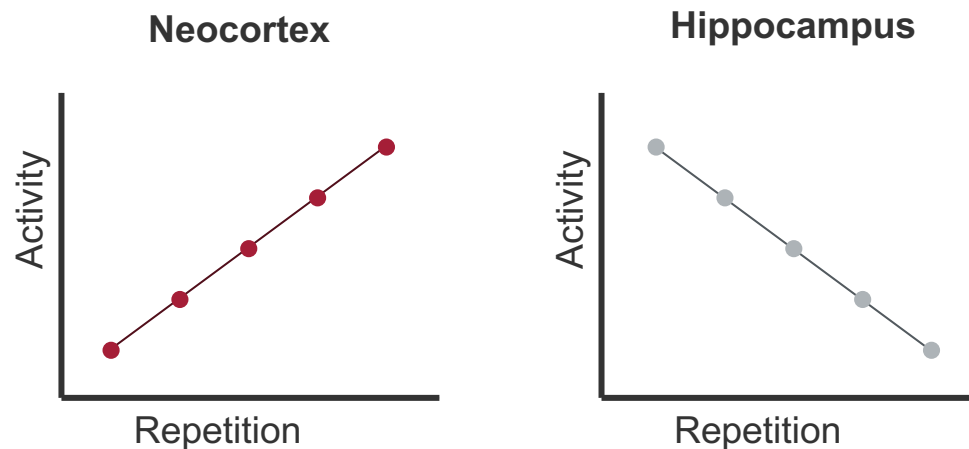
McClelland et al., 1995
Frankland & Bontempi, 2005
Antony et al., 2017

- New memory
- Long-term memory

A paradigm to study systems memory consolidation

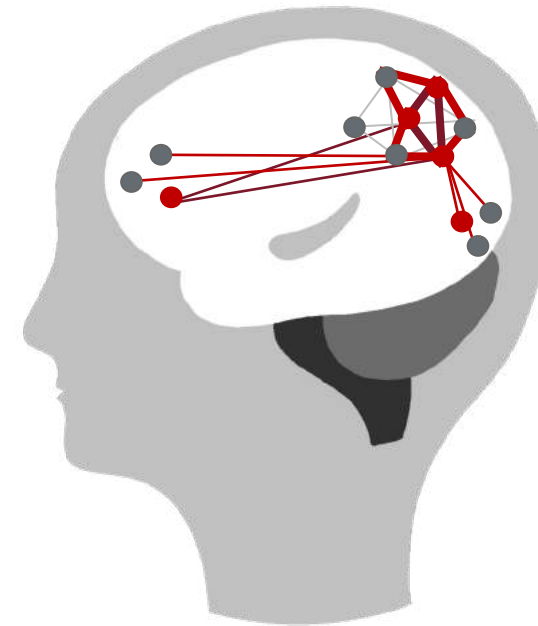
Can we find evidence for systems memory consolidation over rehearsal?

- *Strengthening of neocortical representation*
- *Hippocampal disengagement*



An engram has to be...

- 1) Specific to the experience**
- 2) Stable over time**
- 3) Relevant for behavior**
- 4) Reflected in brain structure**



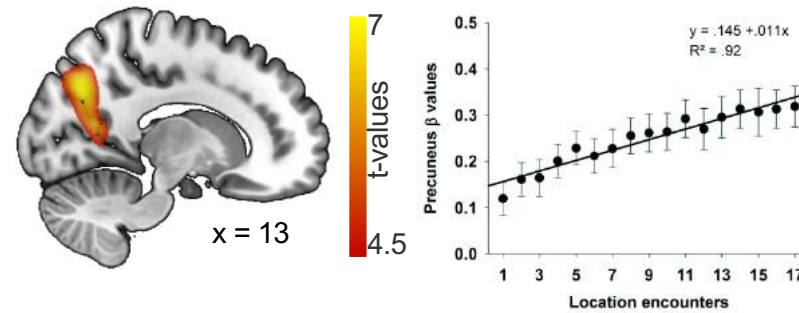
Repetition drives systems memory consolidation

A signature of systems consolidation in brain function

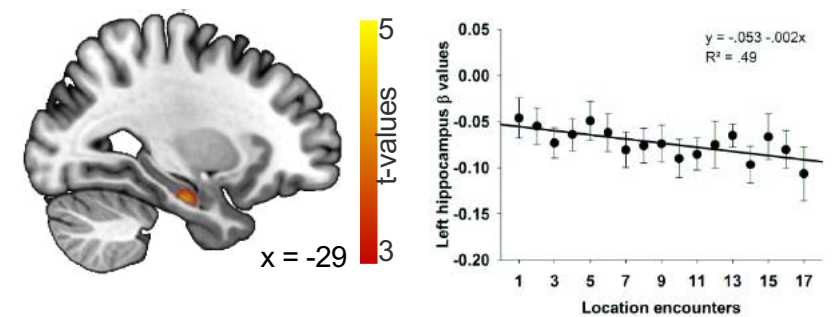


virtual environment

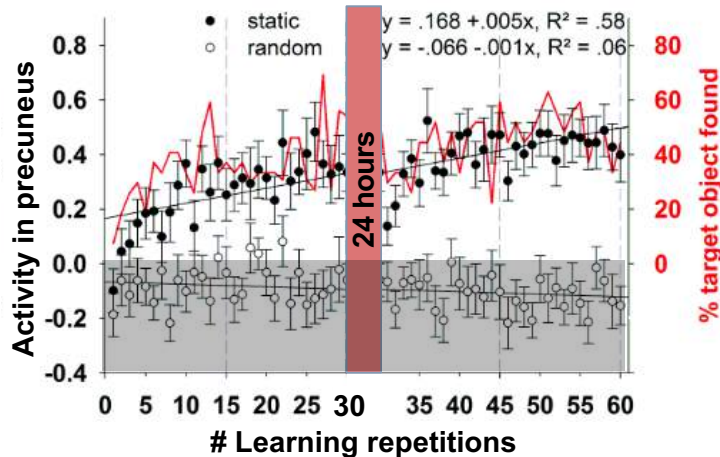
Strengthening of neocortical representation



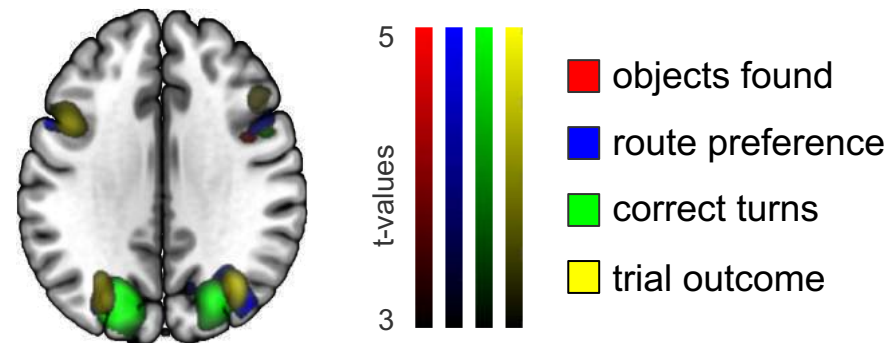
Disengagement of hippocampus



Long-term stability and behavioral relevance

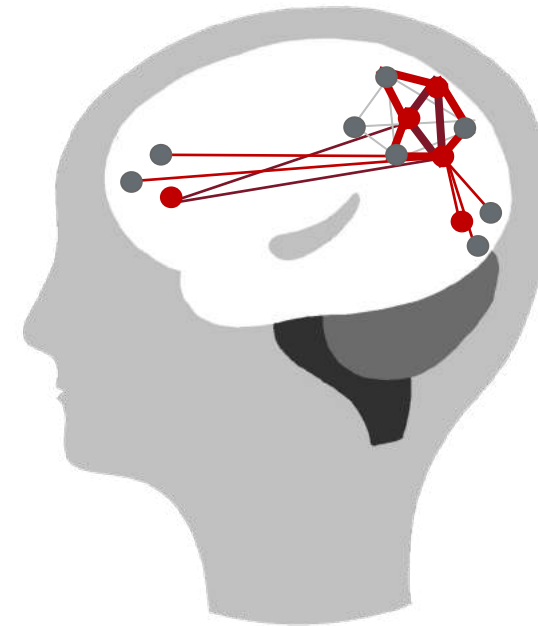


Behavioral relevance



An engram has to be...

- 1) Specific to the experience
- 2) Stable over time
- 3) Relevant for behavior
- 4) **Reflected in brain structure**



Neuron
Article

Cell
PRESS

Learning in the Fast Lane: New Insights into Neuroplasticity

Yaniv Sagi,^{1,2} Ido Tavor,^{1,2} Shir Hofstetter,¹ Shimrit Tzur-Moryosef,¹ Tamar Blumenfeld-Katzir,¹ and Yaniv Assaf^{1,*}

¹Department of Neurobiology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv 69978, Israel

²These authors contributed equally to this work

*Correspondence: assafyan@post.tau.ac.il

DOI 10.1016/j.neuron.2012.01.025

Human Structural Plasticity at Record Speed

Heidi Johansen-Berg,^{1,*} Cassandra Sampaio Baptista,¹ and Adam G. Thomas^{1,2}

¹Oxford Centre for Functional MRI of the Brain, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, Headington, Oxford OX3 9DU, UK

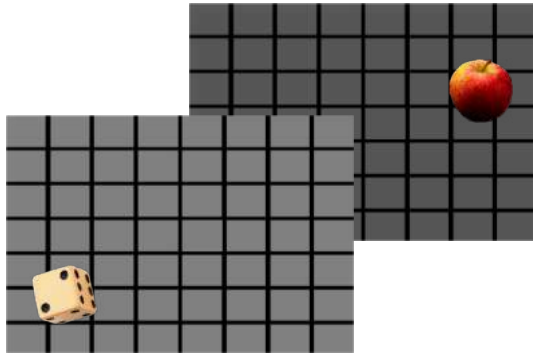
²Functional MRI Facility, NIMH, National Institutes of Health, Bethesda, MD 20892-1148, USA

*Correspondence: heidi@fmrib.ox.ac.uk
DOI 10.1016/j.neuron.2012.03.001

How rapidly does learning shape our brains? A new study in this issue of *Neuron* by Sagi et al. (2012) that uses diffusion magnetic resonance imaging in both humans and rats suggests that just 2 hr of spatial learning is sufficient to change brain structure.

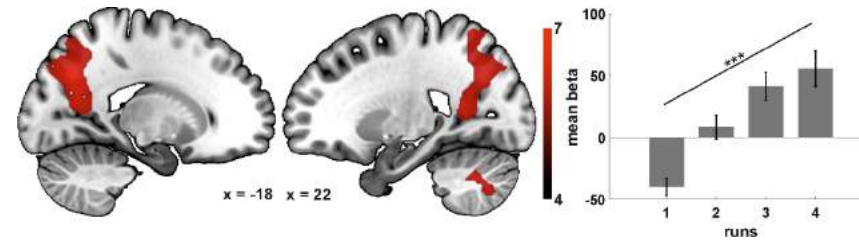
Repetition drives systems memory consolidation

Microstructural plasticity in the neocortex

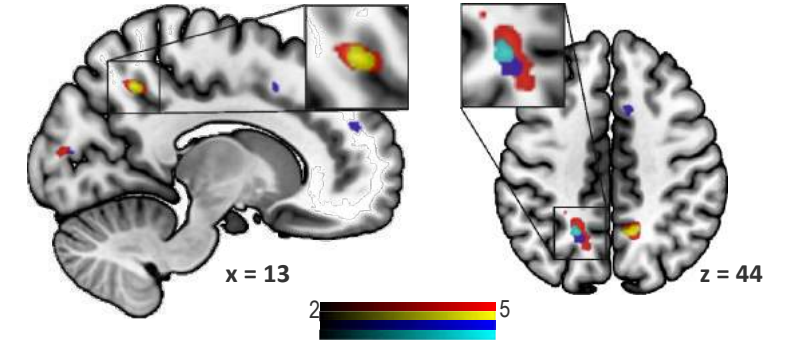


object-location learning

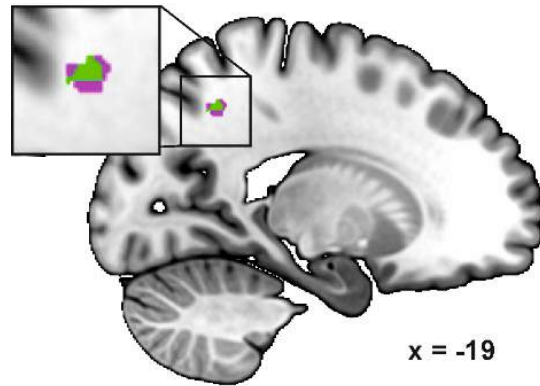
Strengthening of neocortical representation



Microstructural plasticity



Conjunction structural and functional changes



■ Conjunction of the minimum statistic, $p \leq .001$
■ Non-parametric combination, Friston's method, $p_{FWE} \leq .05$



- ✓ experience dependent
- ✓ longterm stable
- ✓ behaviorally relevant

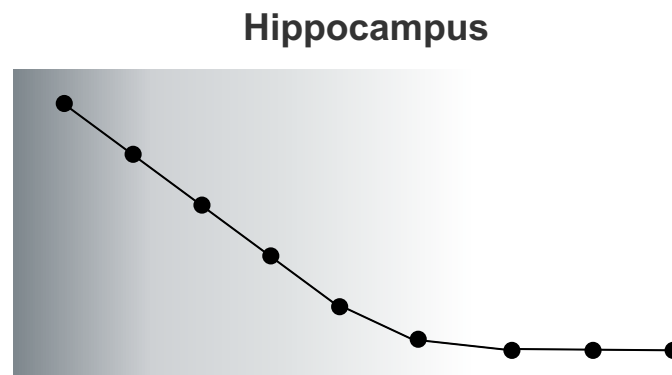
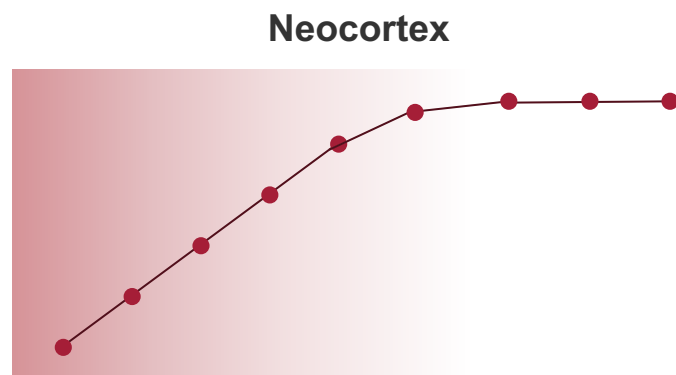


What is the role of sleep in this?

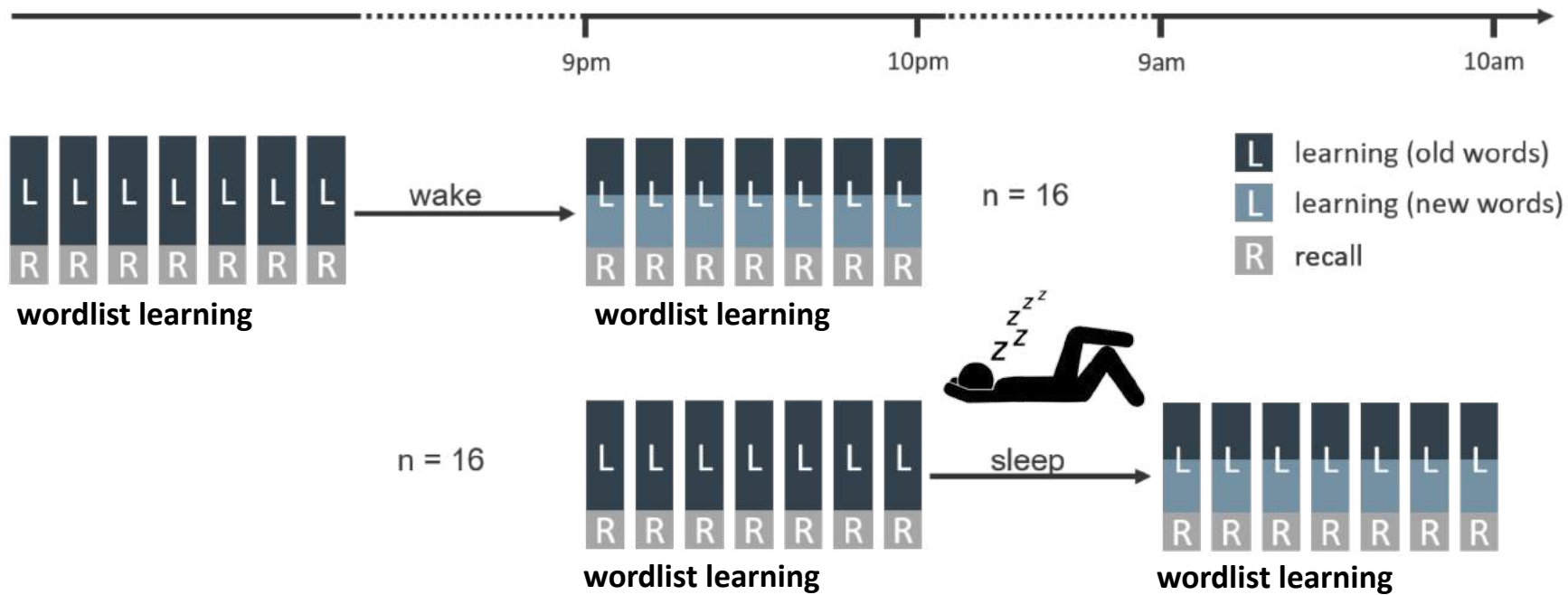
Systems consolidation over learning repetitions

Can we find evidence that sleep supports systems memory consolidation?

- *Strengthening of neocortical representation*
- *Hippocampal disengagement*



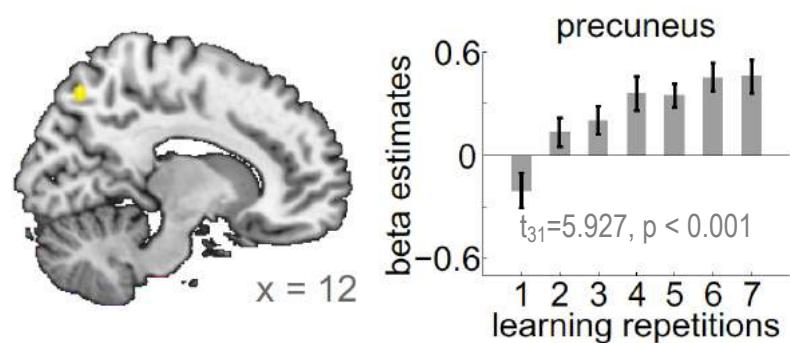
Experimental design



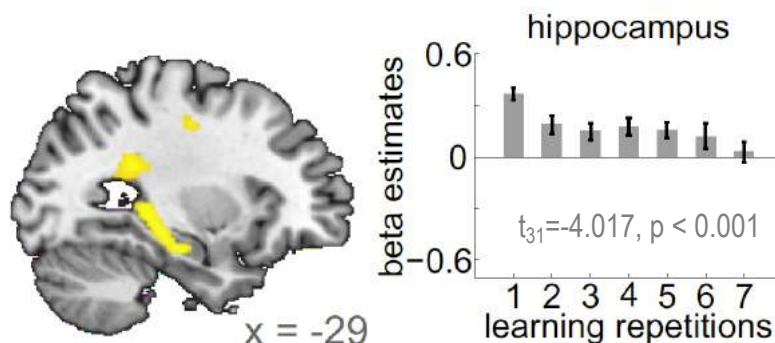
- gasket
- lamplight
- blackboard
- butterfly
- old wordlist**
- armchair
- teapot
- meadow
- bucket
- new wordlist**

Systems consolidation over learning repetitions

Strengthening of neocortical representation

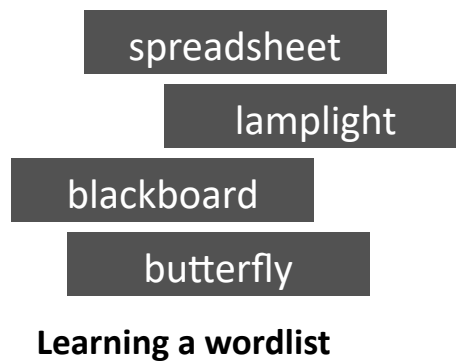
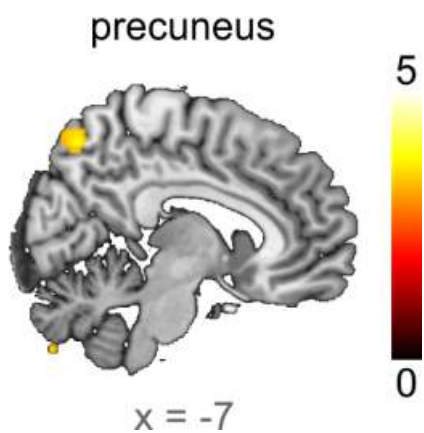


Hippocampal disengagement



Correlation of activation changes of repetitions and performance
precuneus: mean $r = 0.499$, $p < 0.001$
hippocampus: mean $r = -0.366$, $p = 0.001$

Long-term stability



Sleep supports hippocampal disengagement

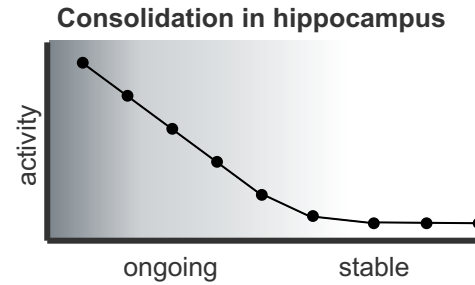
spreadsheet
lamplight
blackboard
butterfly

vs.

armchair
teapot
meadow
bucket

old wordlist
after sleep or wake
(7 learning repetitions)

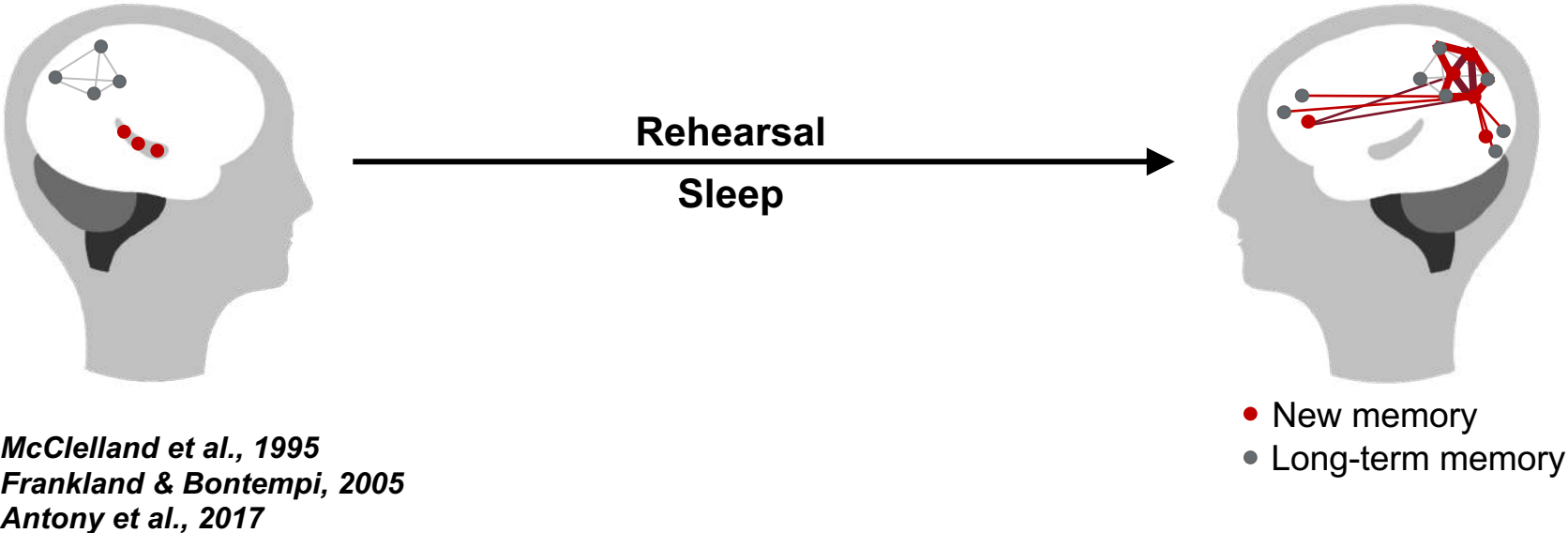
new wordlist





**Rehearsal initiates systems memory consolidation –
Sleep makes it last!**

Mechanisms of systems memory consolidation

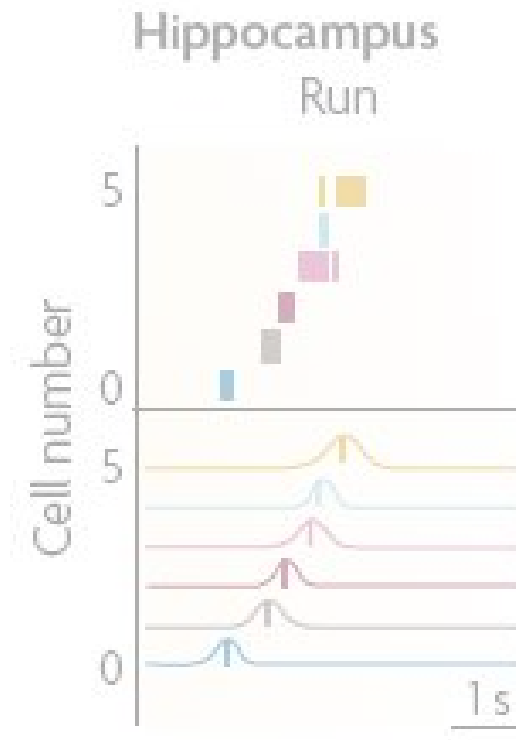
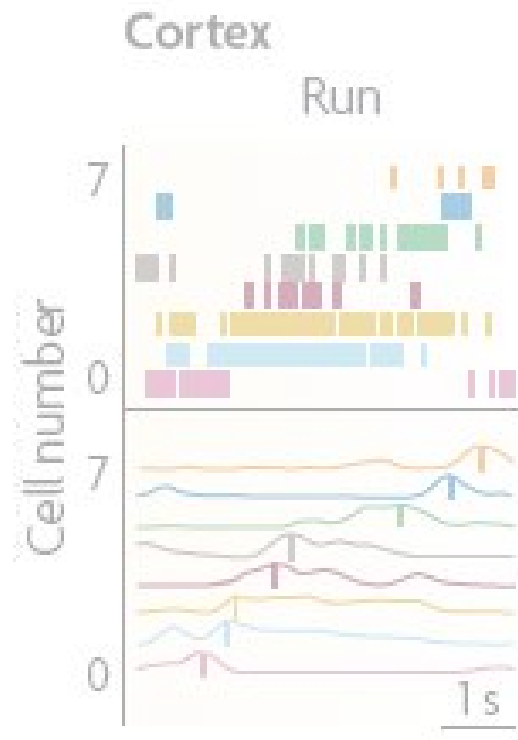


Reactivation of neuronal firing patterns

learning



Replay of neuronal firing patterns



Memory reactivation



**What does spontaneous
memory processing during
sleep look like in humans?**

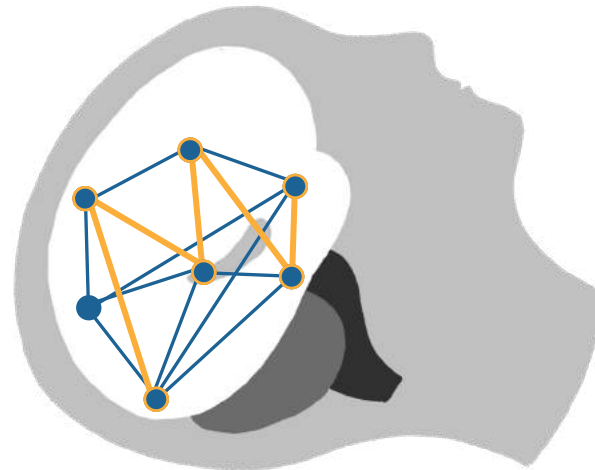


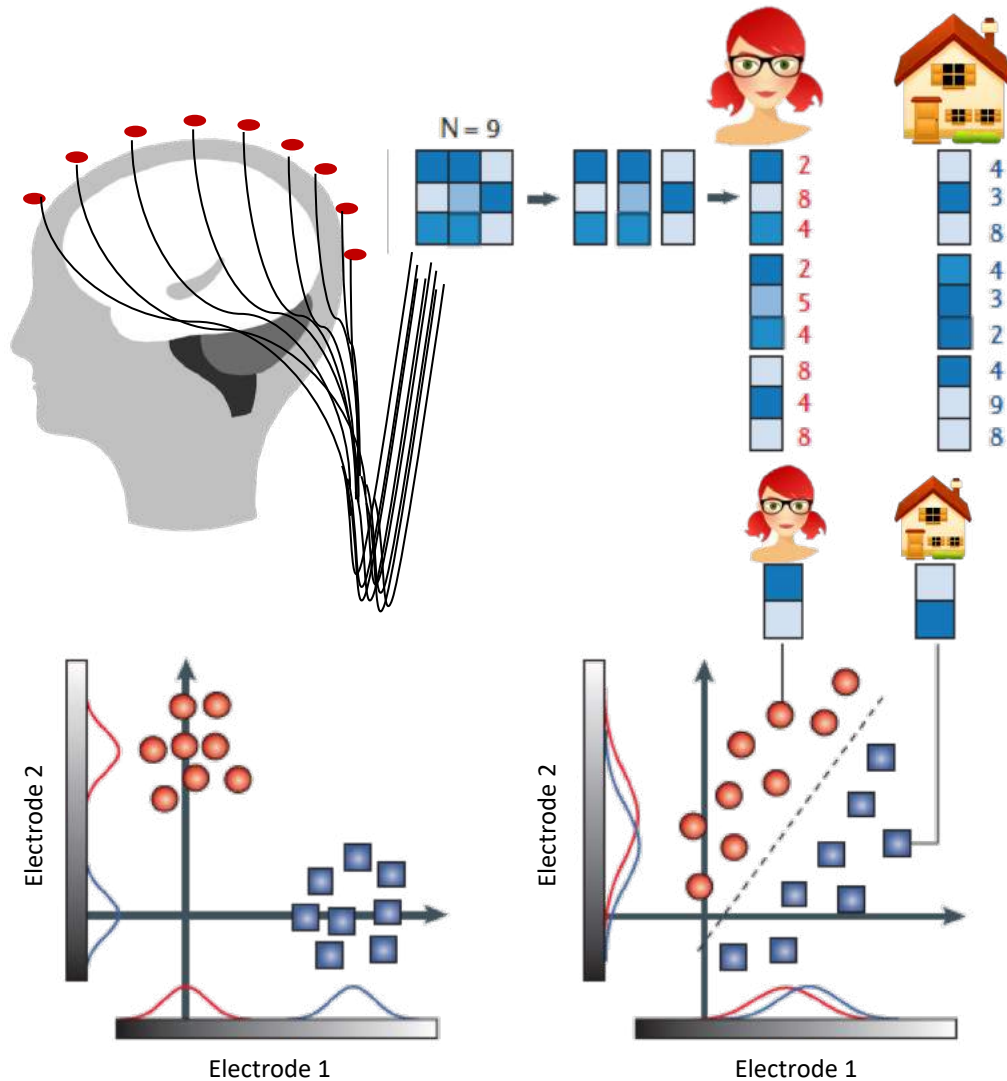
An approach to detect memory reactivation in humans

Spontaneous memory reactivation in humans

In humans: difficult to observe
reactivation of neural firing patterns

Machine learning to detect patterns of
memory processing during sleep!





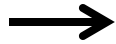
Sensitive test!

Information accumulates across multiple features

Many features – one test!

Avoids increase in type I error due to multiple testing

Spontaneous memory reactivation in humans



Learning

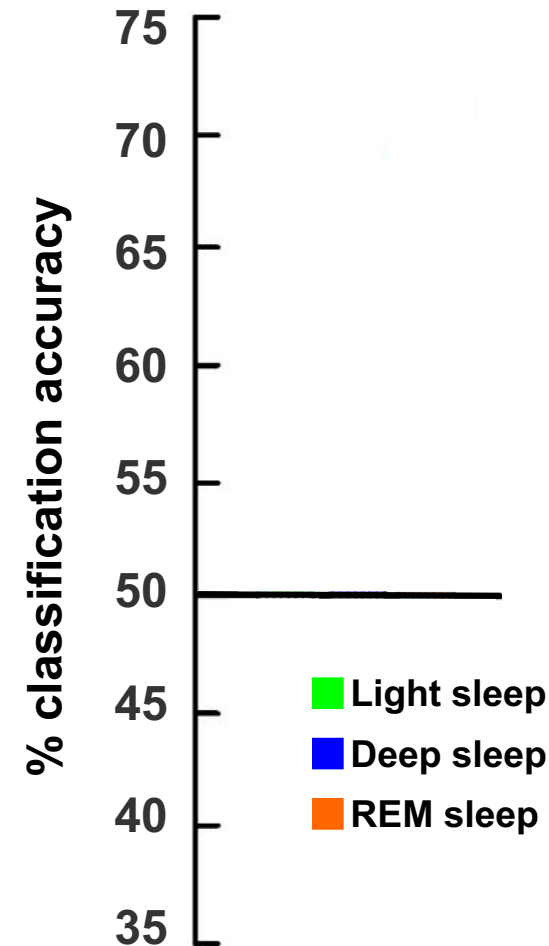
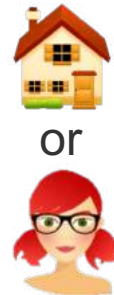
EEG activity in sleep



**Computer algorithm:
What has this person
learned before sleep?**

Spontaneous memory reactivation in humans

- We can predict what someone has learned before sleep!
- Memory is reprocessed during sleep
- Surprising: Memory processing during all sleep stages!
 - Light sleep
 - Deep sleep
 - REM sleep

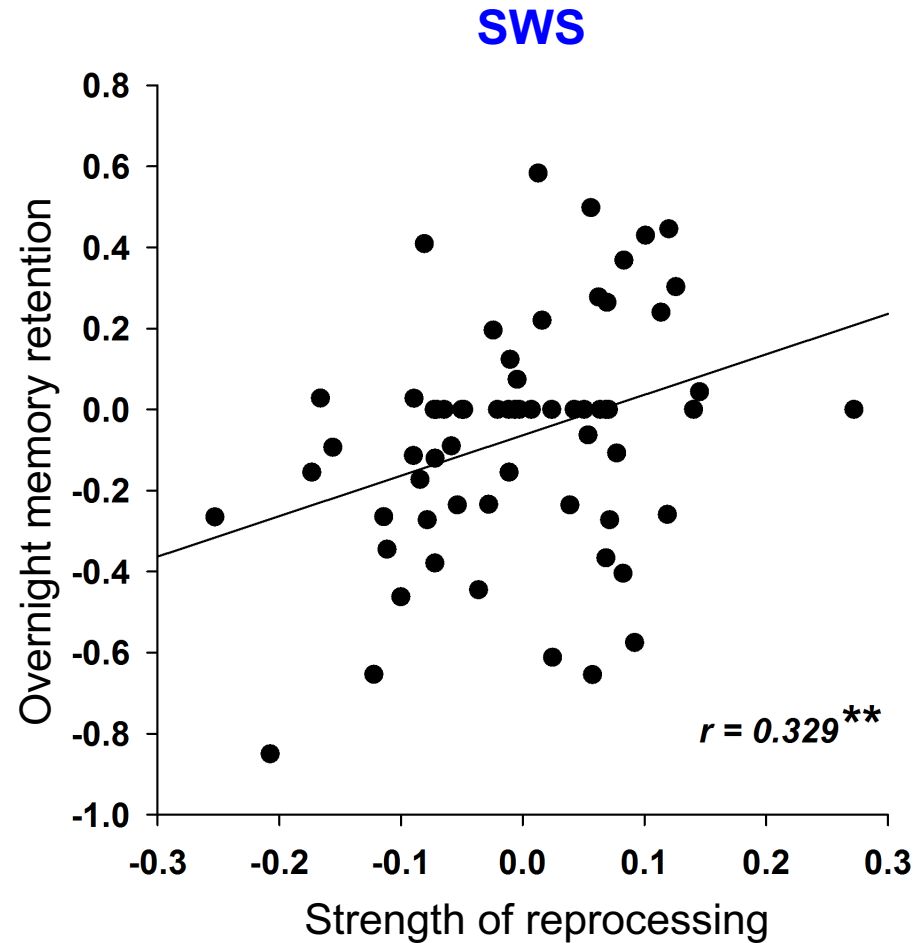


Spontaneous memory reactivation in humans

Does memory processing benefit memory consolidation?

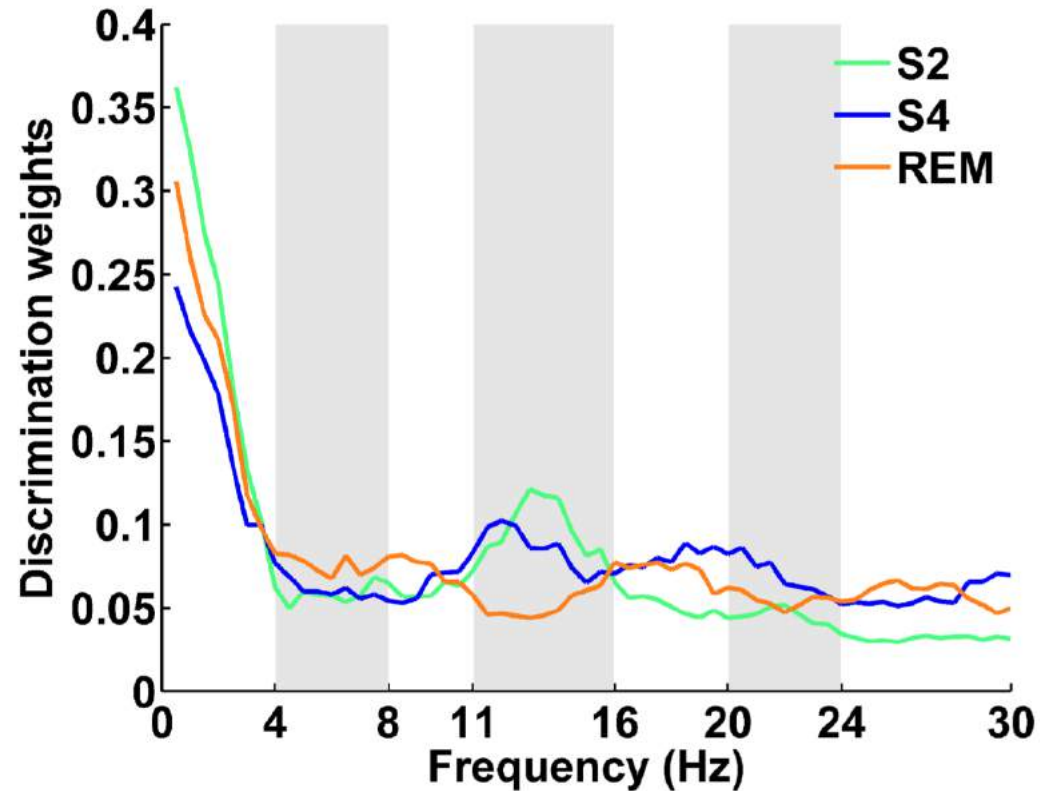
Stronger reprocessing – better memory retention!

Important role of SWS



What are the neural mechanisms underlying spontaneous memory reactivation?

Spontaneous memory reactivation in humans



Different physiological processes support memory consolidation

- **NREM:** Delta, spindles
- **REM:** Theta, alpha, beta

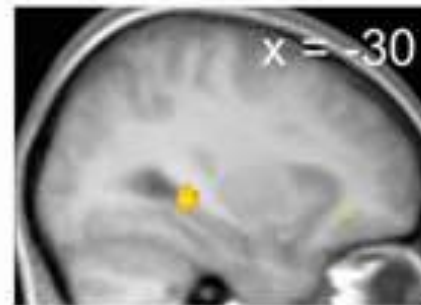
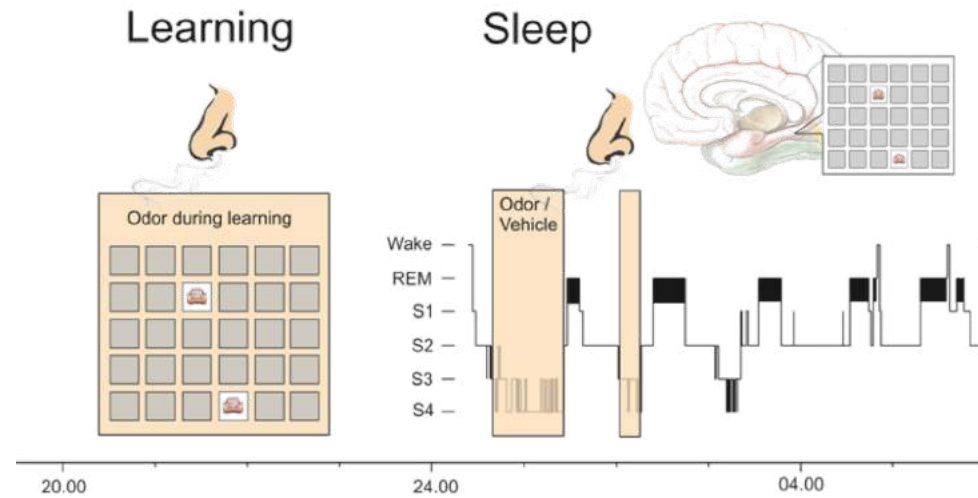
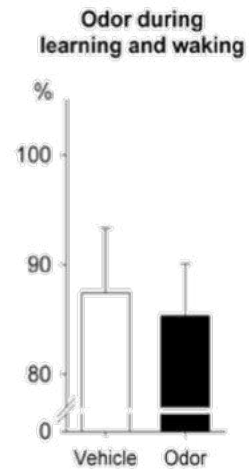
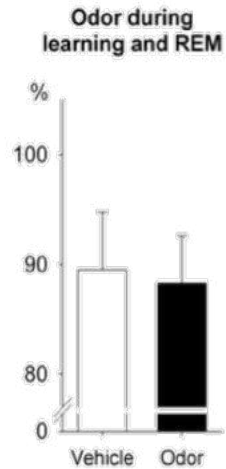
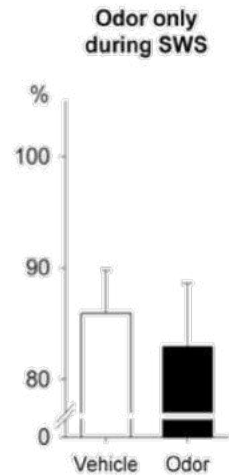
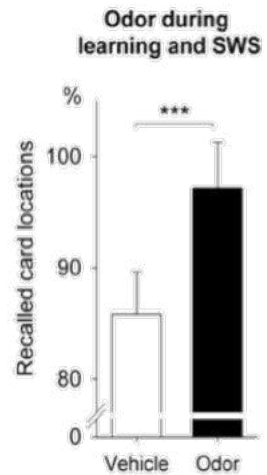
A way to manipulate memory reactivation in humans

What is targeted memory reactivation (TMR)?

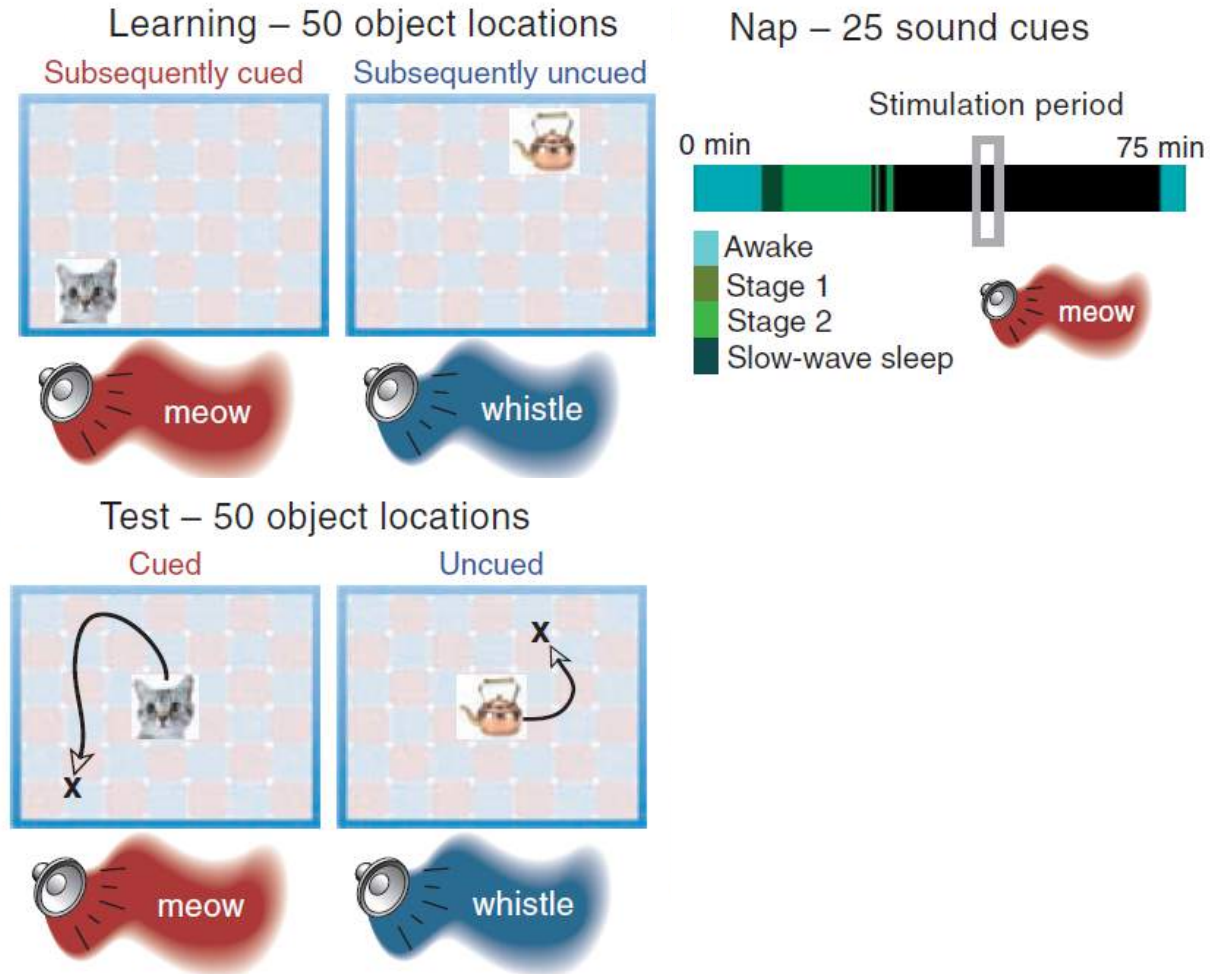


Rasch et al., 2007
Diekelmann et al., 2012
Rihm et al., 2014
Schönauer et al., 2014
Cairney et al., 2016
Schreiner et al., 2015, 2016
Bendor & Wilson, 2012

Targeted reactivation of hippocampal memories during sleep



Cued memory reactivation boosts performance

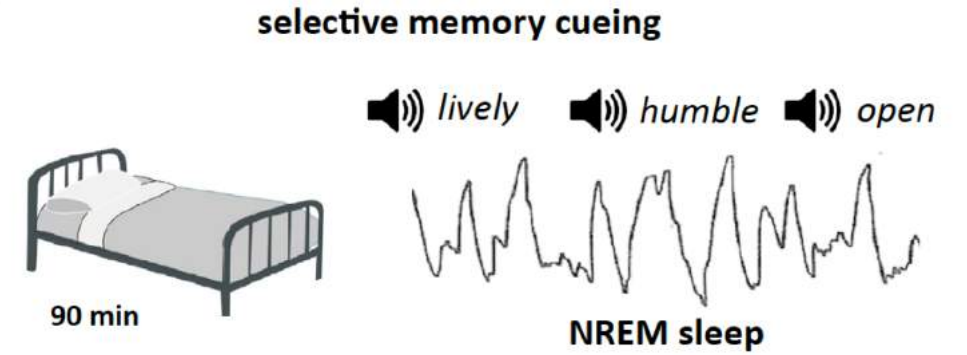
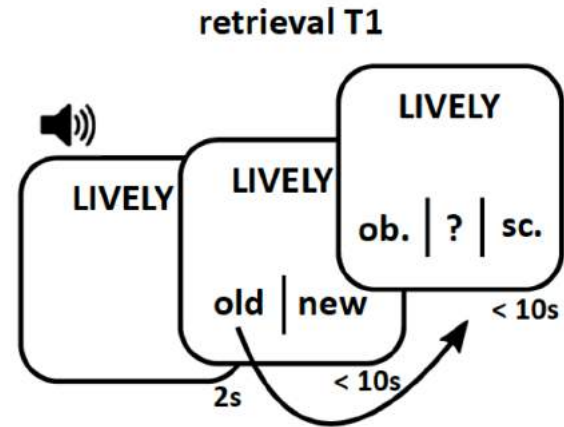
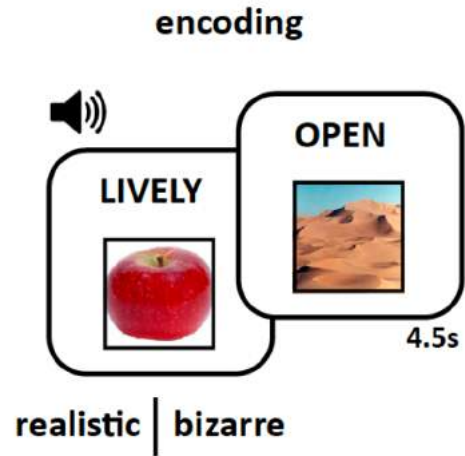


Sound cues are effective stimuli for targeted memory reactivation.

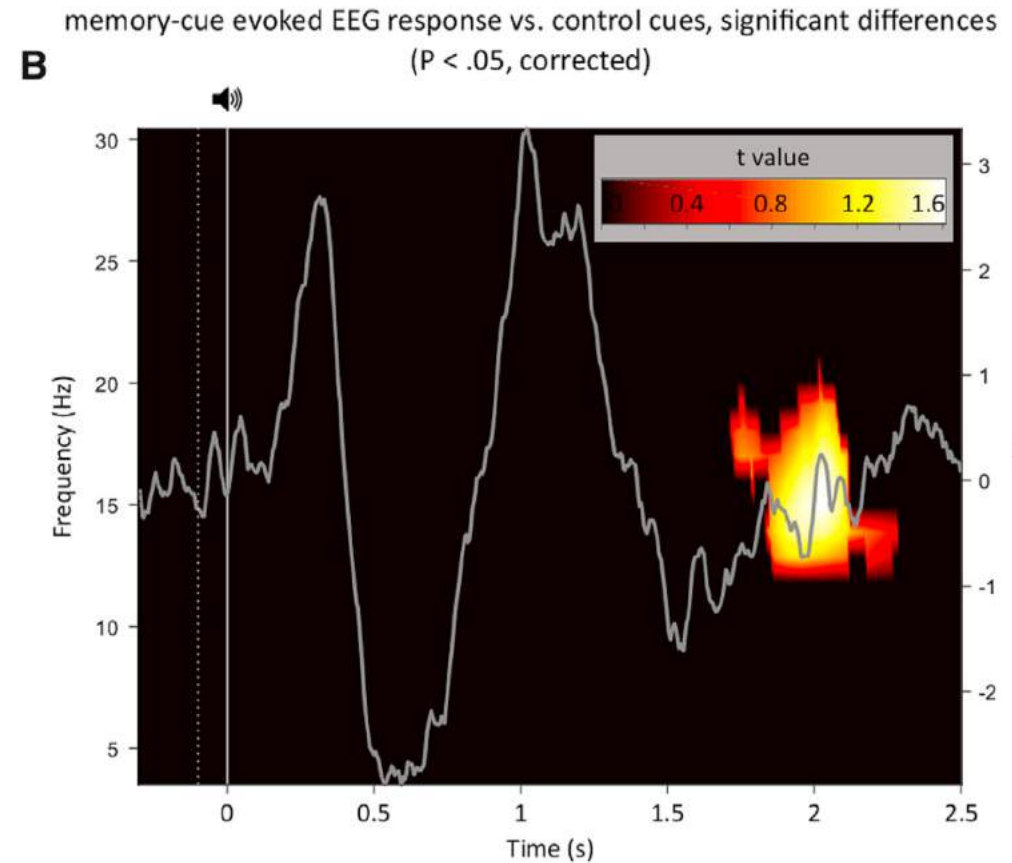
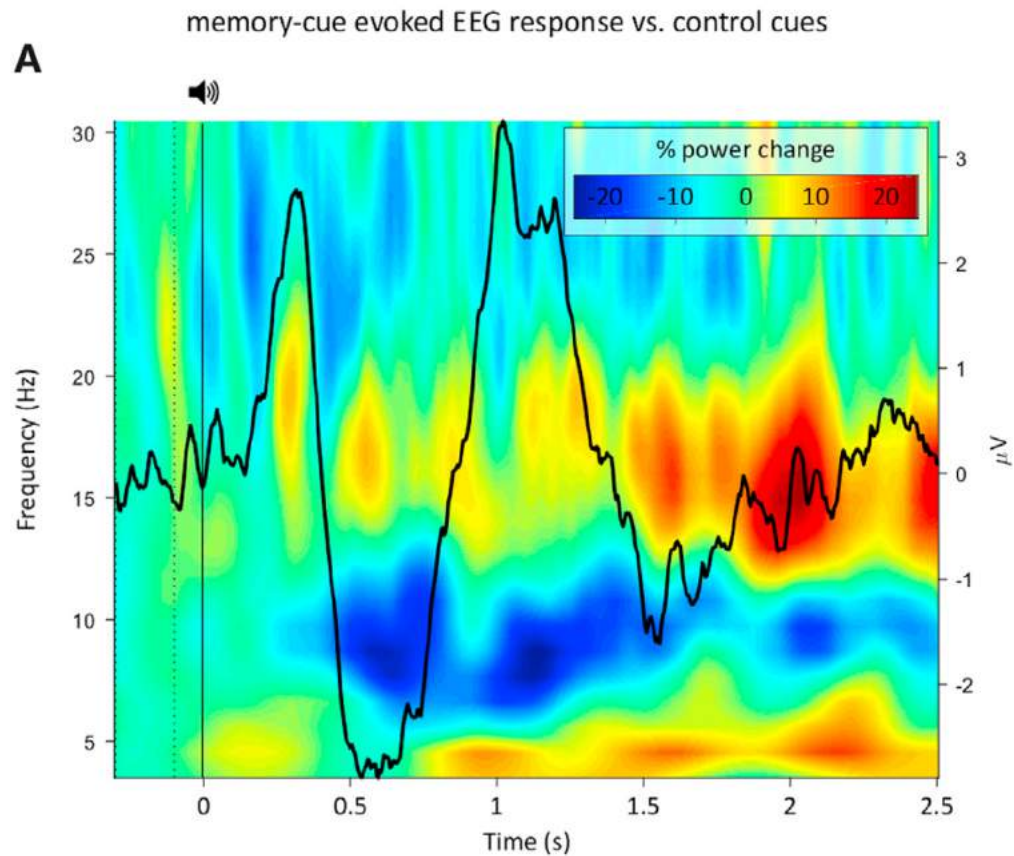
Effects are highly specific to cued content.

What are the neural mechanisms underlying targeted memory reactivation?

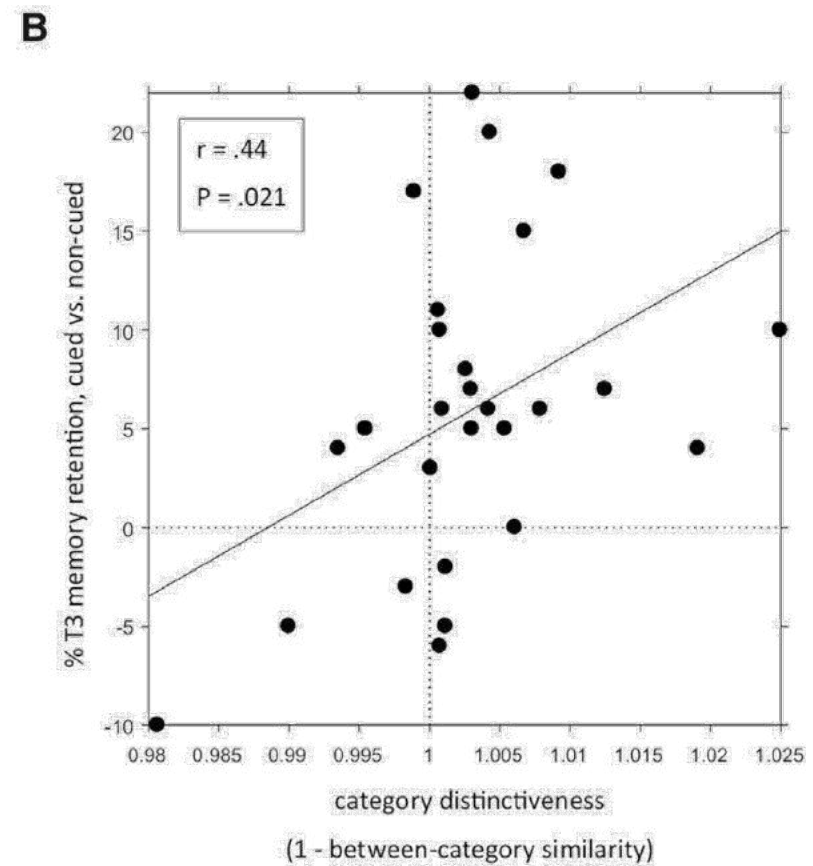
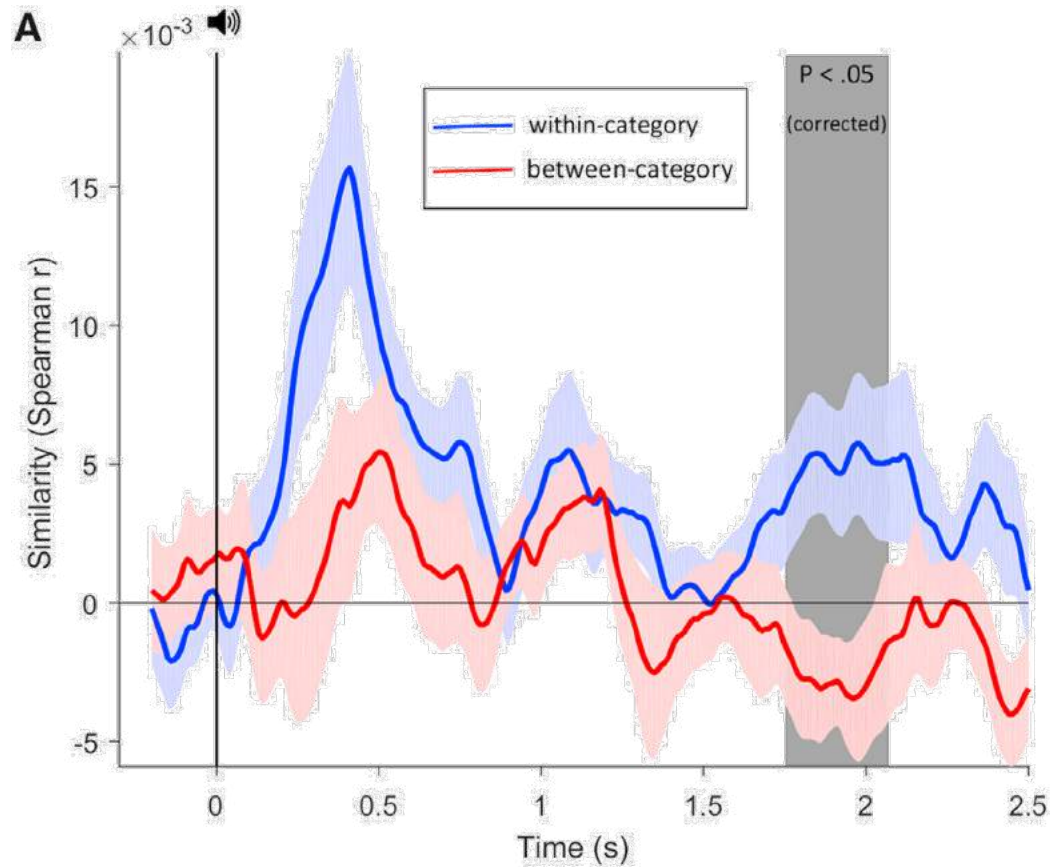
Targeted memory reactivation in humans



Targeted memory reactivation in humans

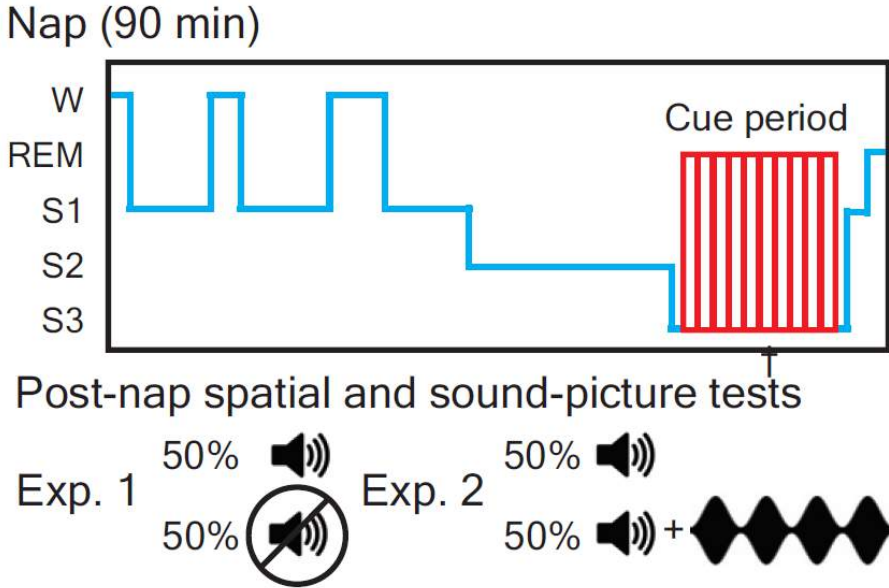
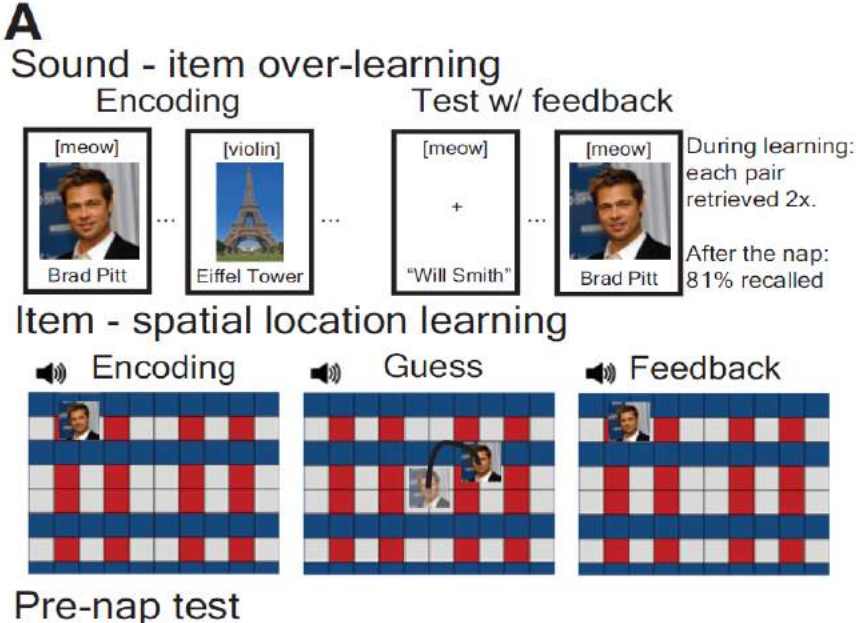


Targeted memory reactivation in humans



**Do spindles have a causal role in memory reprocessing
and the effectiveness of TMR?**

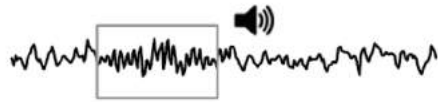
Optimal timing for memory reactivation



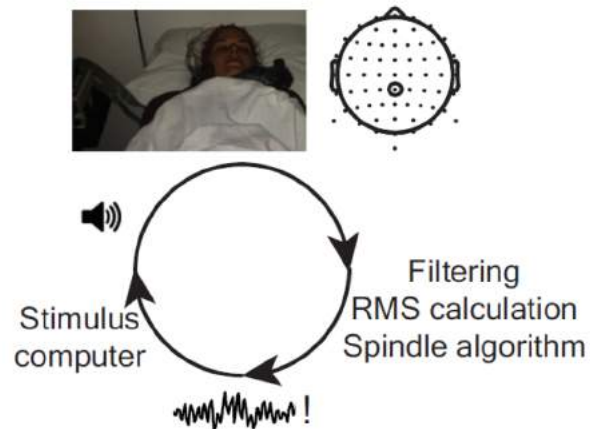
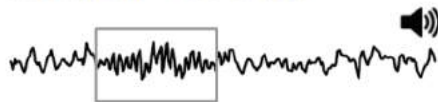
Optimal timing for memory reactivation

A

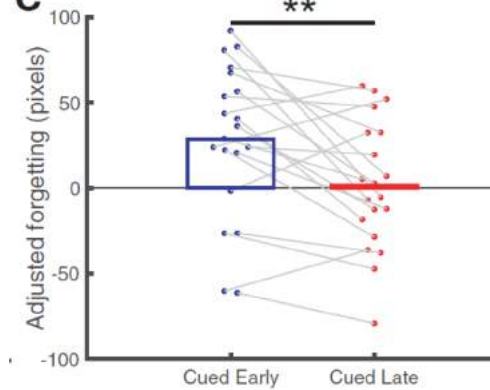
Early condition - 0.25 s ISI



Late condition - 2.5 s ISI

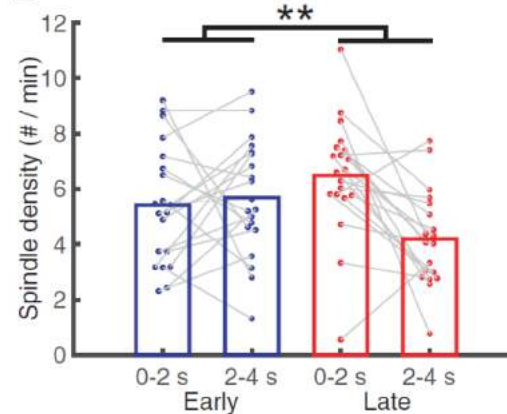


C

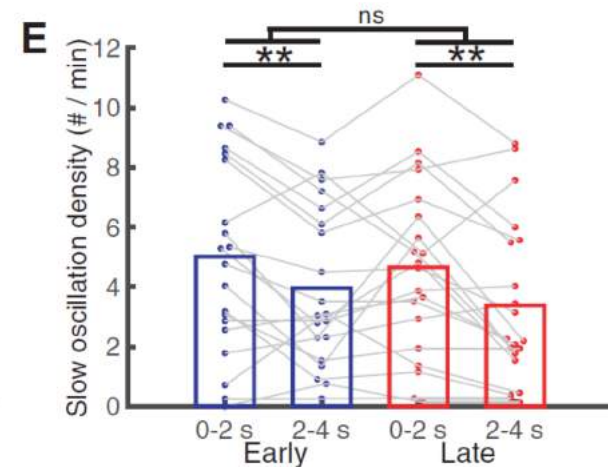


Cues presented outside of the spindle refractory period led to better memory

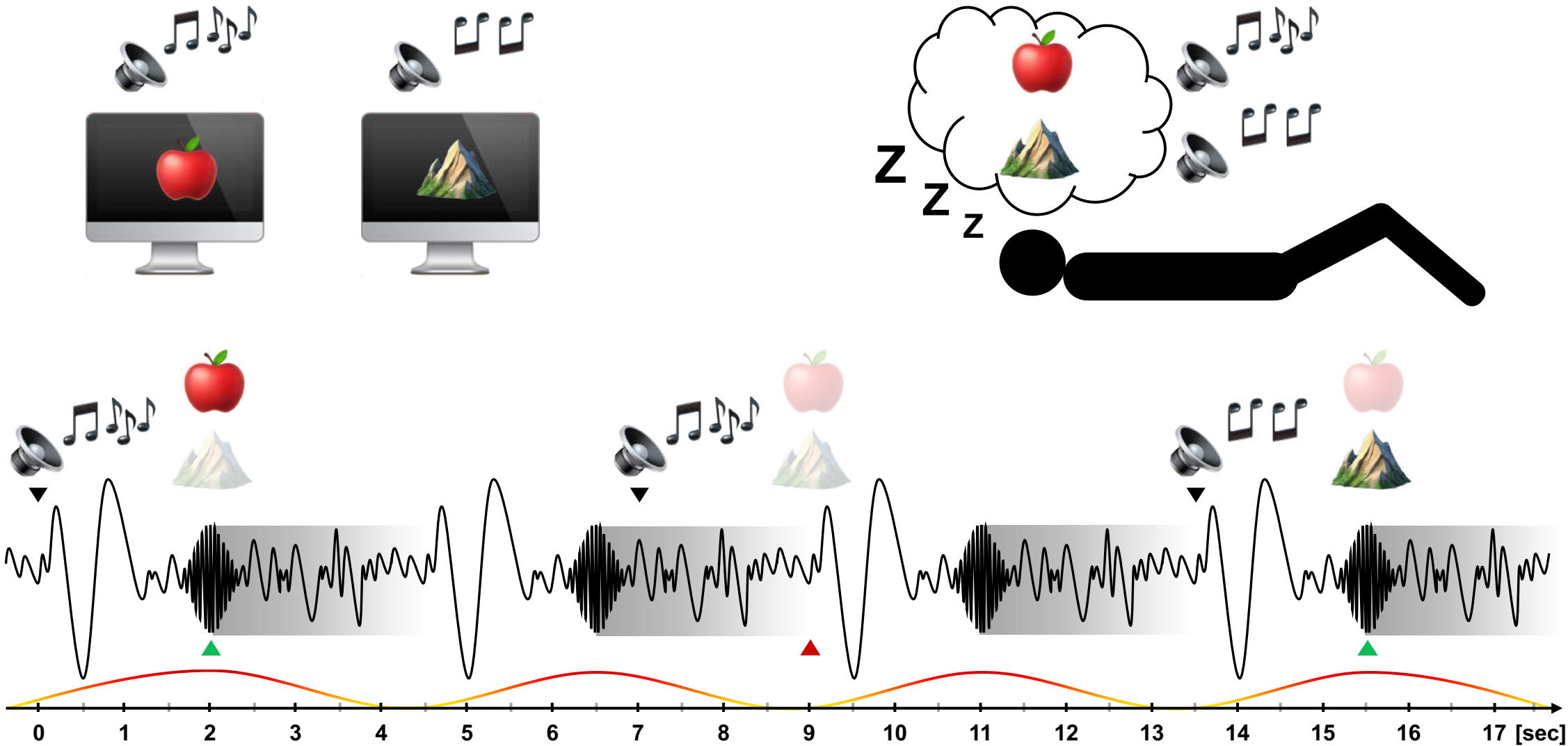
D



E



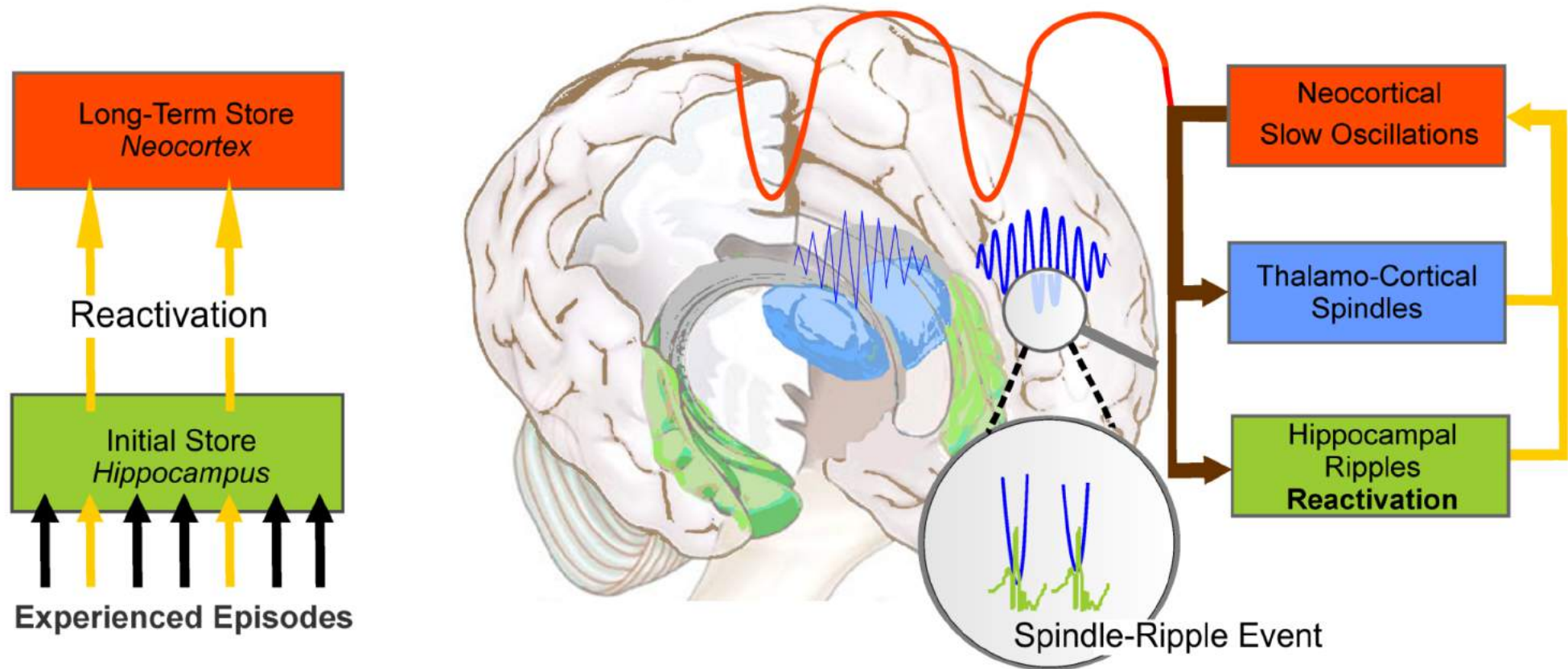
A working model of TMR effects during sleep



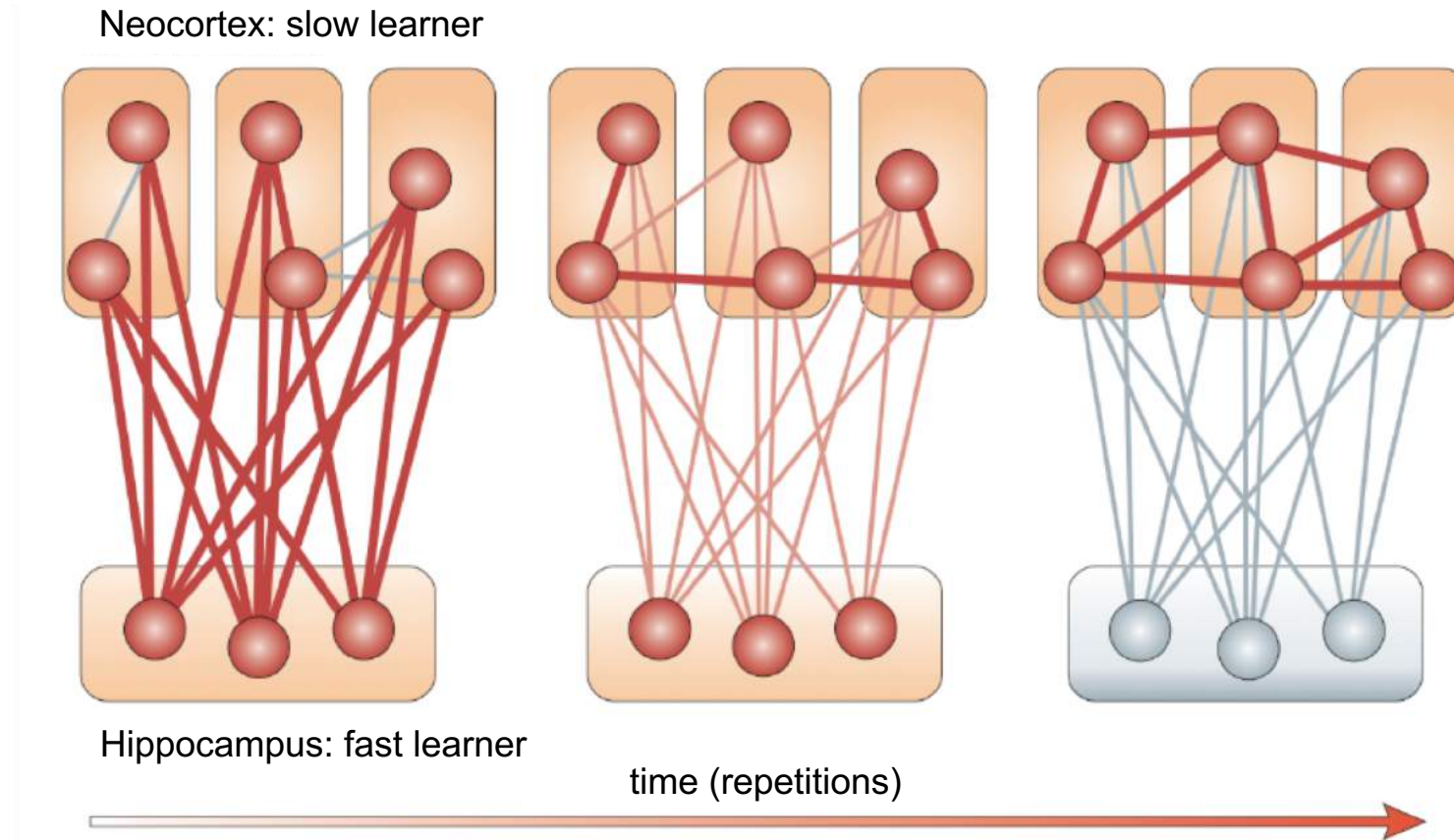
Antony et al., *Curr Biol*, 2018
Cairney et al., *Curr Biol*, 2018
Schönauer, *Curr Biol*, 2018

Prof. Monika Schönauer
Institute of Neuropsychology

Active systems consolidation during sleep



The standard model of memory consolidation



Thank you!

Svenja Brodt



Lea Himmer



Dorothee Pöhlchen



Jonas Beck, Anna Seewald, Annette Abraham, Teresa Geisler, Susanne Kirchner, Max Schneider, Marcel Graetz

Collaborators:

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Stefan Glasauer
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Manuel Schabus
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