

Hippocampus, Brain states and Memory

Master Science et Technologies
Mention Biologie Intégrative et Physiologie
Spécialité Neurosciences

Hippocampus : from cells to physiology and human pathology

Gabrielle GIRARDEAU, PhD, CRCN Inserm
IFM Team 6, « Sleep and Emotional Memory »



@DrGabyGab

gabrielle.girardeau@inserm.fr



Hippocampus, Brain states and Memory

- Reminders
- Experimental design for sleep and memory studies *in vivo*
- Example causal studies
 - Non-REM sleep and ripples
 - REM sleep and theta oscillations
 - Replay
- Hippocampal dialogue with other areas
 - Example correlation study : hippocampus and basolateral amygdala

Vocabulary/Concepts/Methods

Engram

Local Field Potential

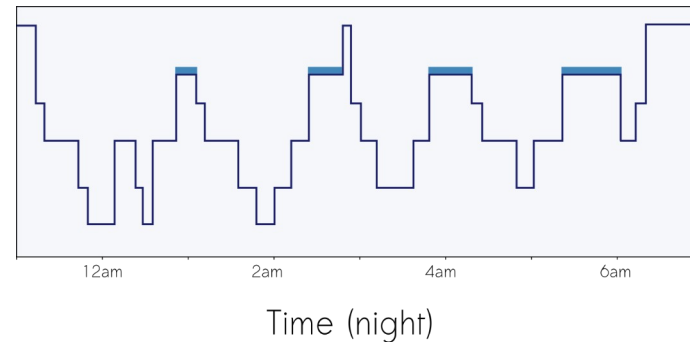
Optogenetics

Neuronal assembly

Replay/Reactivations

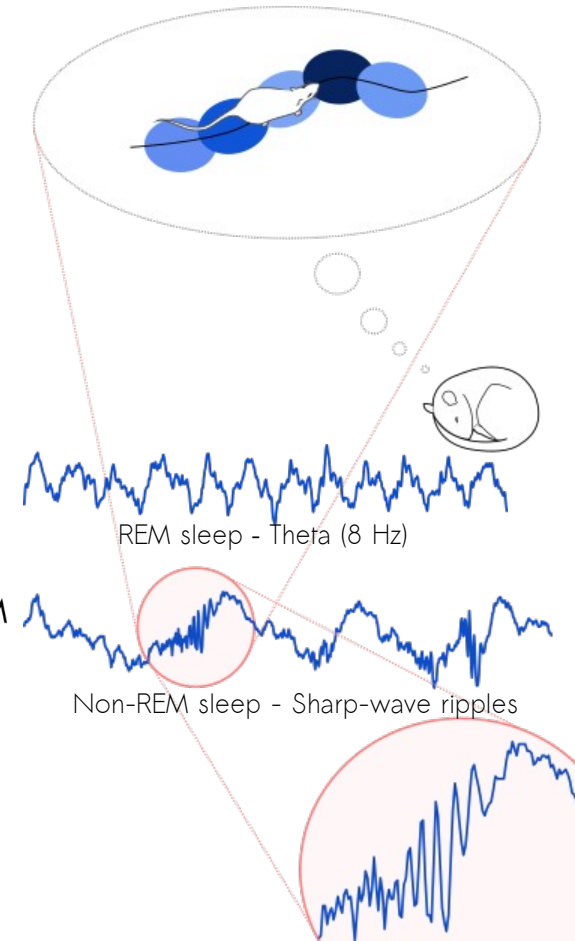
Sleep stages and
hippocampal rhythms

Memory consolidation



Awake
REM

Non-REM

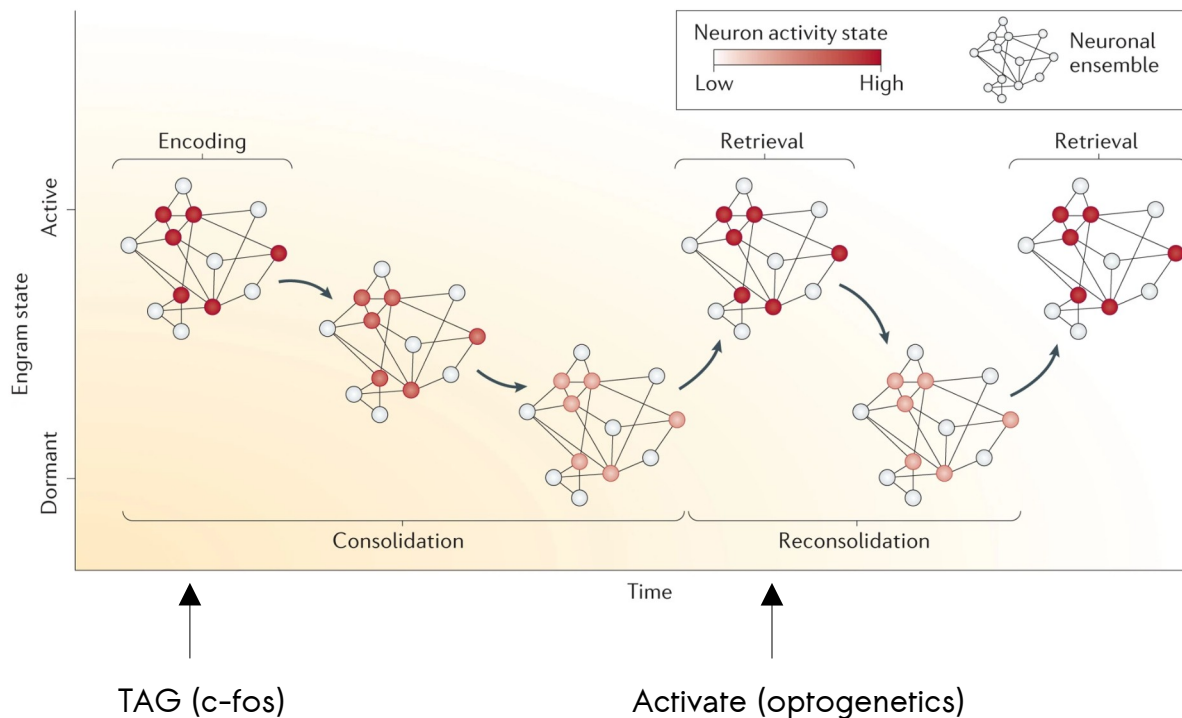


Engram, a buzzword

Finding the engram

Sheena A. Josselyn , Stefan Köhler  & Paul W. Frankland 

Nature Reviews Neuroscience **16**, 521–534(2015) | [Cite this article](#)

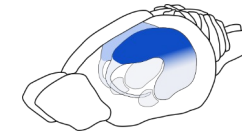
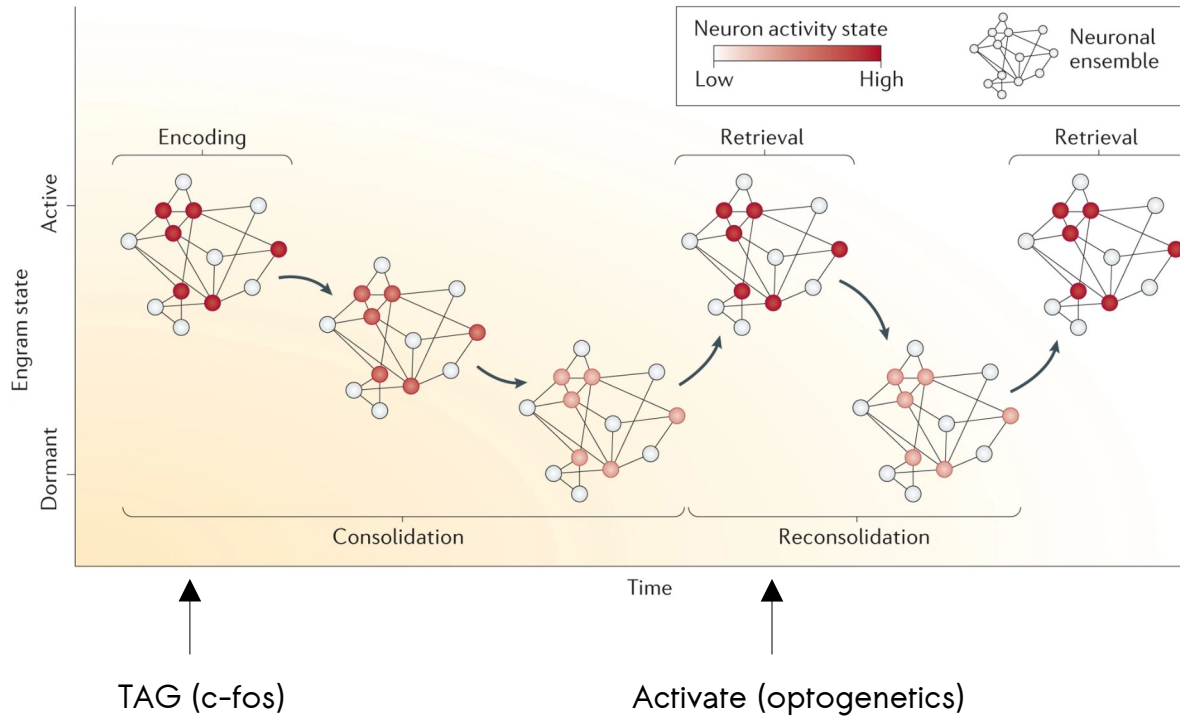


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DG vs CA1

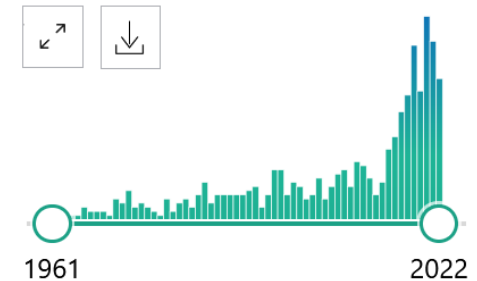
[Nature](#). 2012 Mar 22;484(7394):381-5. doi: 10.1038/nature11028.

Optogenetic stimulation of a hippocampal engram activates fear memory recall

Xu Liu ¹, Steve Ramirez, Petti T Pang, Corey B Puryear, Arvind Govindarajan, Karl Deisseroth, Susumu Tonegawa

« We labelled a population of hippocampal dentate gyrus neurons activated during fear learning with channelrhodopsin-2 (ChR2) and later optically reactivated these neurons in a different context. The mice showed increased freezing only upon light stimulation, indicating light-induced fear memory recall. »

RESULTS BY YEAR



Experimental designs to study sleep and memory

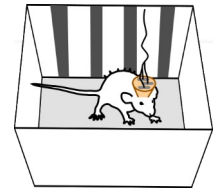
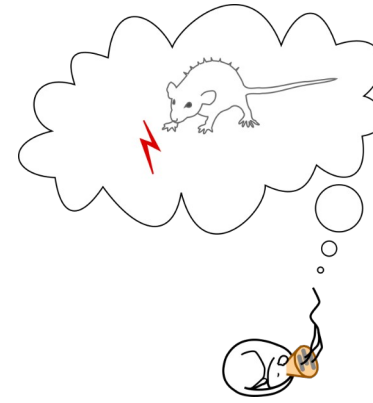
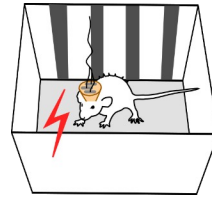
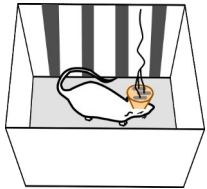
Baseline
Wakefulness

Pre-training
sleep

Training/Exploration
(Acquisition)

Post-training
sleep

Test/Exploration
(retrieval)



Experimental designs to study sleep and memory

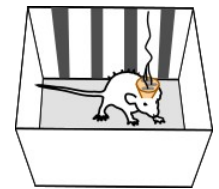
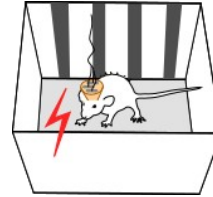
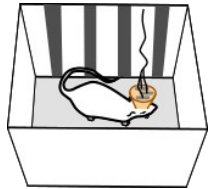
Baseline
Wakefulness

Pre-training
sleep

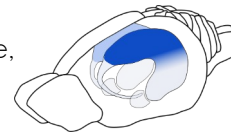
Training/Exploration
(Acquisition)

Post-training
sleep

Test/Exploration
(retrieval)



(Contextual) Fear conditioning
Radial maze, cheeseboard maze,
T-maze...
Simple spatial exploration



Experimental designs to study sleep and memory

Baseline
Wakefulness

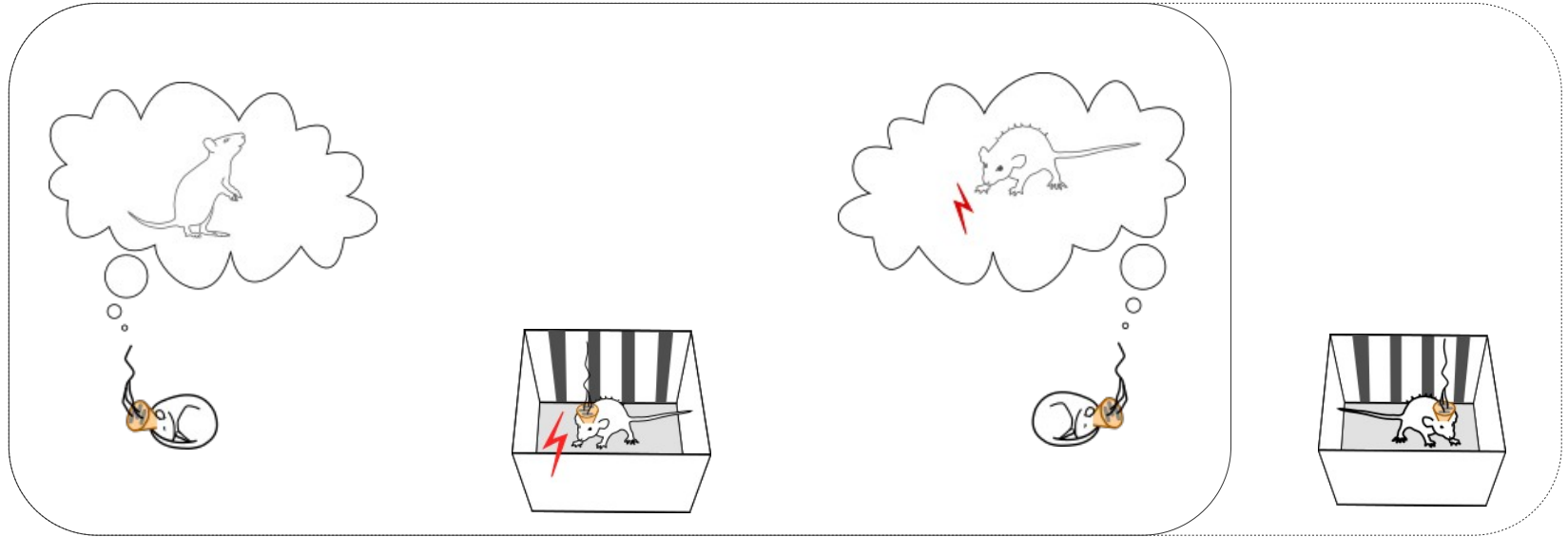
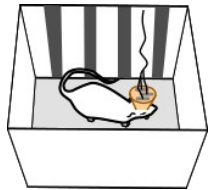
Pre-training
sleep

Training/Exploration
(Acquisition)

Post-training
sleep

Test/Exploration
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Observational/Correlational studies



Sleep Replay/Reactivations

Experimental designs to study sleep and memory

Baseline
Wakefulness

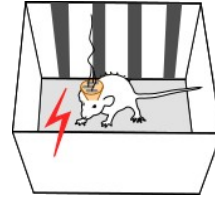
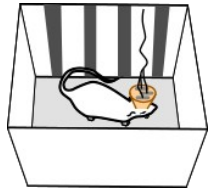
Pre-training
sleep

Training/Exploration
(Acquisition)

Post-training
sleep

Test/Exploration
(retrieval)

Observational/Correlational studies



Sleep-modification
protocol

?
Behavioral
readout

Interventional/causal studies

Hippocampus, Brain states and Memory

- Reminders
- Experimental design for sleep and memory studies *in vivo*
- **Example causal studies**
 - Non-REM sleep and ripples
 - REM sleep and theta oscillations
 - Replay
- Hippocampal dialogue with other areas
 - Example correlation study : hippocampus and basolateral amygdala

Case causal studies : ripples

- How would you test that sleep *ripples* are causally involved in memory consolidation ?

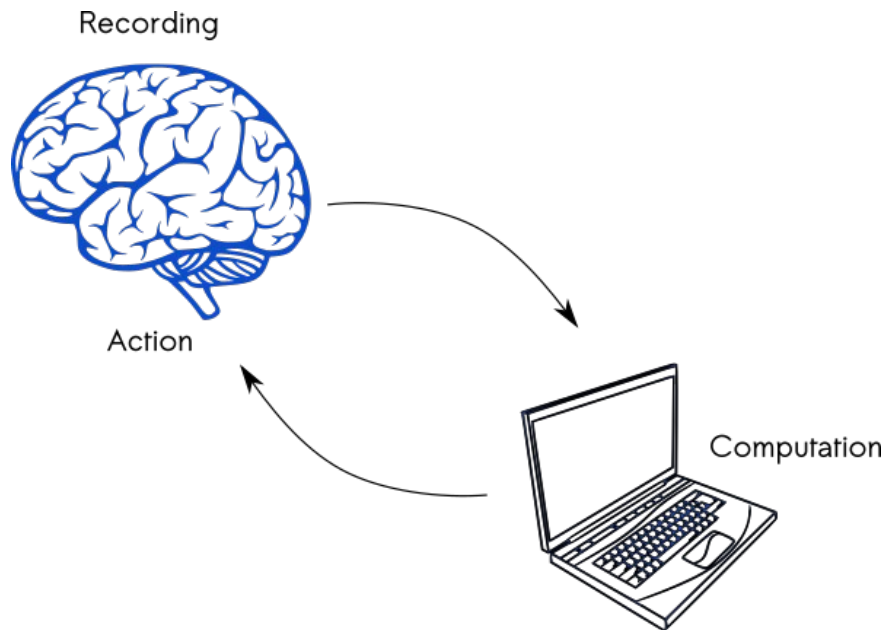
Case causal studies : ripples

- How would you test that sleep *ripples* are causally involved in memory consolidation ?

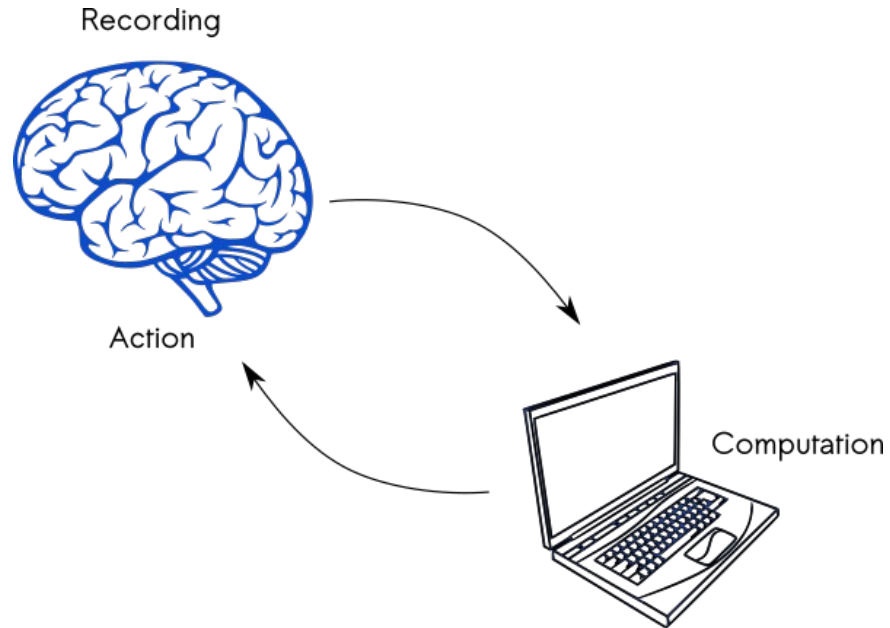


Closed-loop systems

- How would you test that sleep *ripples* are causally involved in memory consolidation ?



Closed-loop systems



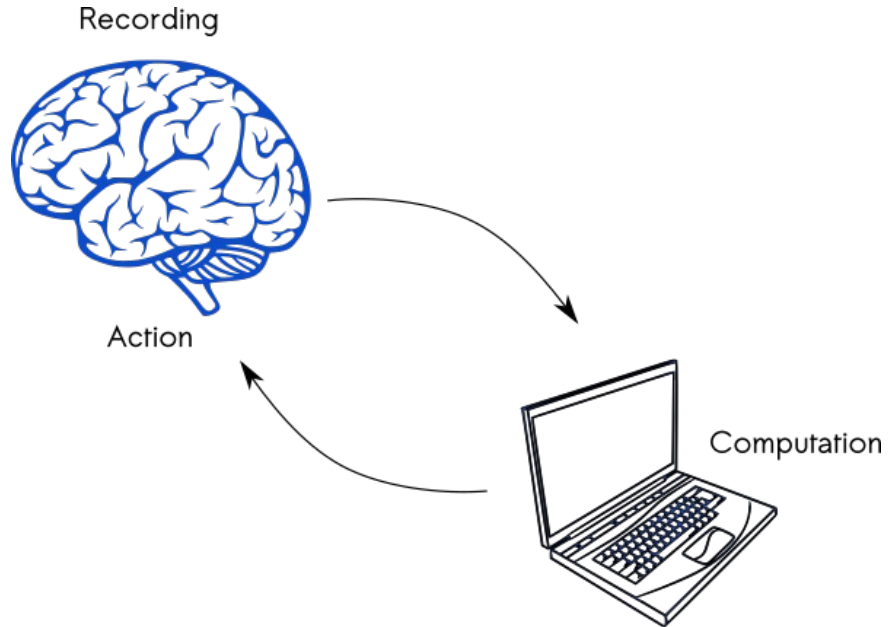
Examples for :

Recording

Computation

Action

Closed-loop systems



Examples for :

Recording :

- Surface EEG
- Intracerebral EEG
- Local Field Potentials
- Ripples, Spindles, theta, Epileptic activity...

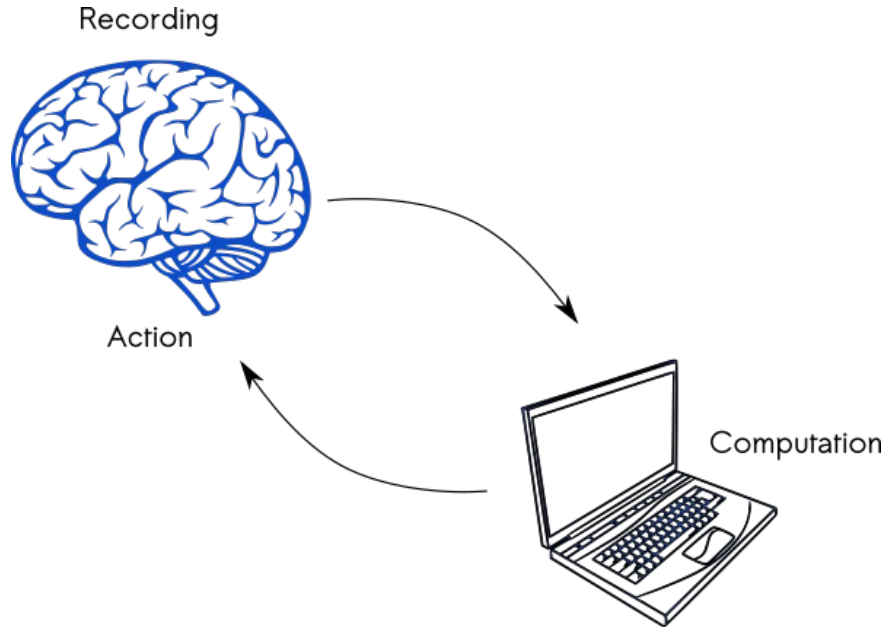
Computation

- Rhythm/Event/Spike detection
- Brain state (sleep stage)
- Specific location...

Action

- Electrical single stimulation
- Optogenetic stimulation
- DBS
- Patterned stimulations...

Closed-loop systems



Neuron

Volume 86, Issue 1, 8 April 2015, Pages 106-139

Review

Closed-Loop and Activity-Guided Optogenetic Control

Logan Grosenick^{1, 2, 3, 6}, James H. Marshel^{1, 2, 6}, Karl Deisseroth^{1, 2, 4, 5, 6} ✉



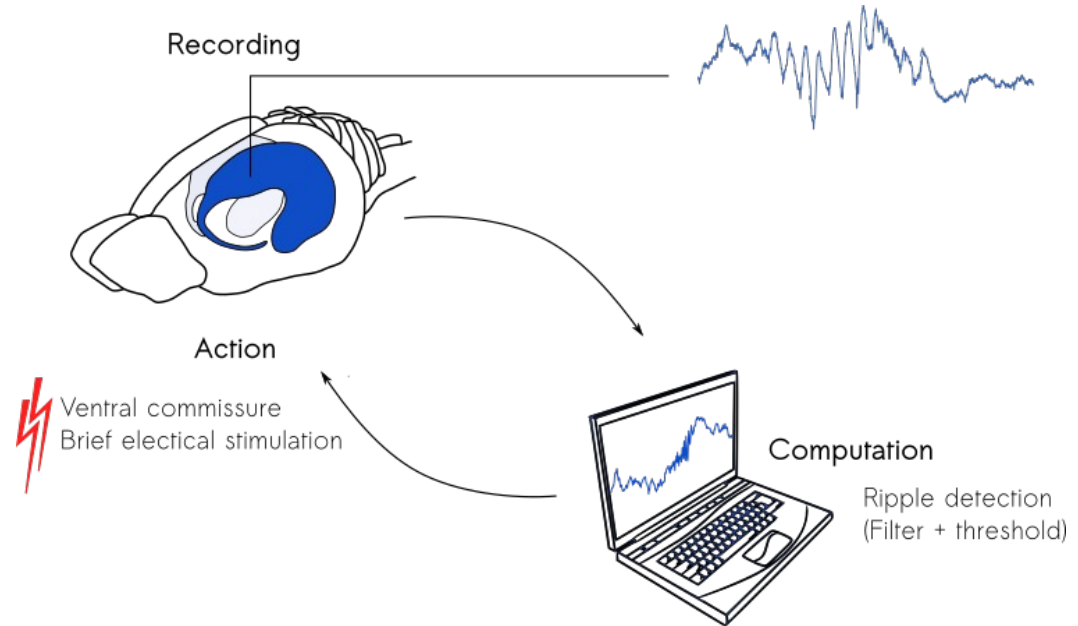
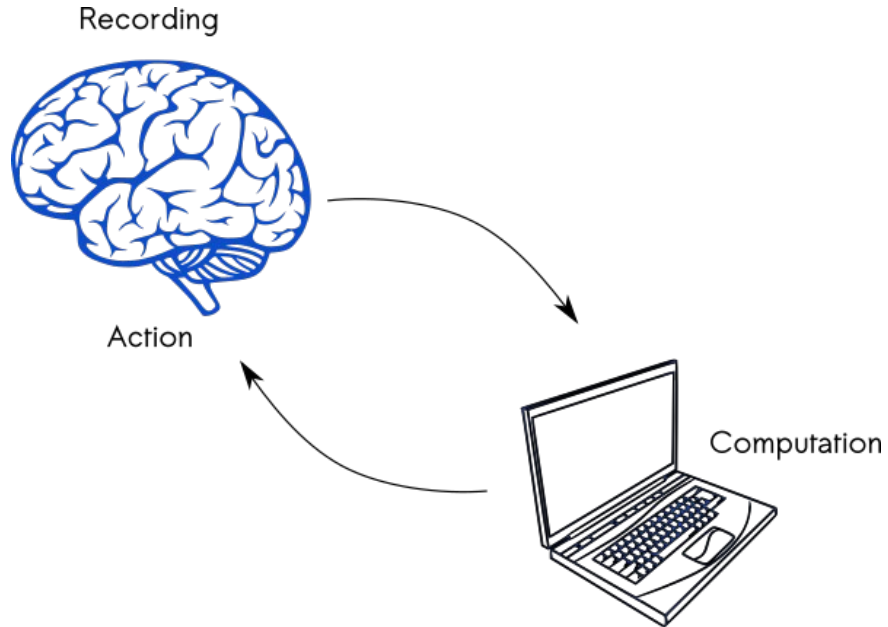
Library Genesis^{2M}

Alternative domains: libgen.gs; libgen.lc; libgen.li; genesis.lib (?)
Official Twitter of the project
Descriptions for 100k European comics are formed in the section [comics](#)
Added materials from torrent tracker [Bibliotik](#) : 250k files in the [fiction](#) section, 150k files in [main section](#)
[Letter of Solidarity](#)

Search in :
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Case causal study 1 : ripples

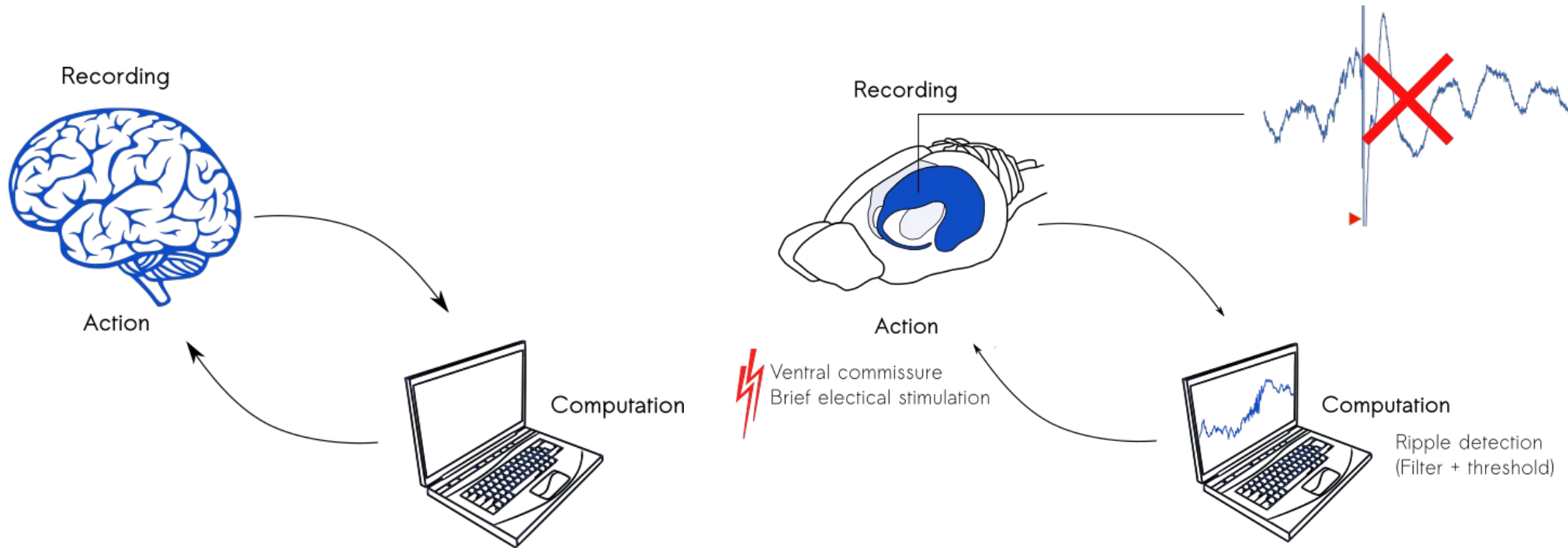


Selective suppression of hippocampal ripples impairs spatial memory

Gabrielle Girardeau, Karim Benchenane, Sidney I Wiener, György Buzsáki  & Michaël B Zugaro 

Nature Neuroscience 12, 1222–1223(2009) | Cite this article

Case causal study 1 : ripples

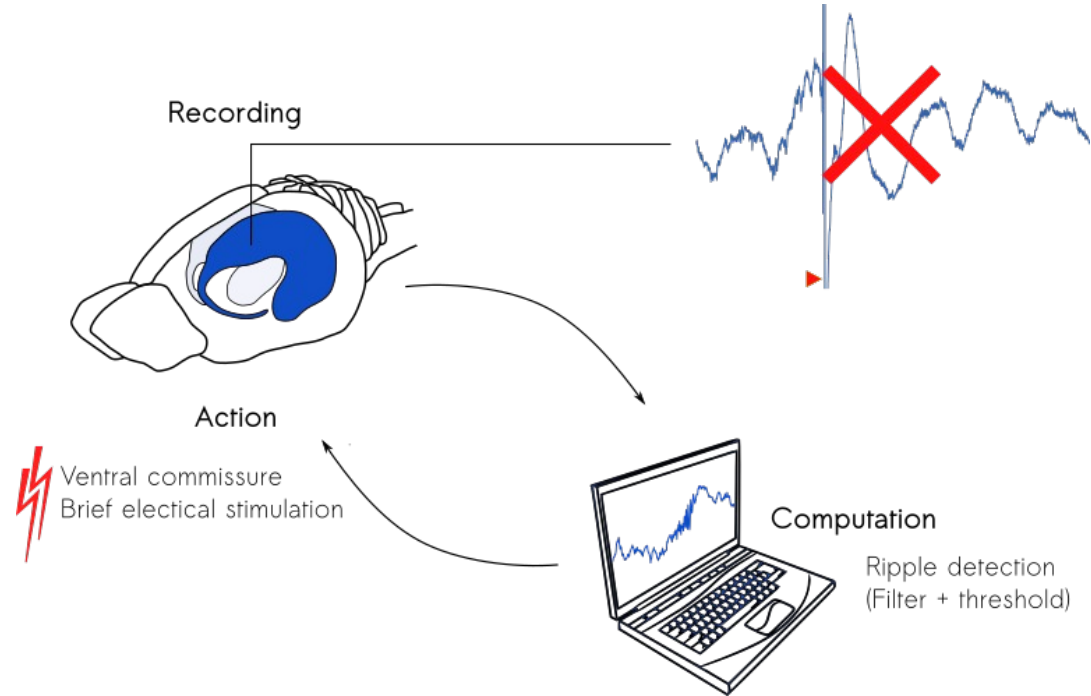
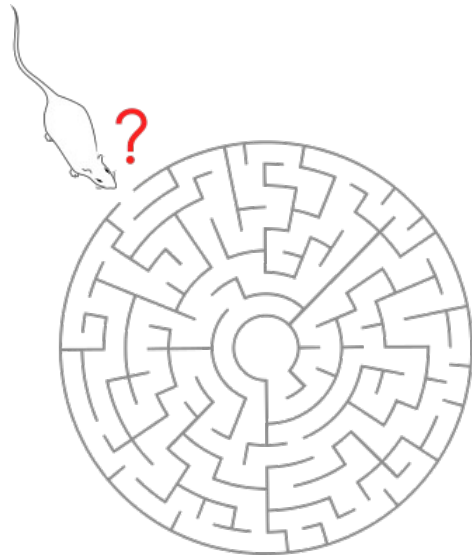


Selective suppression of hippocampal ripples impairs spatial memory

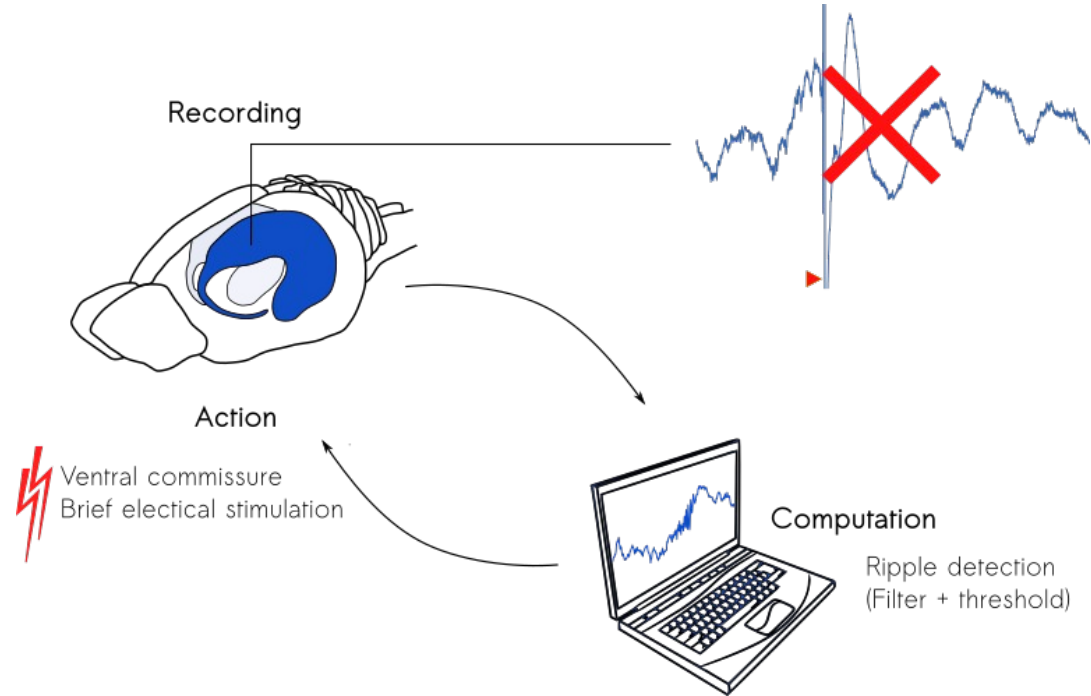
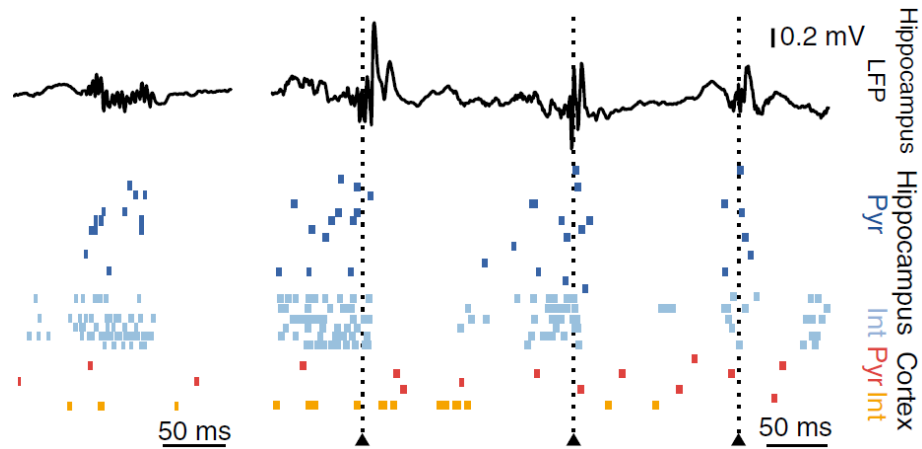
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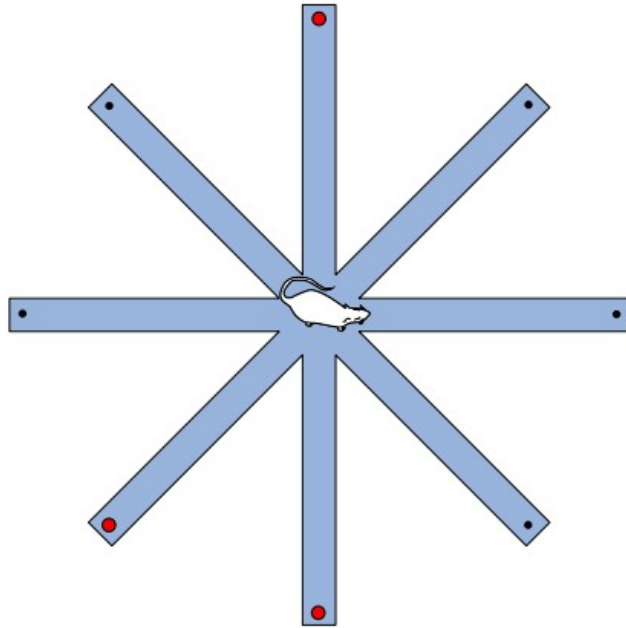
Case causal study 1 : ripples



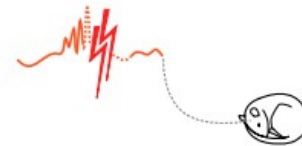
Case causal study 1 : ripples



Case causal study 1 : ripples

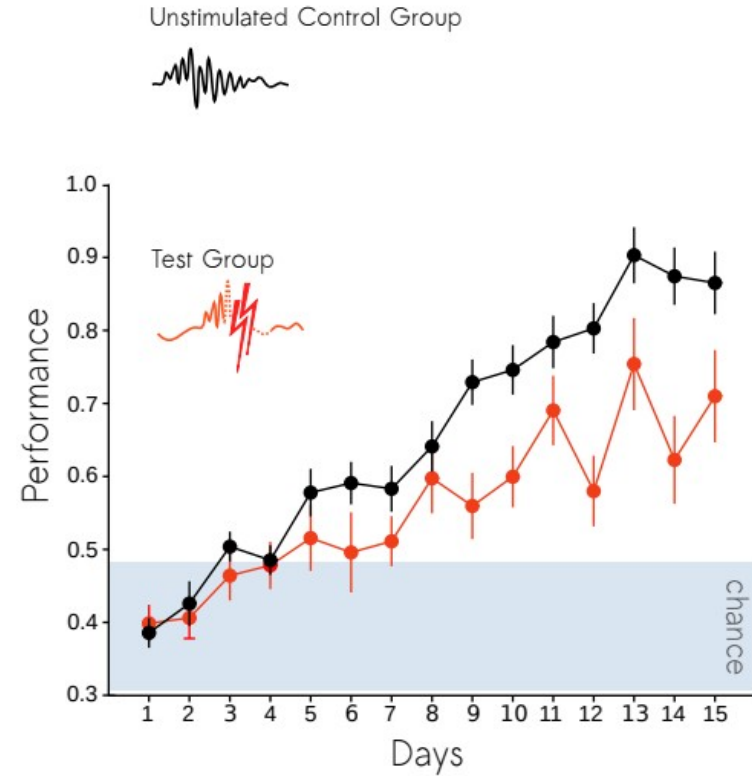
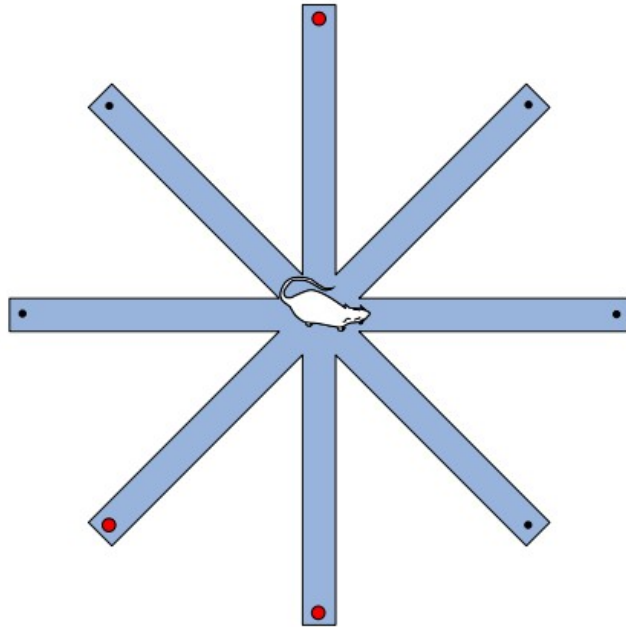


Training on a spatial task : 8-arms radial maze

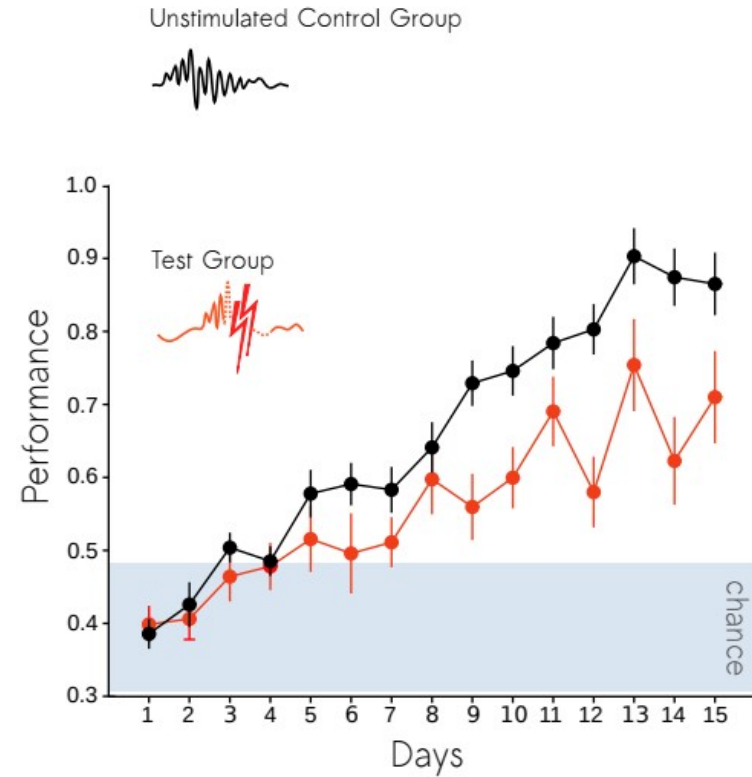
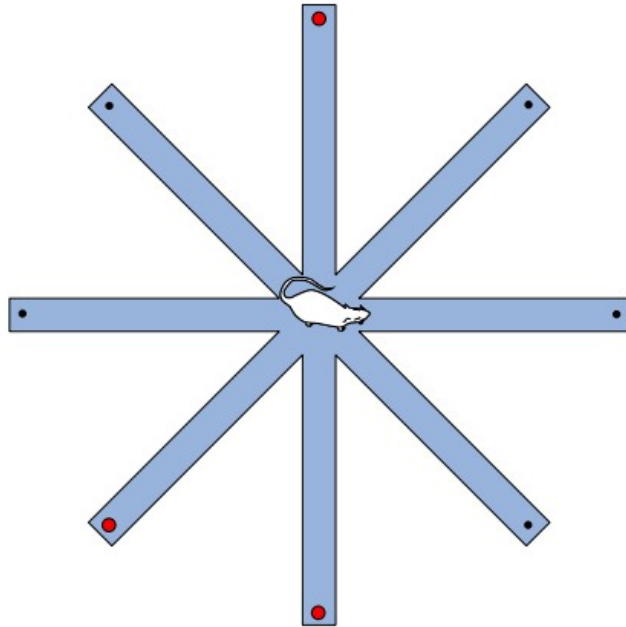


Sleep and rest : 1h ripple suppression

Case causal study 1 : ripples

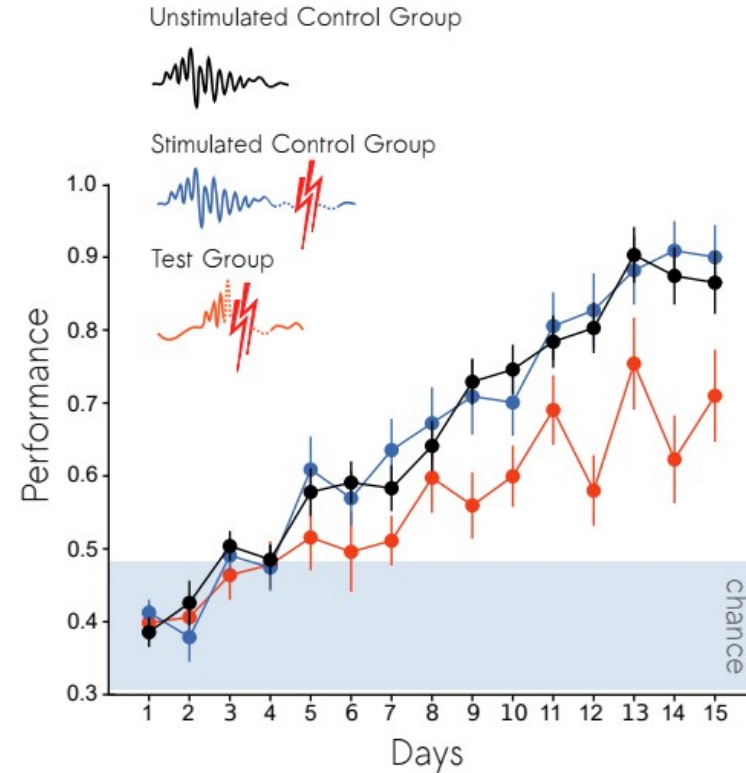
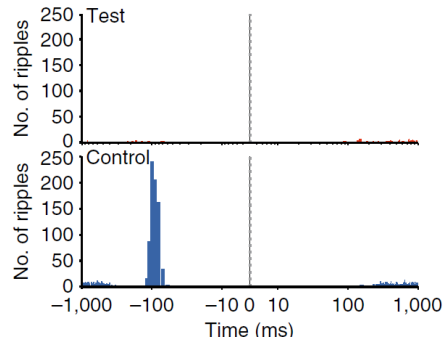
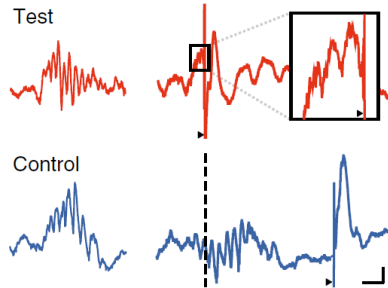


Case causal study 1 : ripples

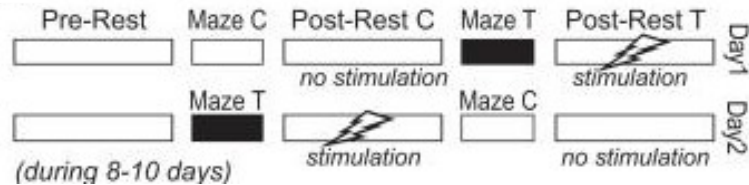
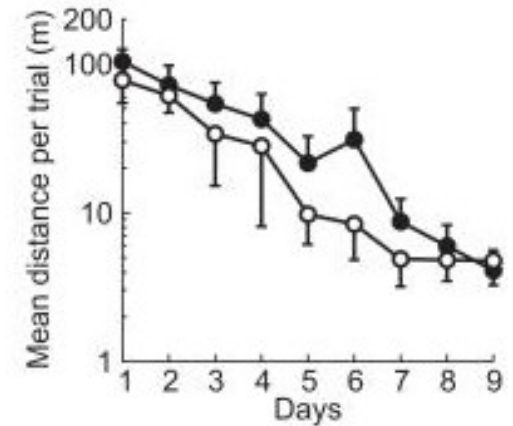
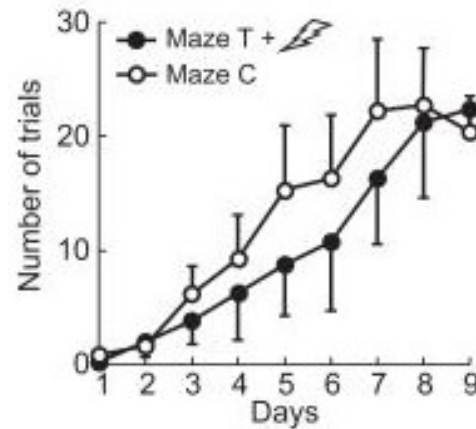
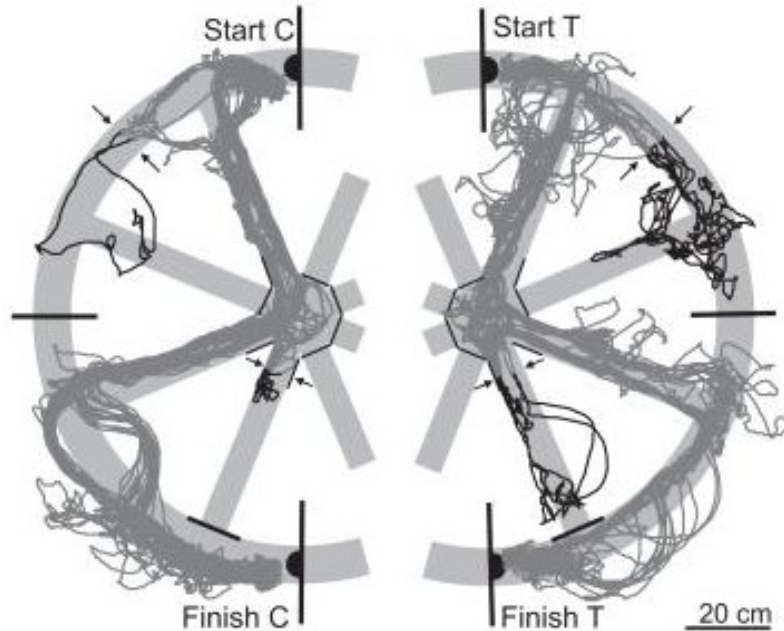


What's missing ?

Case causal study 1 : ripples



Case causal study 2 : ripples

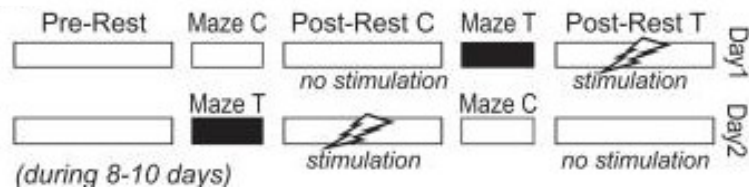
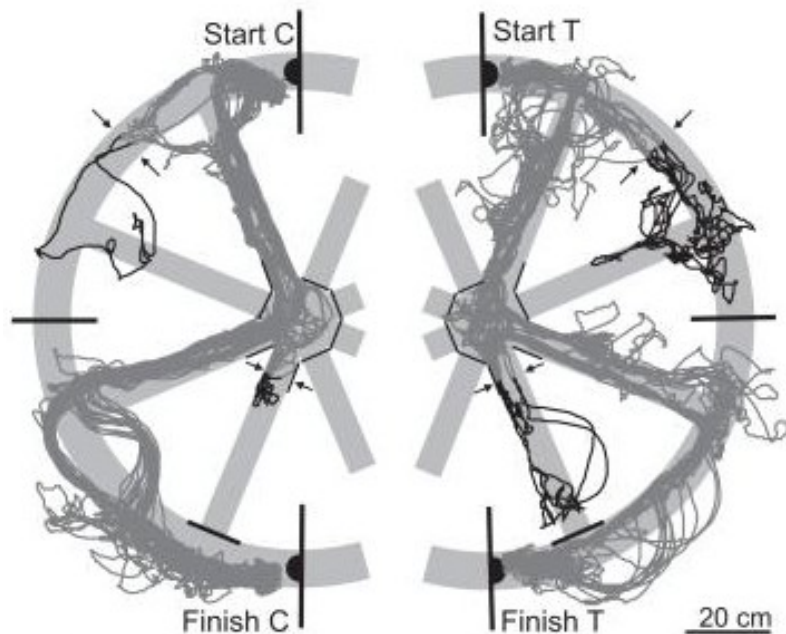


> [Hippocampus](https://doi.org/10.1002/hipo.20707). 2010 Jan;20(1):1-10. doi: 10.1002/hipo.20707.

Disruption of ripple-associated hippocampal activity during rest impairs spatial learning in the rat

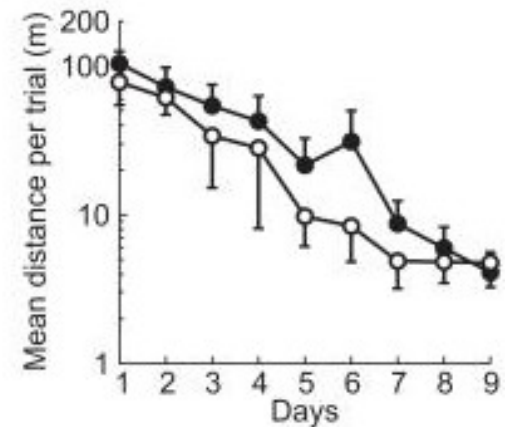
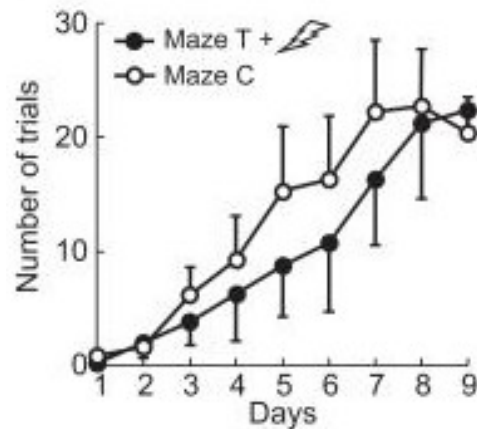
Valérie Ego-Stengel¹, Matthew A Wilson

Case causal study 2 : ripples



What's missing in this experimental design ?

What's good with this experimental design ?



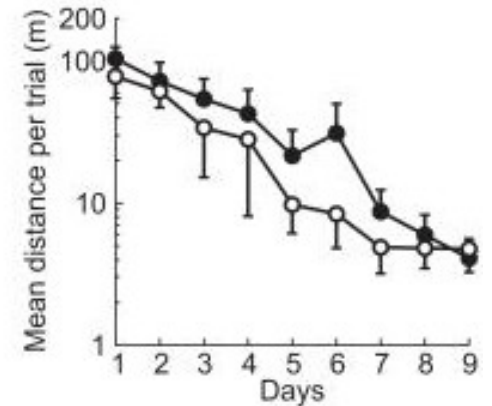
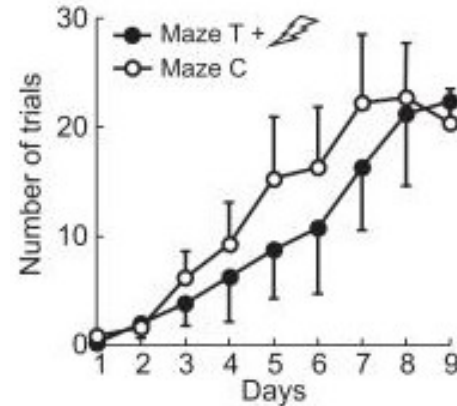
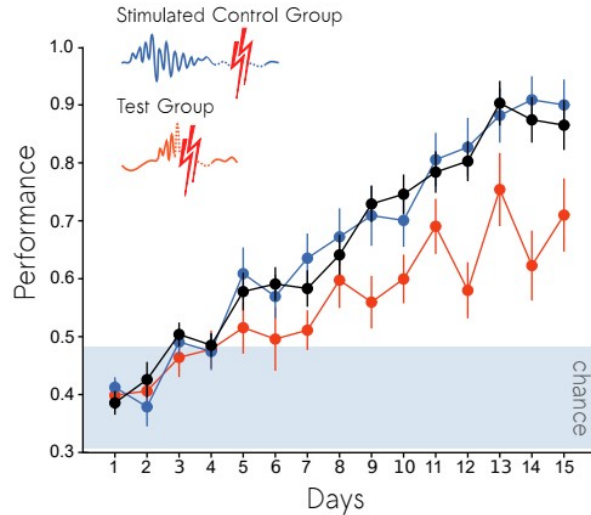
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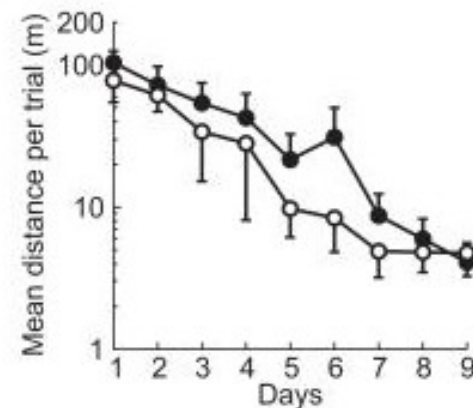
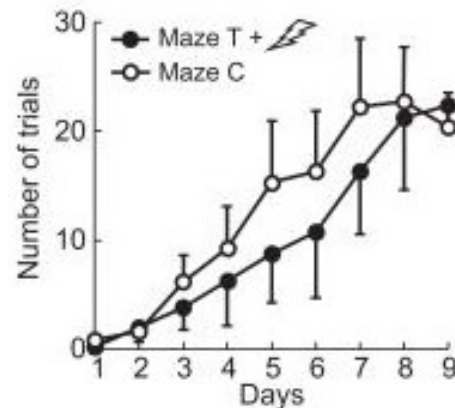
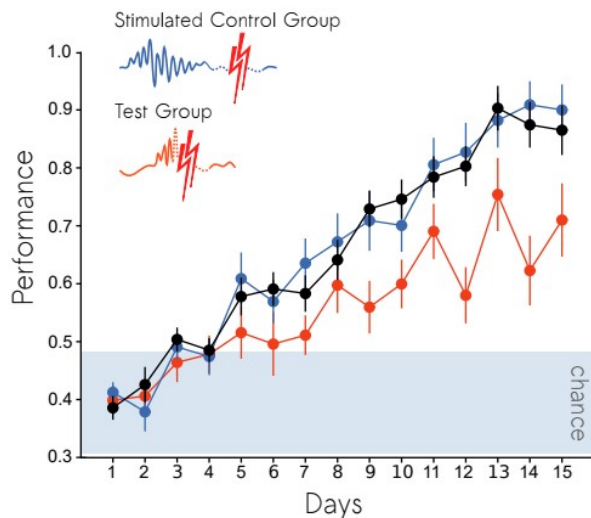
Case causal studies : ripples

- Notice something ?



Case causal studies : ripples

- Notice something ?



These initial task designs were rooted in the idea of consolidation as a *gradual* transfer towards neocortical areas via a hippocampo-cortical dialogue (differential involvement of hippocampus in recent vs remote memories).

Case causal study 3 : ripples

- Different method/task/timescale

Can you think of a good hippocampus-dependent behavioral task that is also a one-shot learning ?

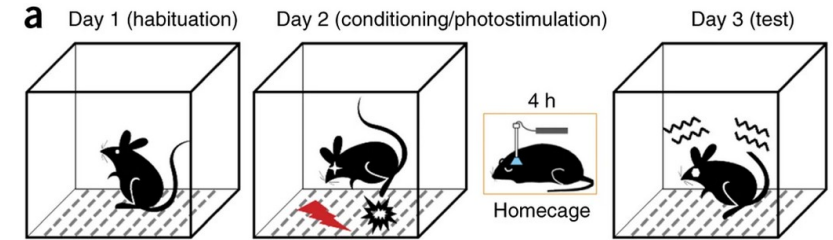
Case causal study 3 : ripples

- Different method/task/timescale

Mesopontine median raphe regulates hippocampal ripple oscillation and memory consolidation

Dong V Wang, Hau-Jie Yau, Carl J Broker, Jen-Hui Tsou, Antonello Bonci & Satoshi Ikemoto 

Nature Neuroscience **18**, 728–735(2015) | [Cite this article](#)



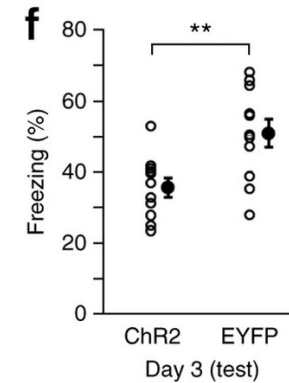
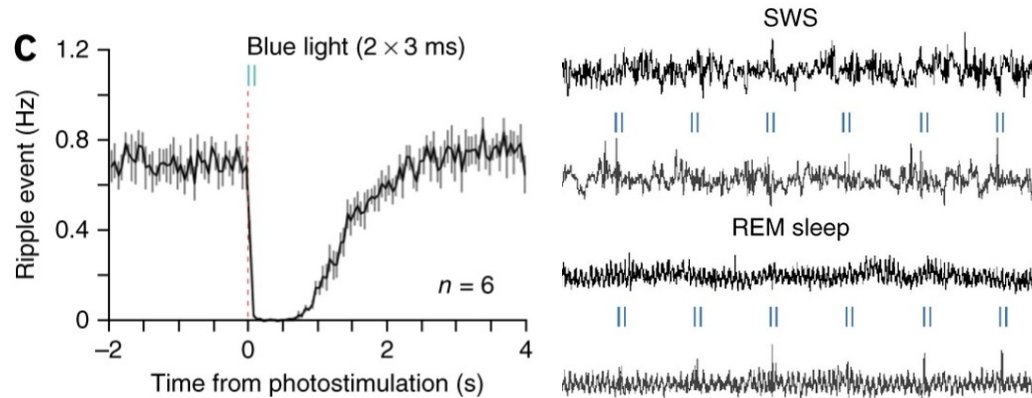
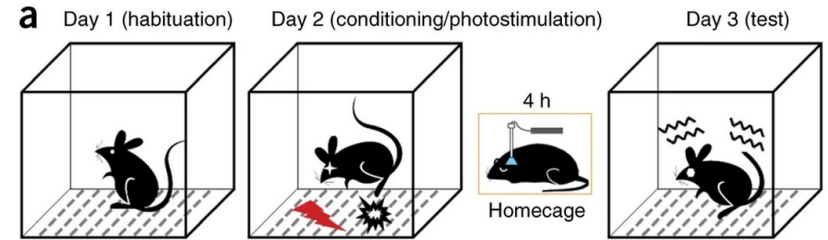
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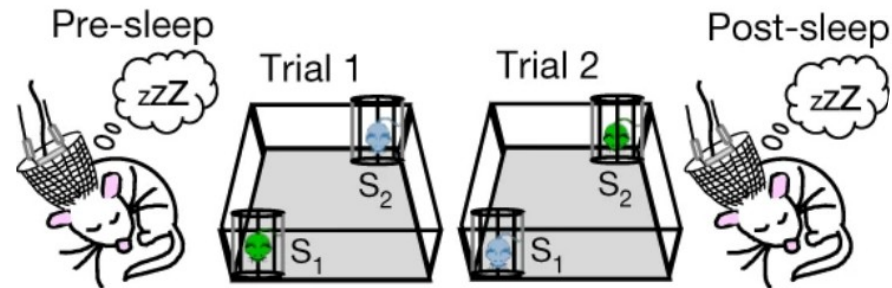


Case causal study 4 : ripples

> [Nature](#). 2020 Nov;587(7833):264-269. doi: 10.1038/s41586-020-2758-y. Epub 2020 Sep 23.

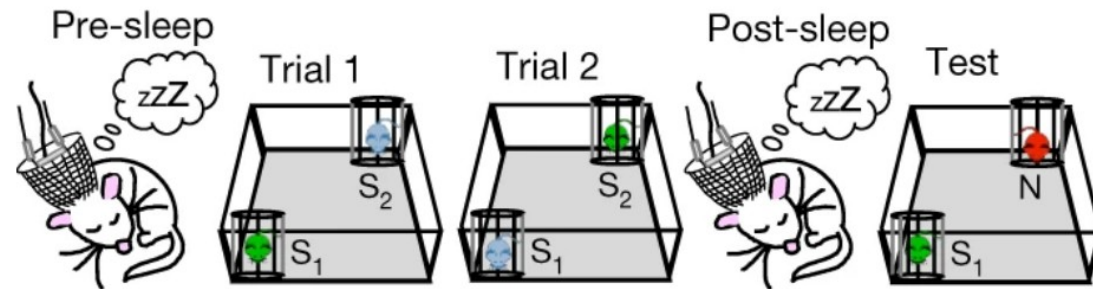
Hippocampal CA2 sharp-wave ripples reactivate and promote social memory

Azahara Oliva ¹, Antonio Fernández-Ruiz ², Felix Leroy ³, Steven A Siegelbaum ^{4 5}

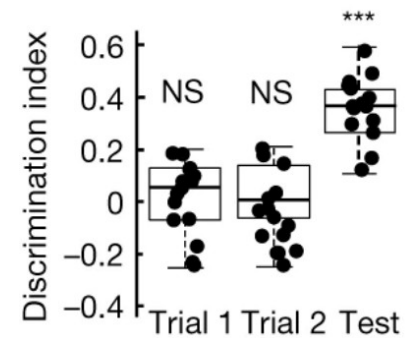
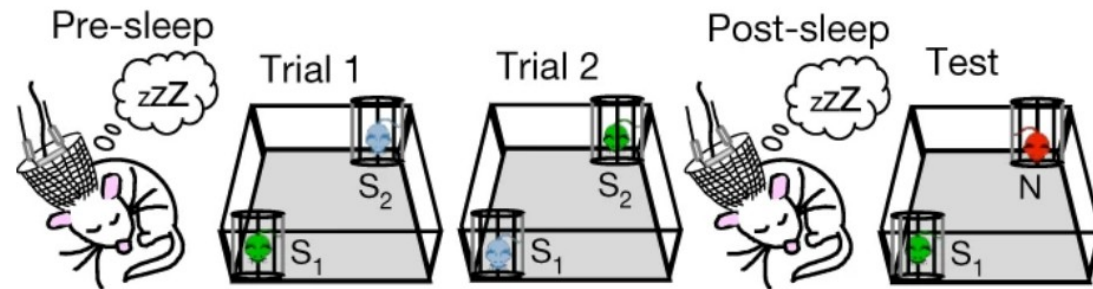


Retrieval
test ?

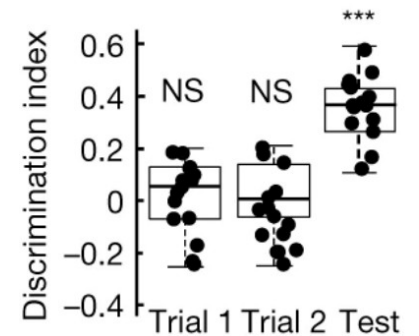
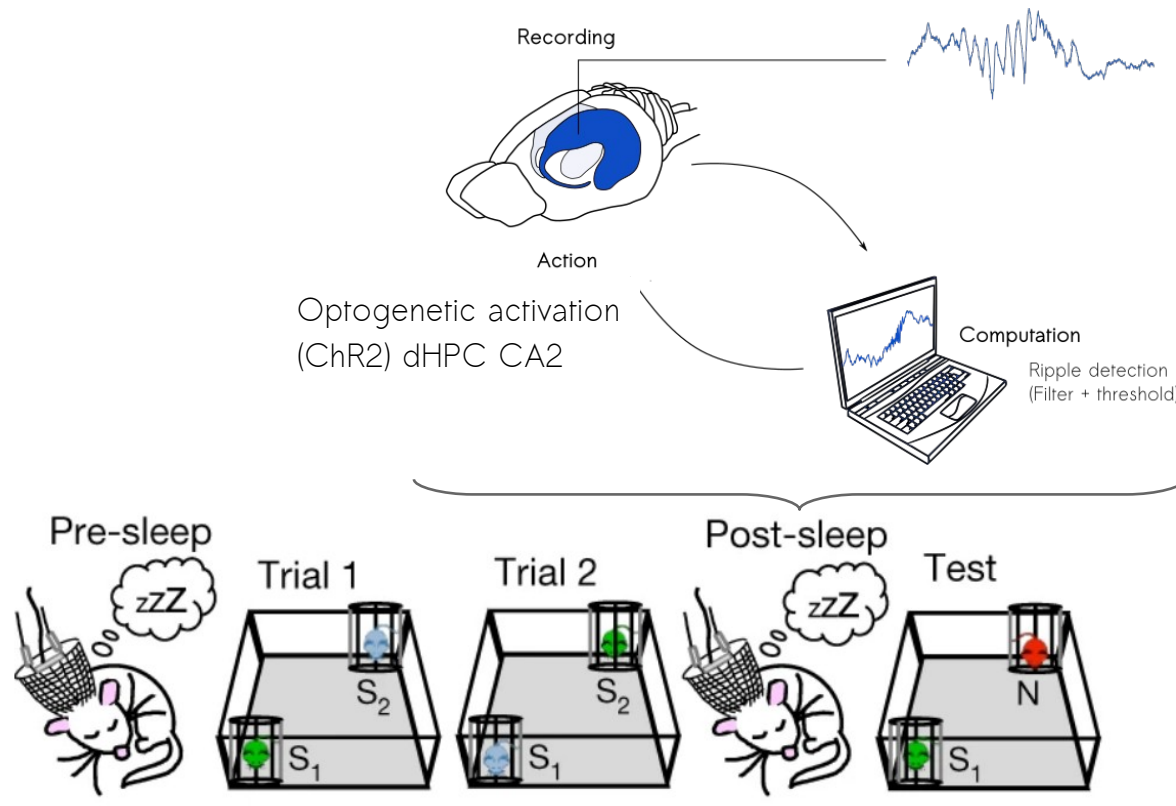
Case causal study 4 : ripples



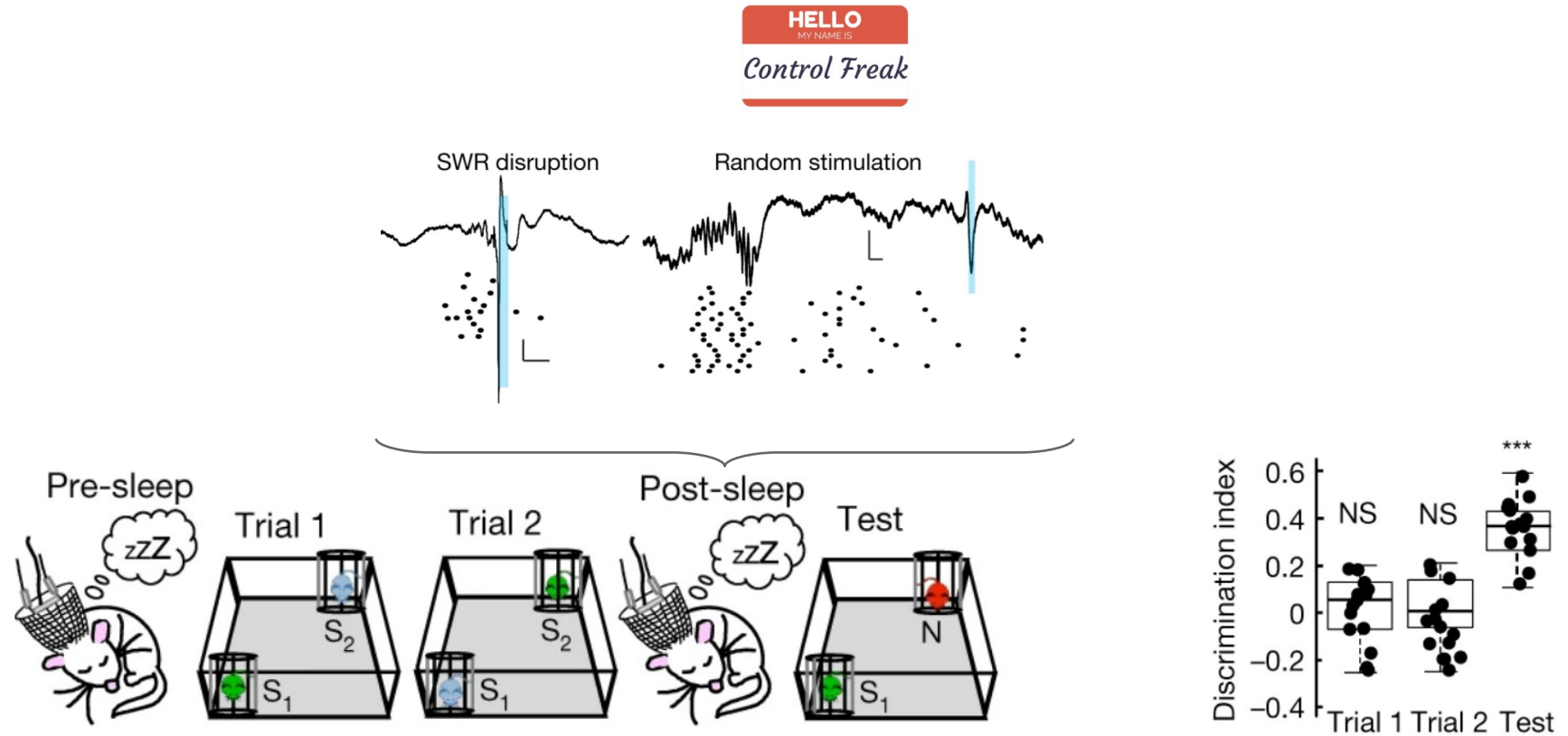
Case causal study 4 : ripples



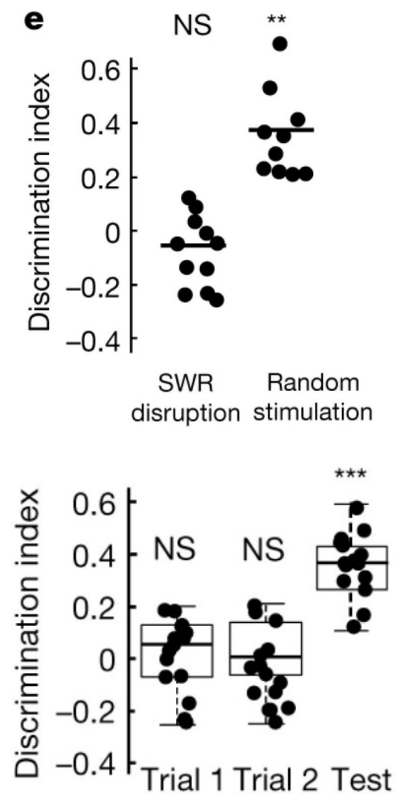
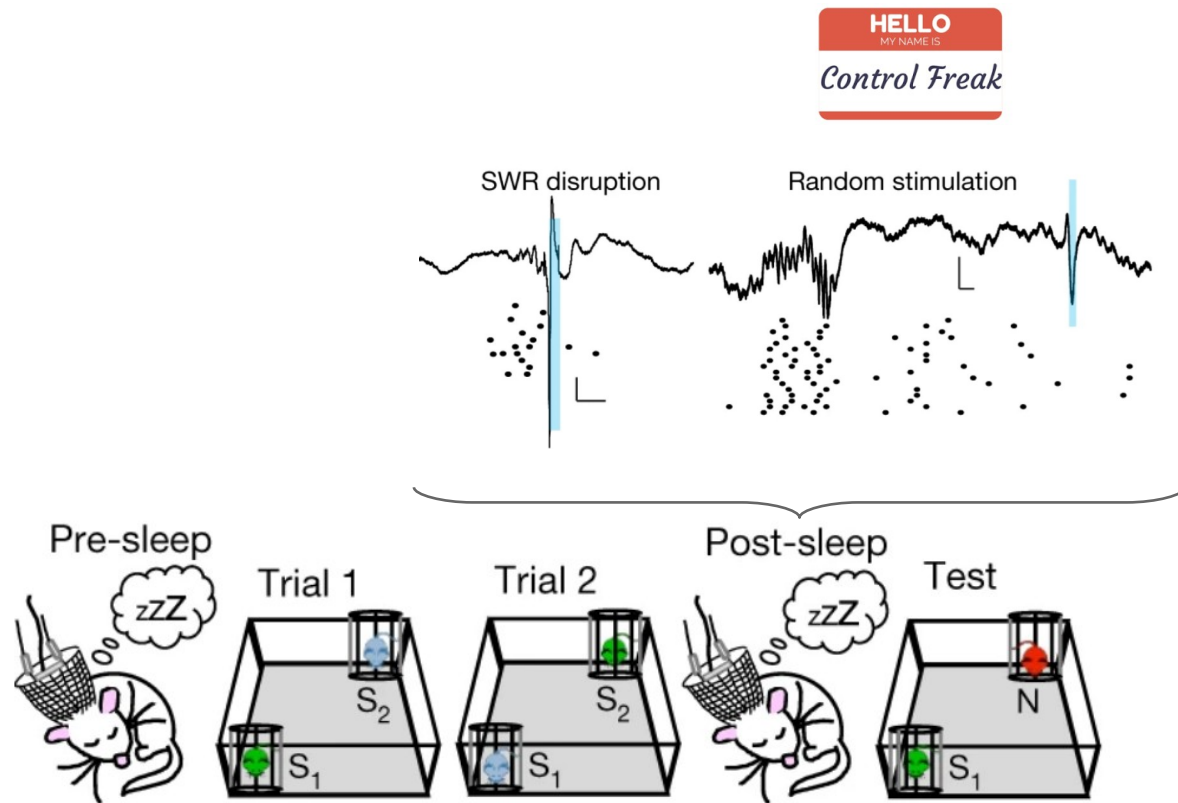
Case causal study 4 : ripples



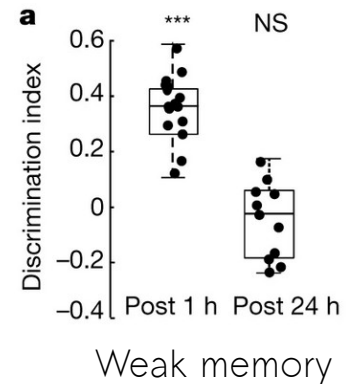
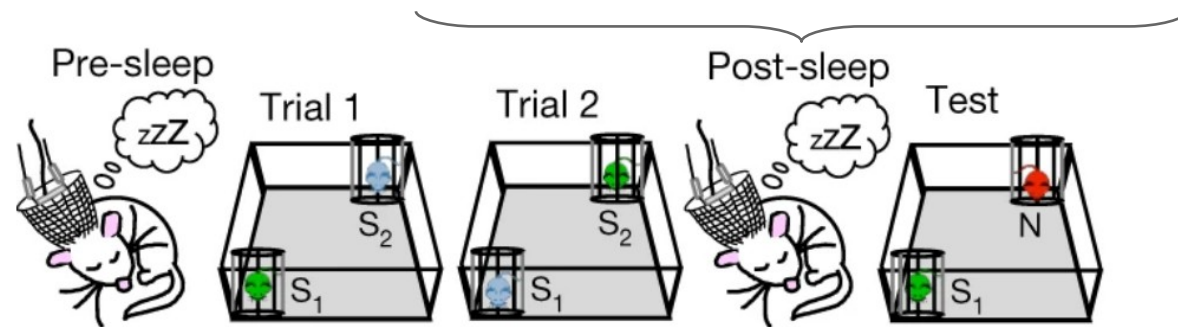
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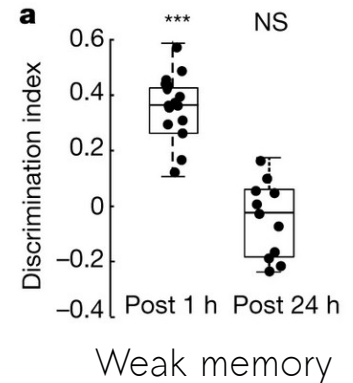
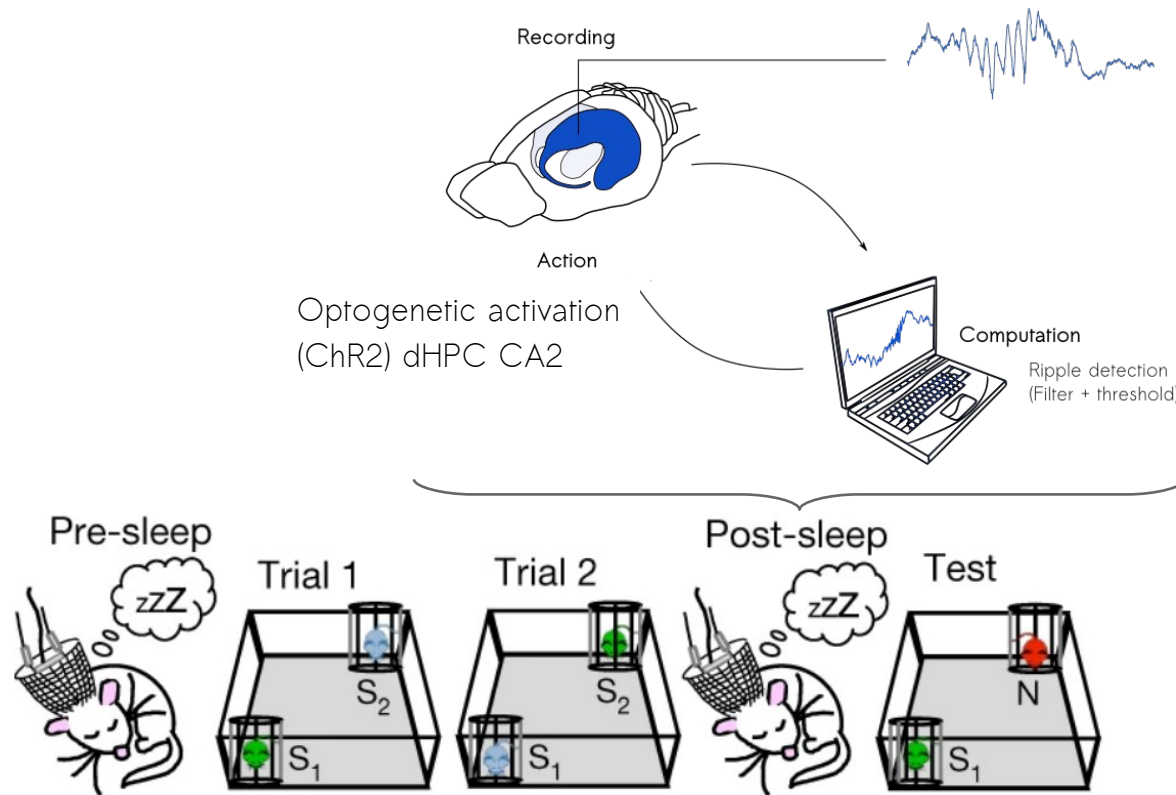
Case causal study 4 : ripples



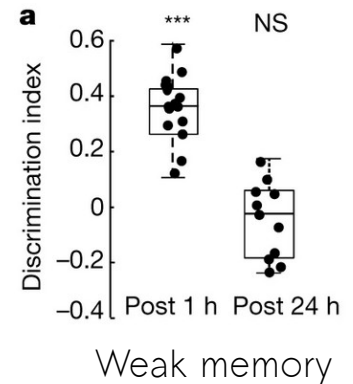
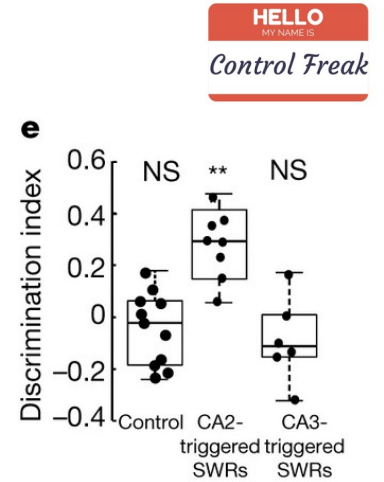
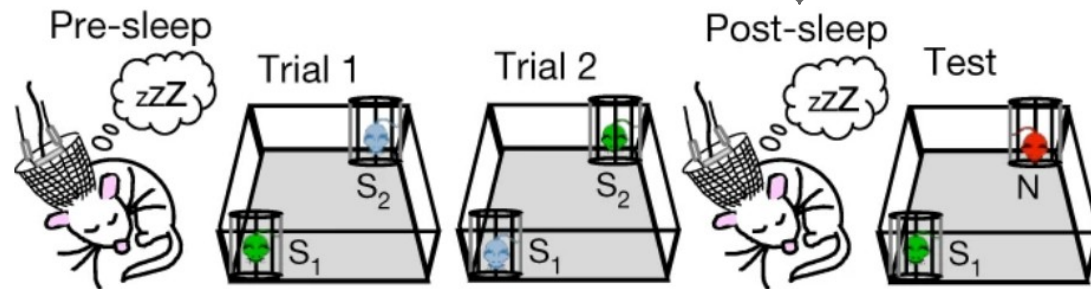
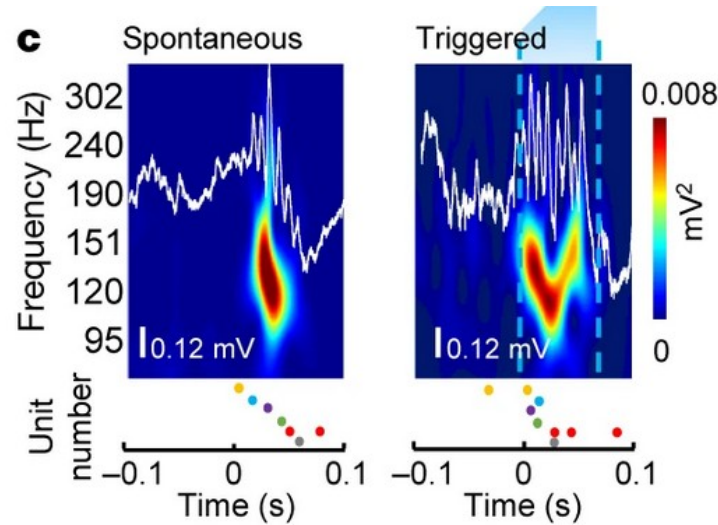
Case causal study 4 : ripples



Case causal study 4 : ripples



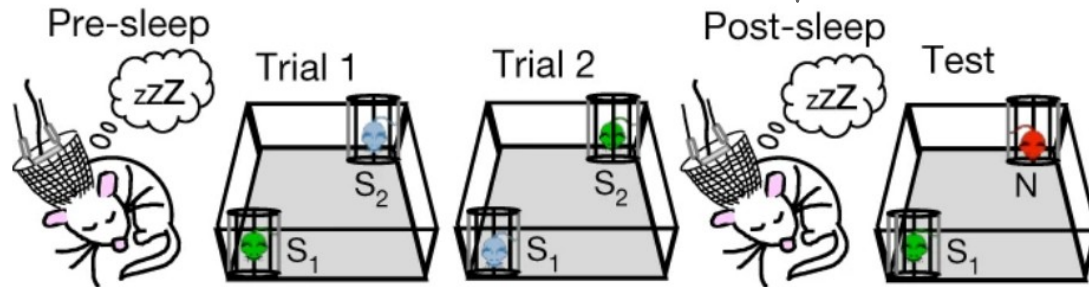
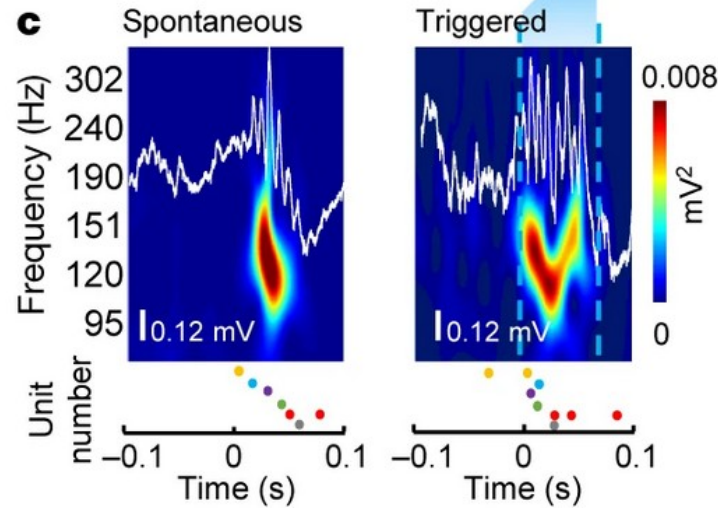
Case causal study 4 : ripples



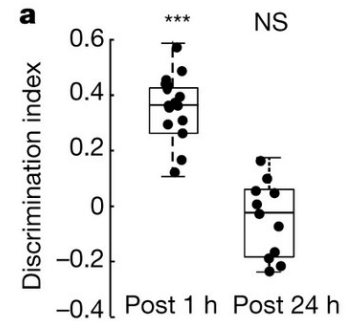
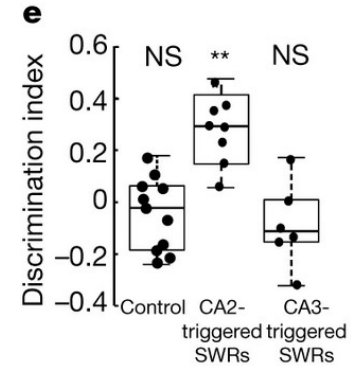
Case causal study 4 : ripples

?

At this point you should be asking yourself a question



HELLO
MY NAME IS
Control Freak



Weak memory

Non-REM sleep sharp-wave ripples

- Can be bidirectionally modified (supressed or enhanced) through electrical or optogenetic stimulations with closed loop or traditional systems
- Are causally involved in spatial and social memory consolidation
- What about replay ?
 - Do you think the previous studies answered whether replay is involved in memory consolidation ?

Non-REM sleep sharp-wave ripples

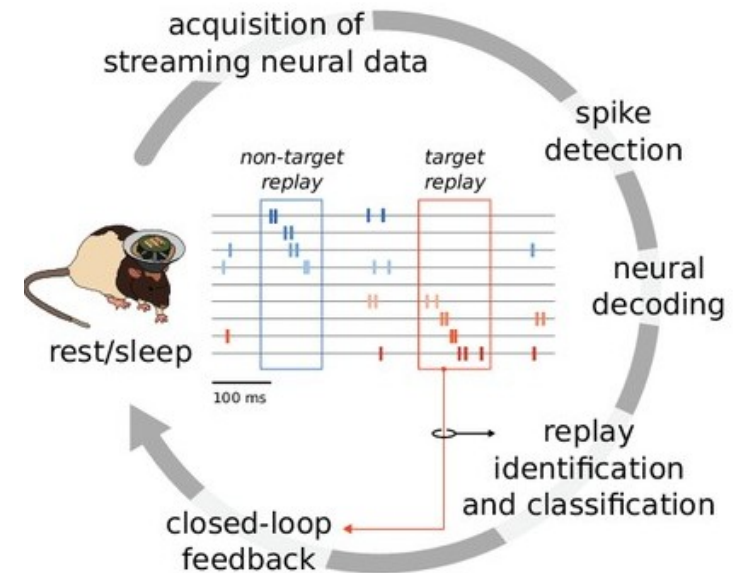
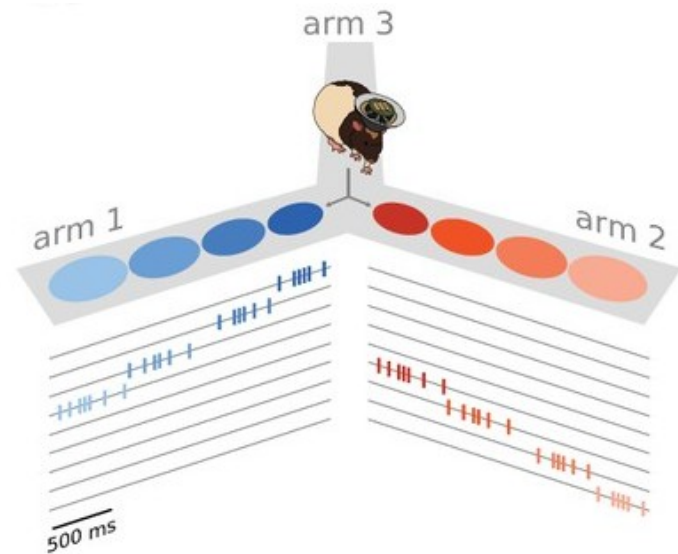
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- Are causally involved in spatial and social memory consolidation
- What about replay ?
 - Do you think the previous studies answered whether replay is involved in memory consolidation ?
 - Try and think of an experiment that would

Replay ?

> [Elife](#). 2018 Oct 30;7:e36275. doi: 10.7554/eLife.36275.

Real-time classification of experience-related ensemble spiking patterns for closed-loop applications

Davide Ciliberti ^{1 2 3}, Frédéric Michon ^{1 2 3}, Fabian Kloosterman ^{1 2 3 4}

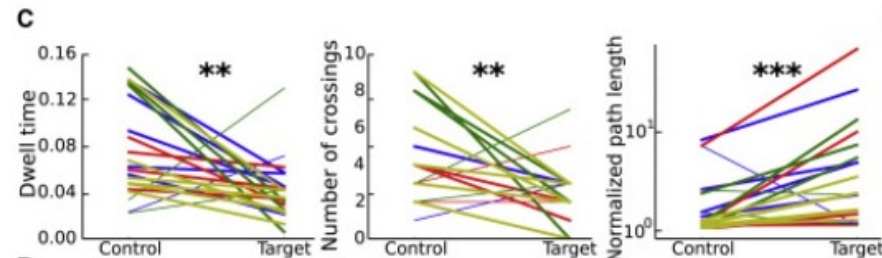
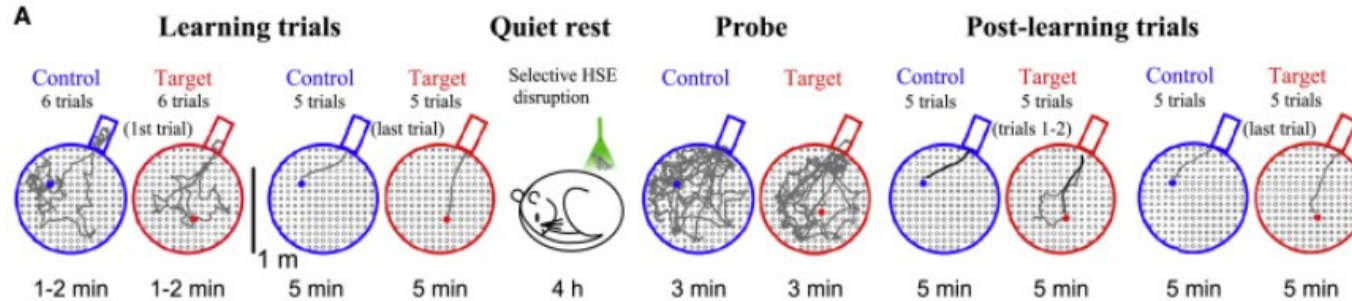


Replay ?

> *Neuron*. 2020 Apr 22;106(2):291-300.e6. doi: 10.1016/j.neuron.2020.01.021. Epub 2020 Feb 17.

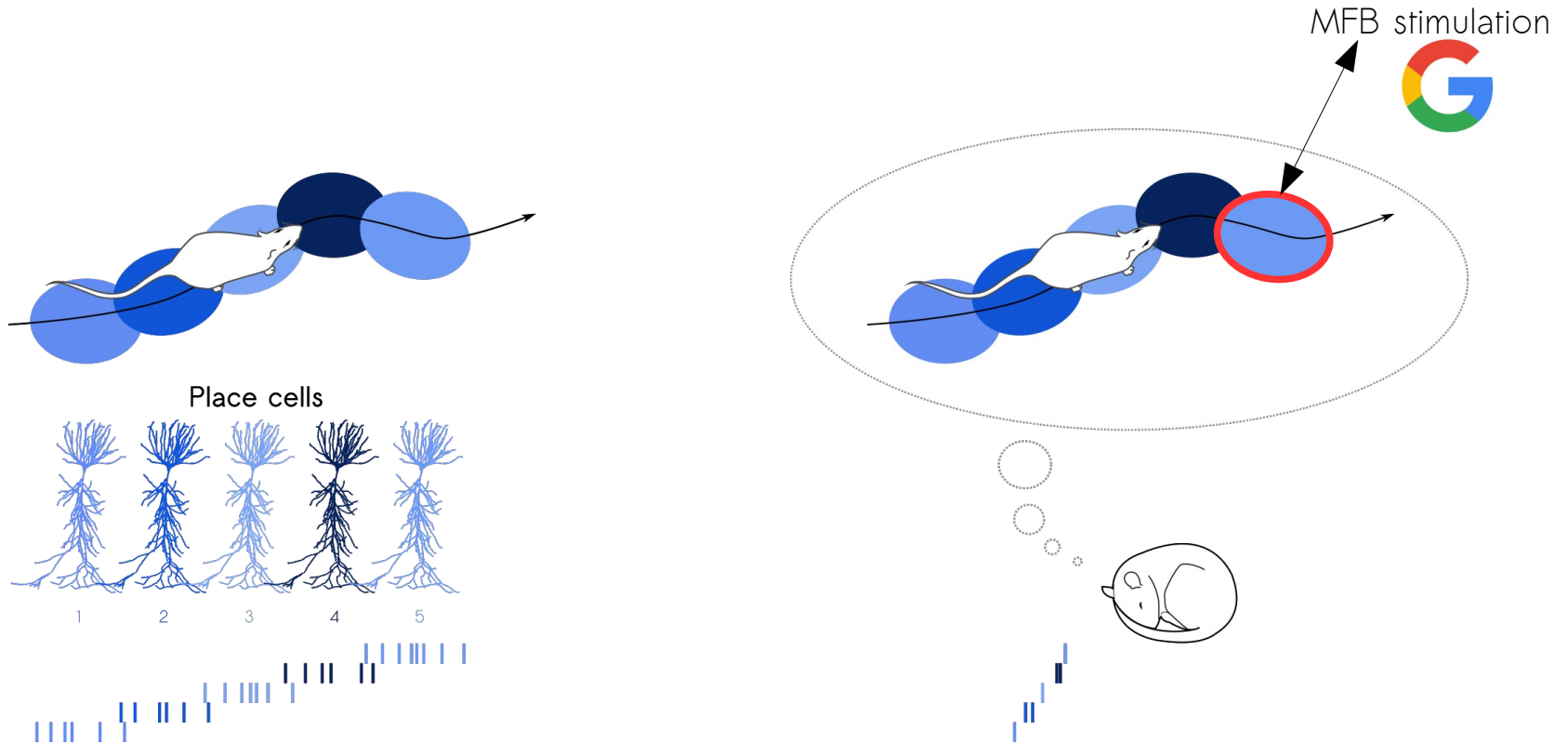
Assembly-Specific Disruption of Hippocampal Replay Leads to Selective Memory Deficit

Igor Gridchyn¹, Philipp Schoenenberger¹, Joseph O'Neill¹, Jozsef Csicsvari²

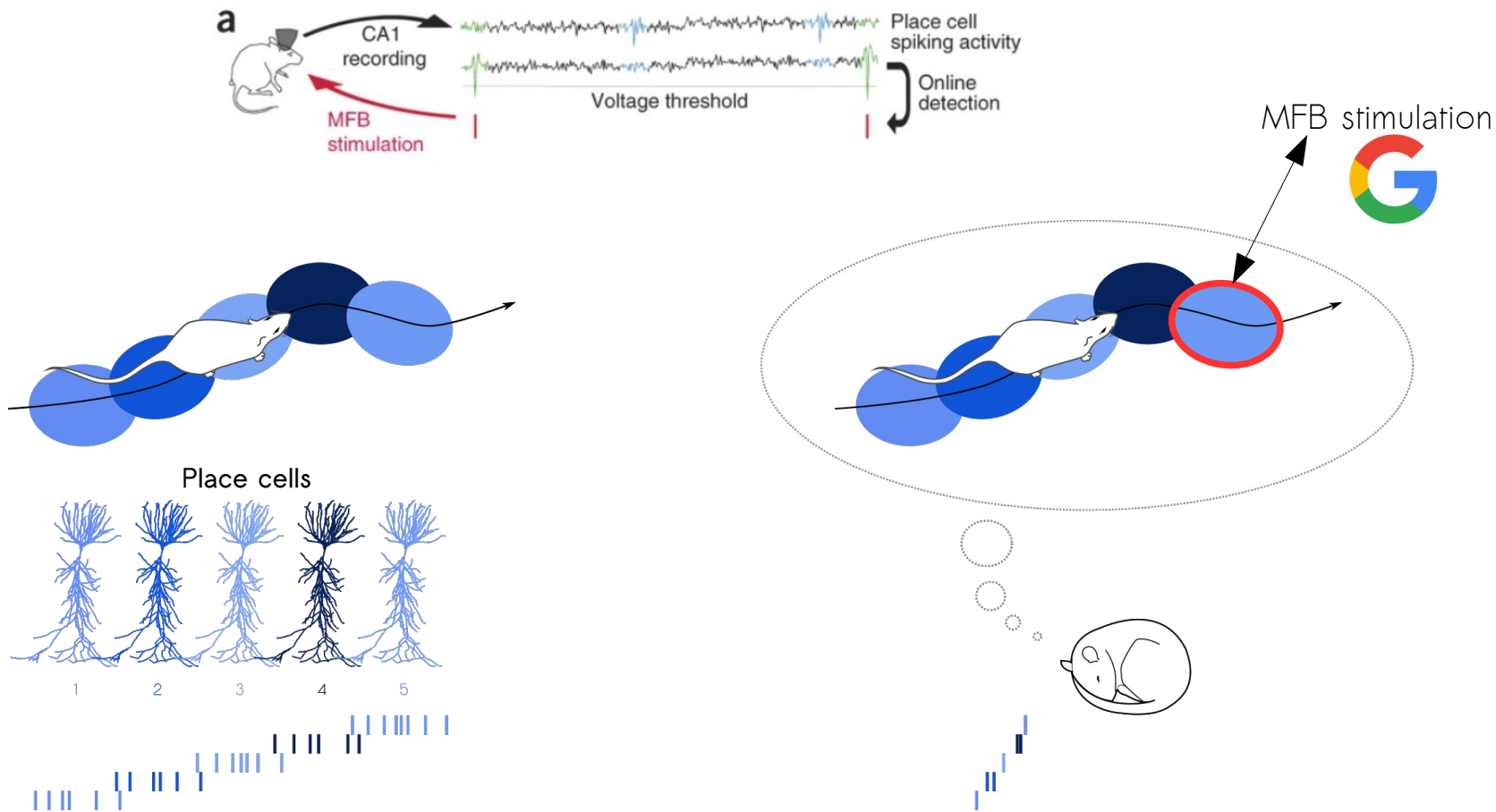


Replay : the prequel

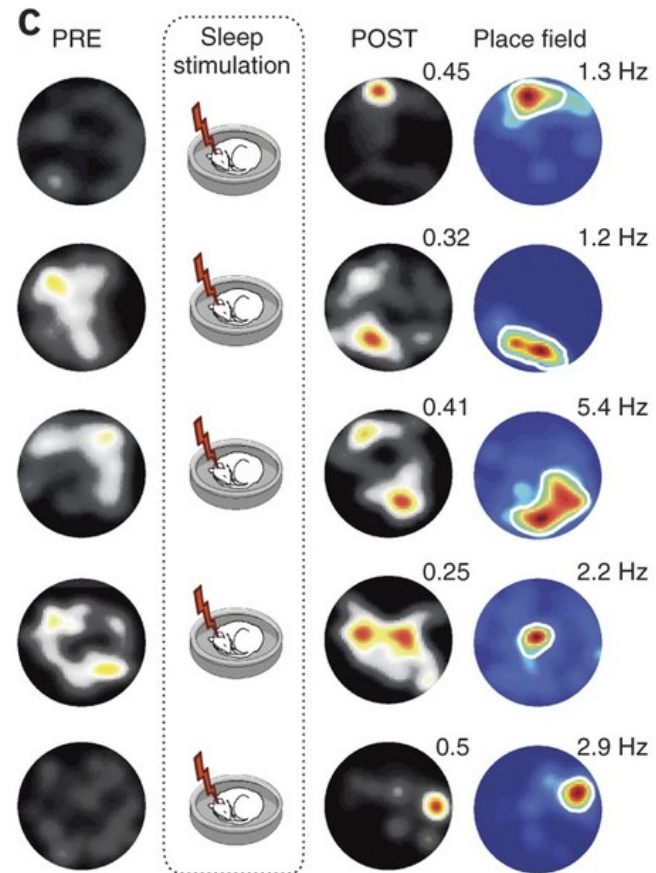
- Search MFB (Medial forebrain bundle) on The Internet and take a minute to try and figure out what is the experimental design and the results



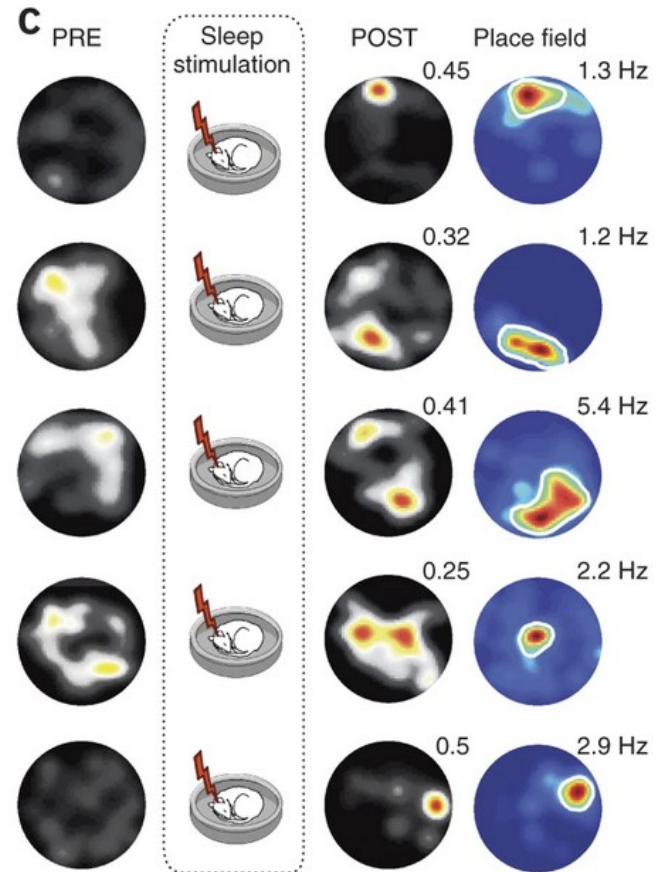
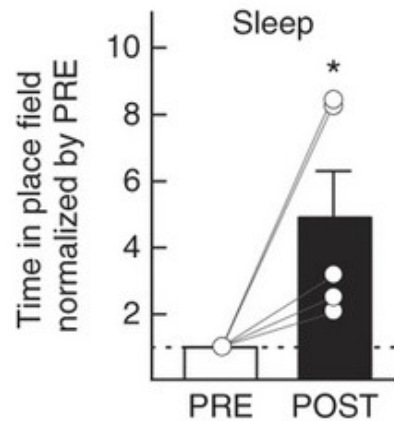
Replay : the prequel



Replay : the prequel



Replay : the prequel

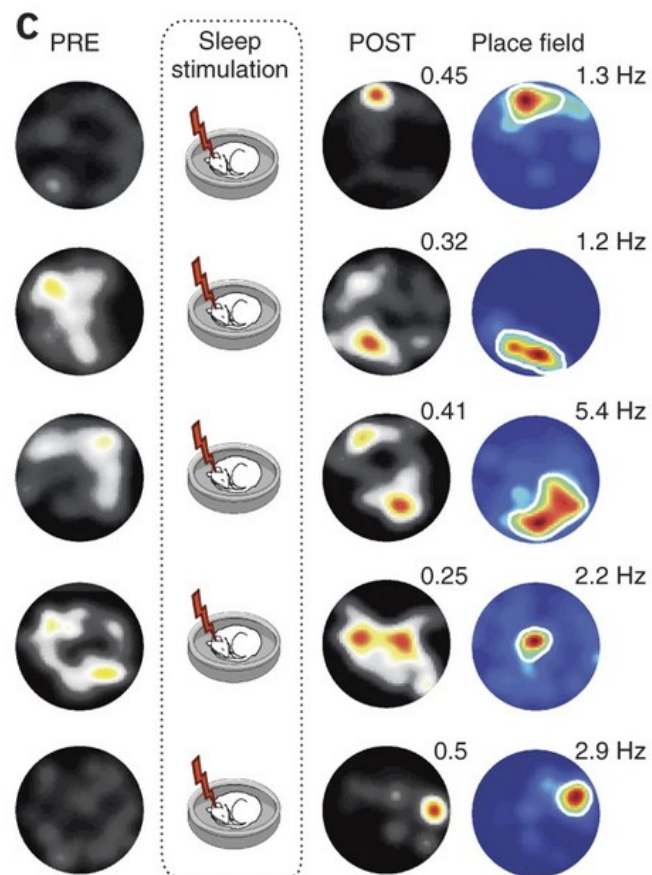
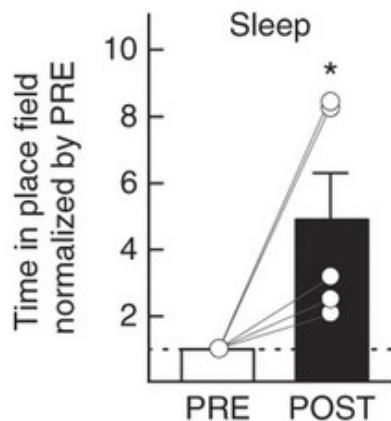


Replay : the prequel

Explicit memory creation during sleep demonstrates a causal role of place cells in navigation

Gaetan de Lavilléon, Marie Masako Lacroix, Laure Rondi-Reig & Karim Benchenane ✉

Nature Neuroscience 18, 493–495(2015) | [Cite this article](#)



Non-REM sleep sharp-wave ripples

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 - *Awake* sharp-wave ripples (several closed-loop bidirectional modification experiments)
 - Forward and reverse *replay*, during awake and sleep ripples
 - Sharp-wave ripples and *plasticity* : more detailed analysis on the physiology of the hippocampus and the mechanisms underlying the role of ripples in memory. Correlational AND Interventional studies : i.e. closed-loop can also be used to get a *physiological* readout of the pertubation.

Recommended readings

Reviews

Review > [Hippocampus](#). 2015 Oct;25(10):1073-188. doi: 10.1002/hipo.22488.

Hippocampal sharp wave-ripple: A cognitive biomarker for episodic memory and planning

György Buzsáki¹

> [Hippocampus](#). 2020 Jan;30(1):39-49. doi: 10.1002/hipo.22997. Epub 2018 Nov 13.

Hippocampal ripples as a mode of communication with cortical and subcortical areas

Ralitsa Todorova¹, Michaël Zugaro¹



> [Nat Neurosci](#). 2017 Jun;20(6):845-853. doi: 10.1038/nn.4543. Epub 2017 Apr 10.

Sharp wave ripples during learning stabilize the hippocampal spatial map

Lisa Roux¹, Bo Hu¹, Ronny Eichler¹, Eran Stark^{1,2}, György Buzsáki^{1,3,4}

> [PLoS One](#). 2016 Oct 19;11(10):e0164675. doi: 10.1371/journal.pone.0164675. eCollection 2016.

Optogenetically Blocking Sharp Wave Ripple Events in Sleep Does Not Interfere with the Formation of Stable Spatial Representation in the CA1 Area of the Hippocampus

Krisztián A Kovács¹, Joseph O'Neill¹, Philipp Schoenenberger¹, Markku Penttonen², Damaris K Ranguel Guerrero¹, Jozsef Csicsvari¹

Plasticity/Spatial Map

Awake ripples

> [Science](#). 2019 Jun 14;364(6445):1082-1086. doi: 10.1126/science.aax0758.

Long-duration hippocampal sharp wave ripples improve memory

Antonio Fernández-Ruiz¹, Azahara Oliva^{1,2}, Eliezyer Fermino de Oliveira^{1,3}, Florbela Rocha-Almeida^{1,4}, David Tingley¹, György Buzsáki^{5,6}

> [Science](#). 2012 Jun 15;336(6087):1454-8. doi: 10.1126/science.1217230. Epub 2012 May 3.

Awake hippocampal sharp-wave ripples support spatial memory

Shantanu P Jadhav¹, Caleb Kemere, P Walter German, Loren M Frank

> [Neuron](#). 2016 Dec 7;92(5):968-974. doi: 10.1016/j.neuron.2016.10.020. Epub 2016 Nov 10.

Hippocampal Offline Reactivation Consolidates Recently Formed Cell Assembly Patterns during Sharp Wave-Ripples

Gido M van de Ven¹, Stéphanie Trouche², Colín G McNamara², Kevin Allen³, David Dupret⁴

> [Science](#). 2018 Mar 30;359(6383):1524-1527. doi: 10.1126/science.aao0702. Epub 2018 Feb 8.

Hippocampal ripples down-regulate synapses

Hiroaki Norimoto^{1,2}, Kenichi Makino¹, Mengxuan Gao¹, Yu Shikano¹, Kazuki Okamoto¹, Tomoe Ishikawa¹, Takuya Sasaki¹, Hiroyuki Hioki^{3,4}, Shigeyoshi Fujisawa⁵, Yuji Ikegaya^{6,7}

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- REM-sleep ?

Case causal study : REM-sleep

- How would you test the causal rôle of REM sleep in memory consolidation ?
(2 answers)
- Based on your knowledge of the origin of theta, can you think of an experimental design ?

Case causal study : REM-sleep

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An old school causal method ?



Problem ?



The flowerpot method for REM-sleep deprivation.

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REPORT

Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation

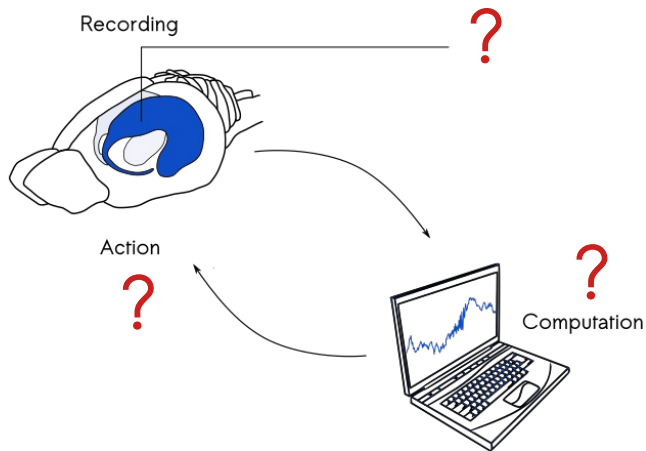
Richard Boyce¹, Stephen D. Glasgow², Sylvain Williams^{2,*†}, Antoine Adamantidis^{2,3,*†}

+ See all authors and affiliations

Science 13 May 2016:
Vol. 352, Issue 6287, pp. 812-816
DOI: 10.1126/science.aad5252

Case causal study : REM-sleep

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REPORT

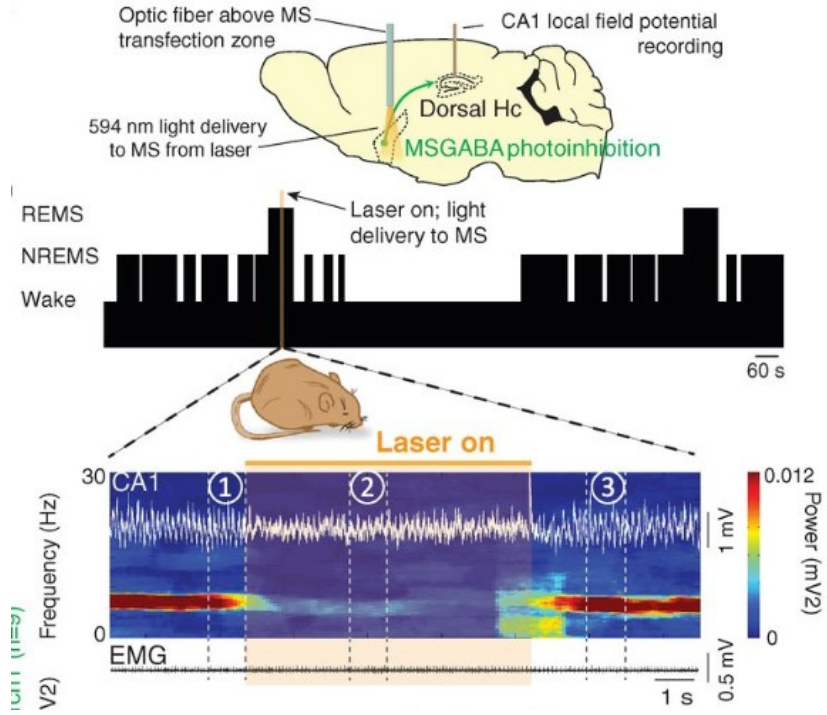
Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation

Richard Boyce¹, Stephen D. Glasgow², Sylvain Williams^{2,*†}, Antoine Adamantidis^{2,3,*†}

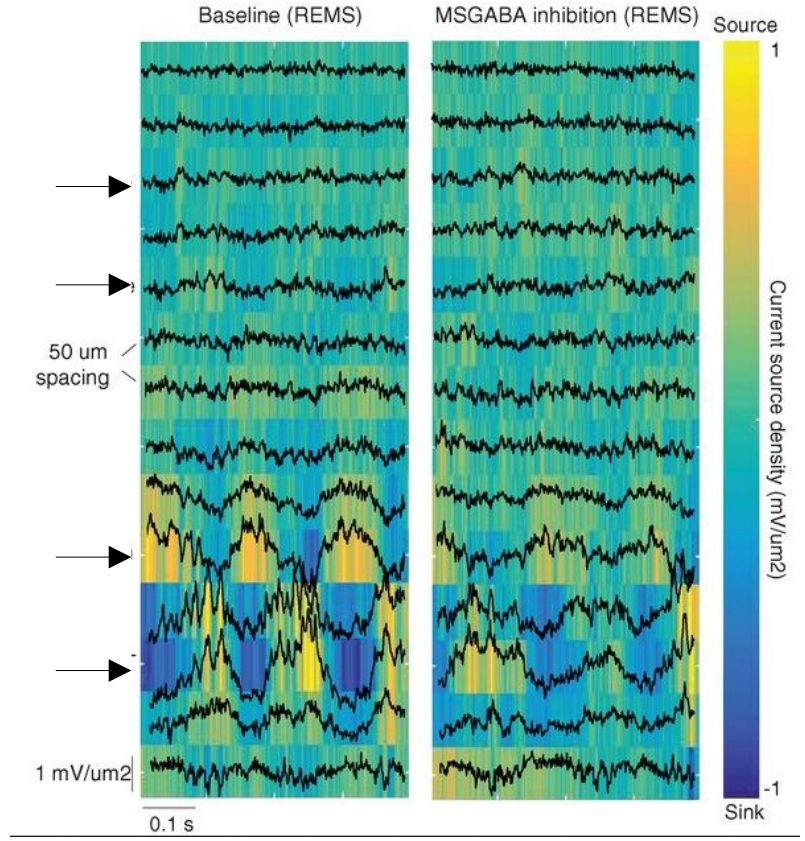
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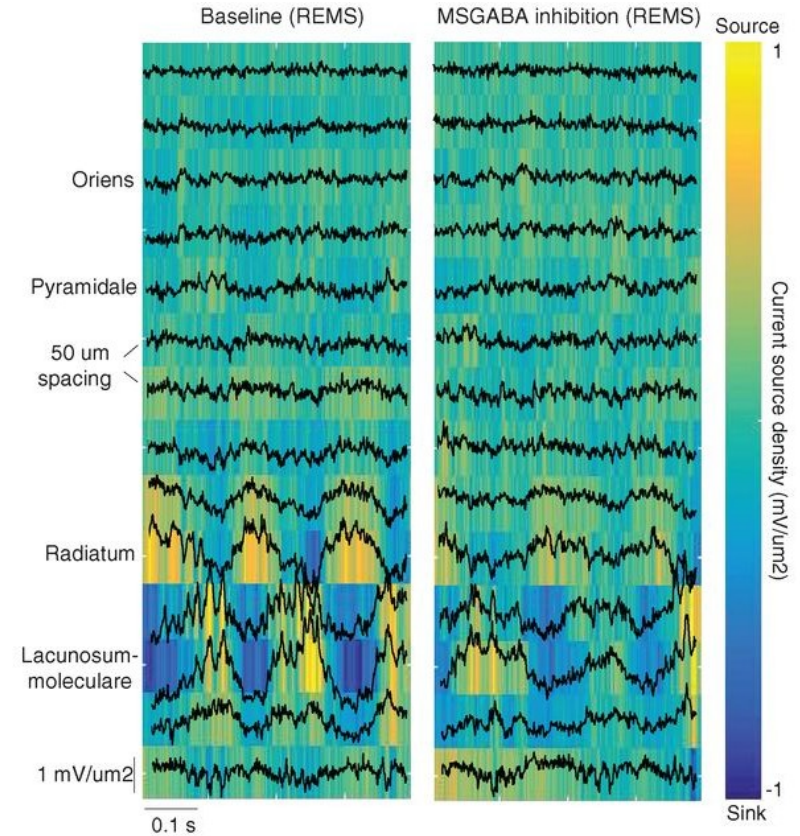
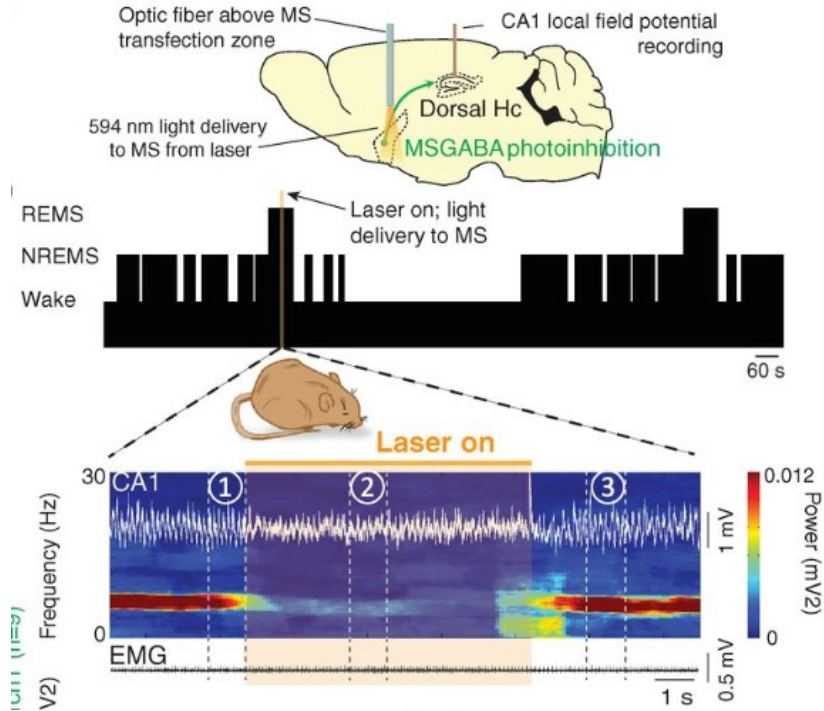
Case causal study : REM-sleep



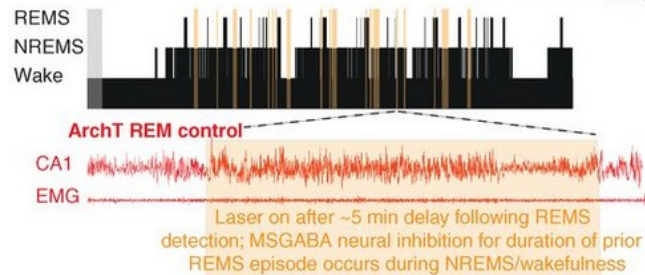
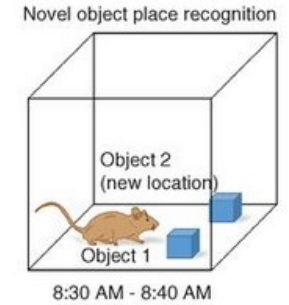
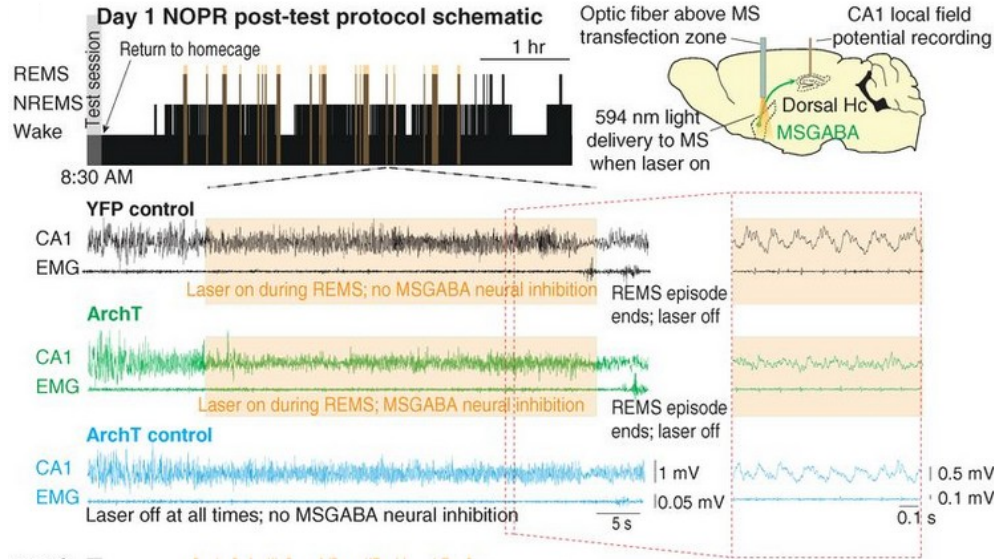
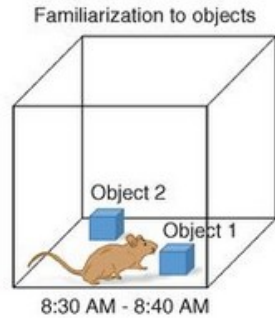
Layers ?



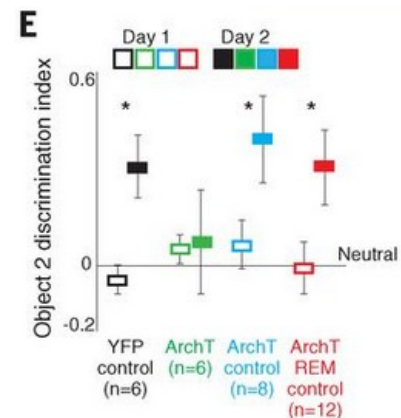
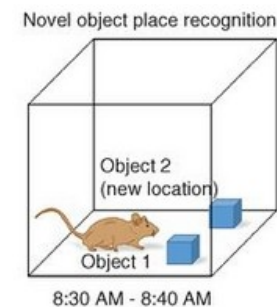
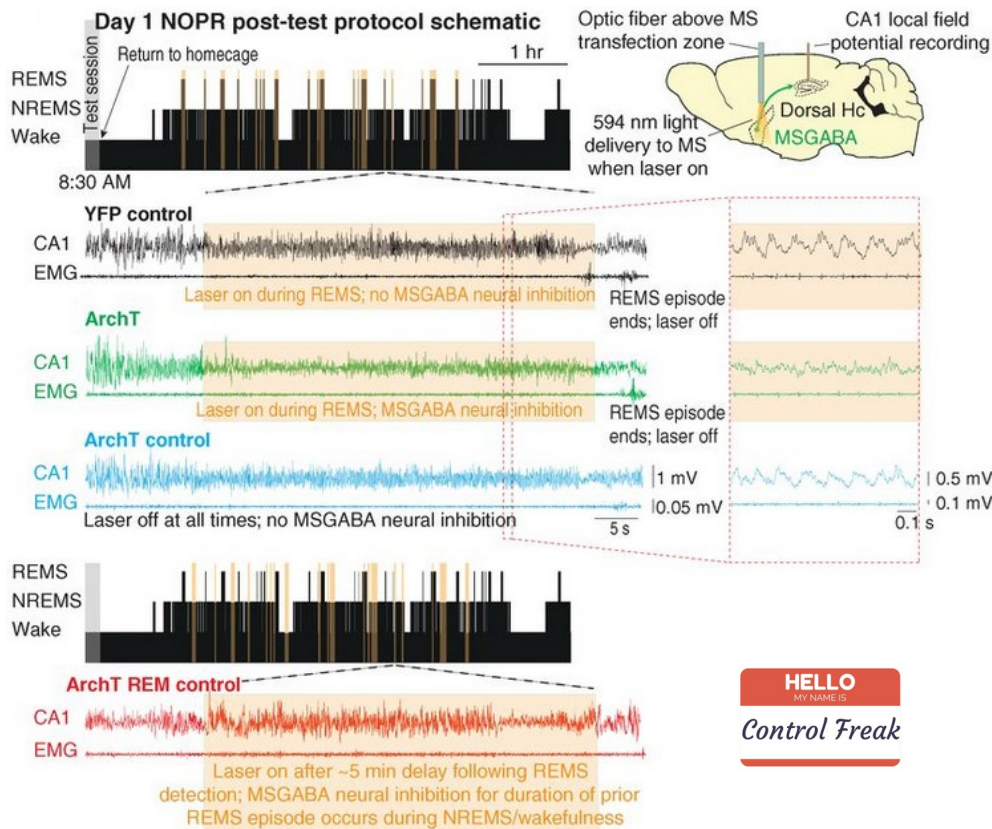
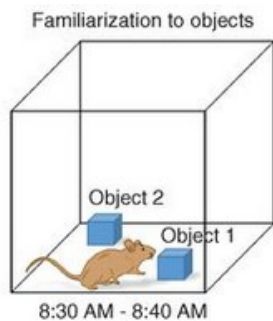
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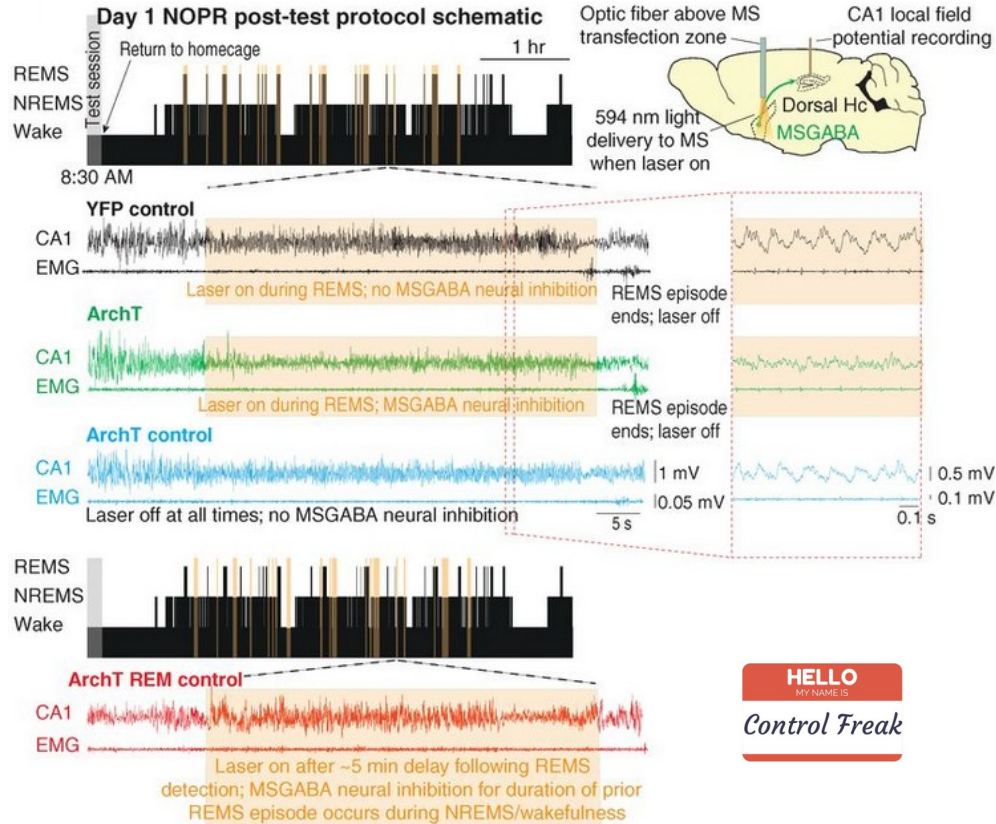
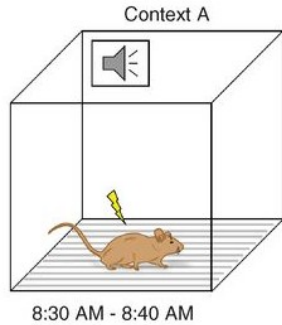
Case causal study : REM-sleep



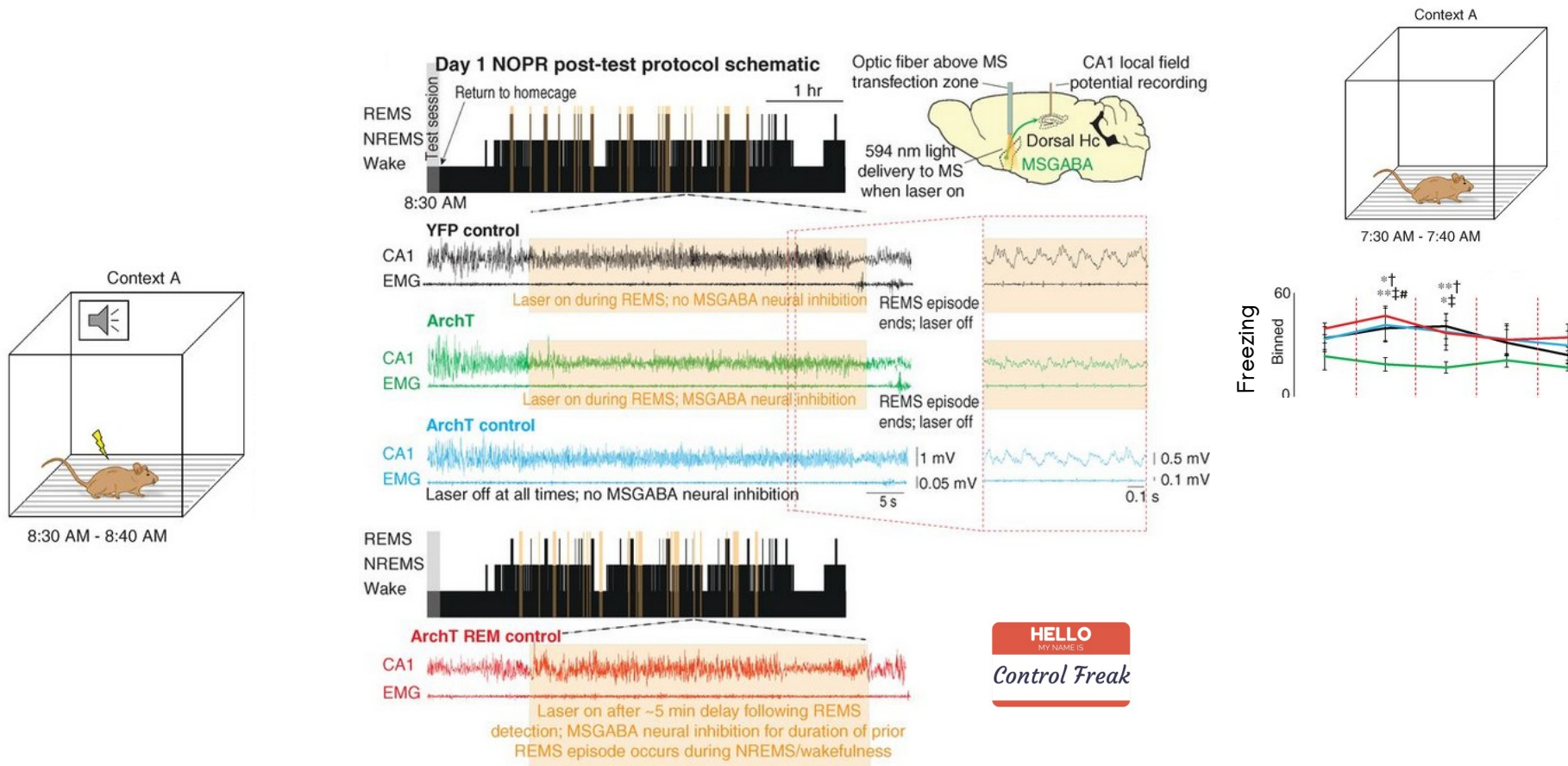
Case causal study : REM-sleep



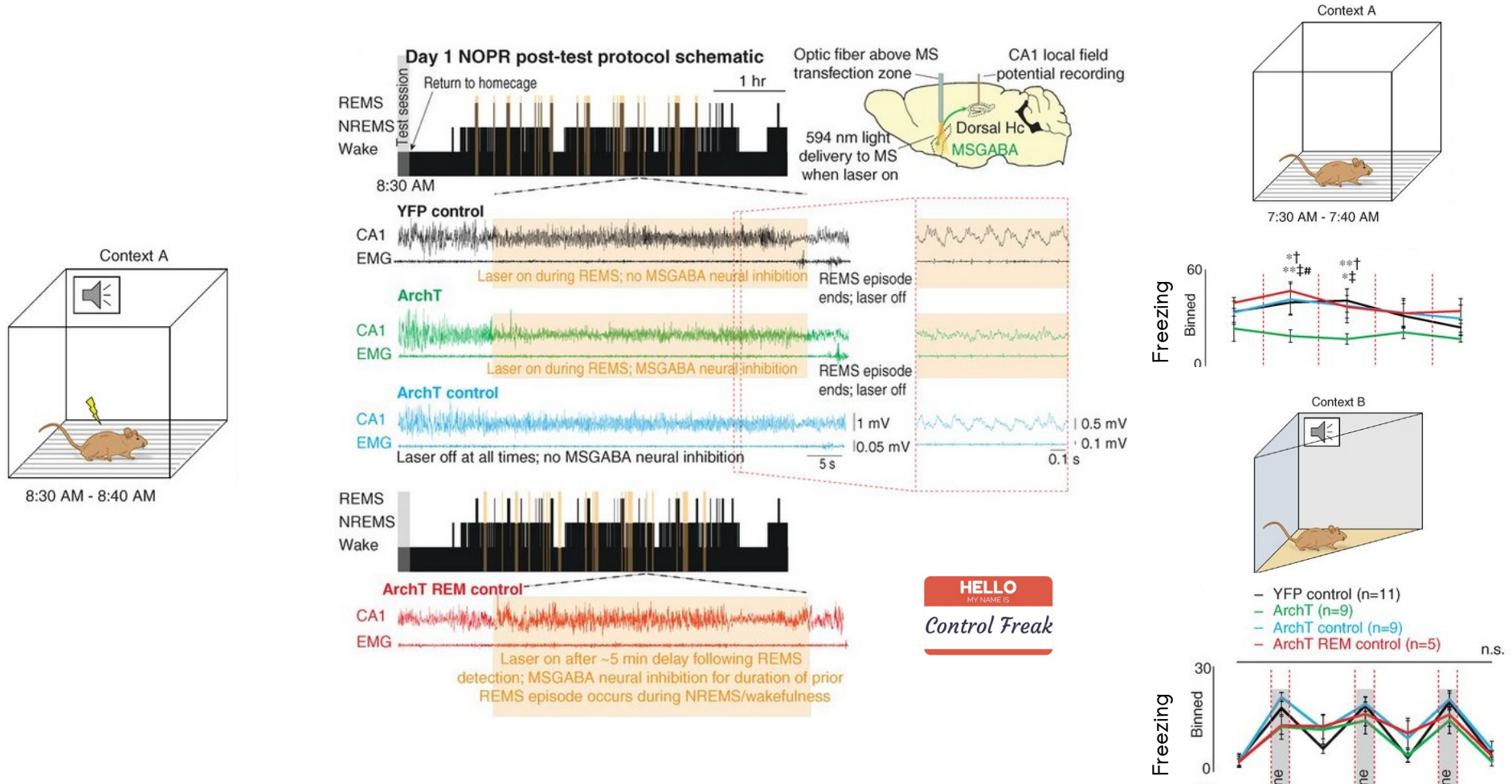
Case causal study : REM-sleep



Case causal study : REM-sleep



Case causal study : REM-sleep



REM-sleep and theta : under construction

- No « obvious » candidate mechanism for memory consolidation during REM-sleep (no replay)
- Less studied (only a few minutes per hour : scarce data)
- Specific or complementary role ? Homeostasis ?

› [Neuron](#). 2020 Aug 5;107(3):552-565.e10. doi: 10.1016/j.neuron.2020.05.008. Epub 2020 Jun 4.

Sparse Activity of Hippocampal Adult-Born Neurons during REM Sleep Is Necessary for Memory Consolidation

Deependra Kumar ¹, Iyo Koyanagi ¹, Alvaro Carrier-Ruiz ², Pablo Vergara ¹, Sakthivel Srinivasan ¹, Yuki Sugaya ², Masatoshi Kasuya ¹, Tzong-Shiue Yu ³, Kaspar E Vogt ¹, Masafumi Muratani ⁴, Takaaki Ohnishi ⁵, Sima Singh ¹, Catia M Teixeira ⁶, Yoan Chérasse ¹, Toshie Naoi ¹, Szu-Han Wang ⁷, Pimpimon Nondhalee ¹, Boran A H Osman ¹, Naoko Kaneko ⁸, Kazunobu Sawamoto ⁹, Steven G Kernie ³, Takeshi Sakurai ¹, Thomas J McHugh ¹⁰, Masanobu Kano ², Masashi Yanagisawa ¹, Masanori Sakaguchi ¹¹

› [Neuron](#). 2012 Sep 20;75(6):1001-7. doi: 10.1016/j.neuron.2012.08.015.

REM sleep reorganizes hippocampal excitability

Andres D Grosmark ¹, Kenji Mizuseki, Eva Pastalkova, Kamran Diba, György Buzsáki

› [Science](#). 2019 Sep 20;365(6459):1308-1313. doi: 10.1126/science.aax9238.

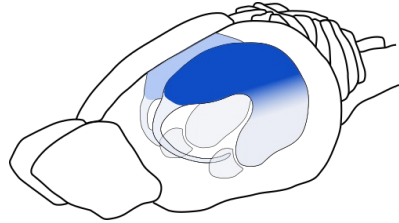
REM sleep-active MCH neurons are involved in forgetting hippocampus-dependent memories

Shuntaro Izawa ^{1 2 3 4}, Srikanta Chowdhury ^{1 2 3}, Toh Miyazaki ^{1 2 3 4}, Yasutaka Mukai ^{1 2 3 4}, Daisuke Ono ^{1 2 3}, Ryo Inoue ^{1 2}, Yu Ohmura ⁵, Hiroyuki Mizoguchi ⁶, Kazuhiro Kimura ⁷, Mitsuhiro Yoshioka ⁵, Akira Terao ^{7 8}, Thomas S Kilduff ⁹, Akihiro Yamanaka ^{10 2 3}

Hippocampus, Brain states and Memory

- Reminders
- Experimental design for sleep and memory studies *in vivo*
- Example causal studies
 - Non-REM sleep and ripples
 - REM sleep and theta oscillations
 - Replay
- **Hippocampal dialogue with other areas**
 - Example correlation study : hippocampus and basolateral amygdala

Hippocampus vs The rest of the Brain



Hippocampo-*cortical* coordination for memory consolidation
(Ripples, spindles, up/downstates)

> [Elife](#). 2015 Oct 14;4:e05360. doi: 10.7554/eLife.05360.

VTA neurons coordinate with the hippocampal reactivation of spatial experience

Stephen N Gomperts ^{1 2 3}, Fabian Kloosterman ^{4 5 6}, Matthew A Wilson ^{2 3}

> [PLoS Biol](#). 2009 Aug;7(8):e1000173. doi: 10.1371/journal.pbio.1000173. Epub 2009 Aug 18.

Hippocampus leads ventral striatum in replay of place-reward information

Carien S Lansink ¹, Pieter M Goltstein, Jan V Lankelma, Bruce L McNaughton, Cyriel M A Pennartz

Reward

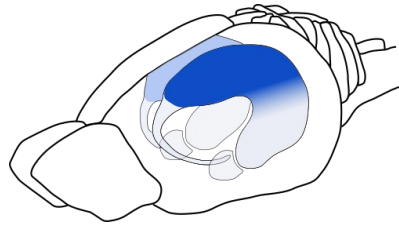
Aversion

Reactivations of emotional memory in the hippocampus-amygdala system during sleep

Gabrielle Girardeau, Ingrid Inema & György Buzsáki [✉](#)

[Nature Neuroscience](#) **20**, 1634–1642(2017) | [Cite this article](#)

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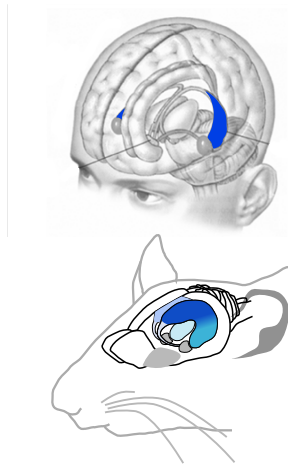
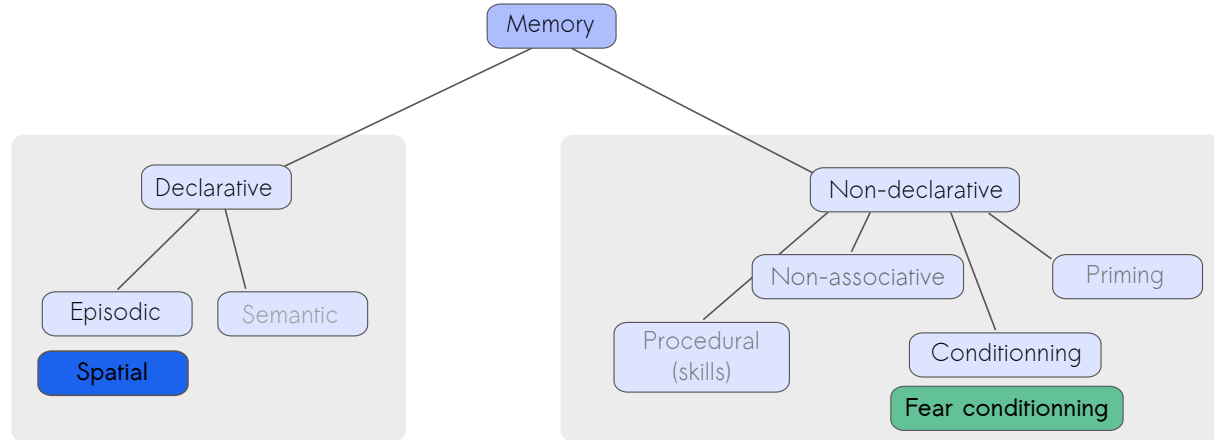
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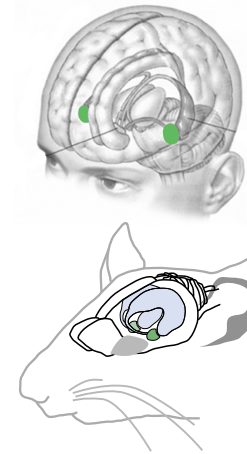
[Nature Neuroscience](#) **20**, 1634–1642(2017) | [Cite this article](#)

Hippocampus-amygdala dialogue (correlation study)



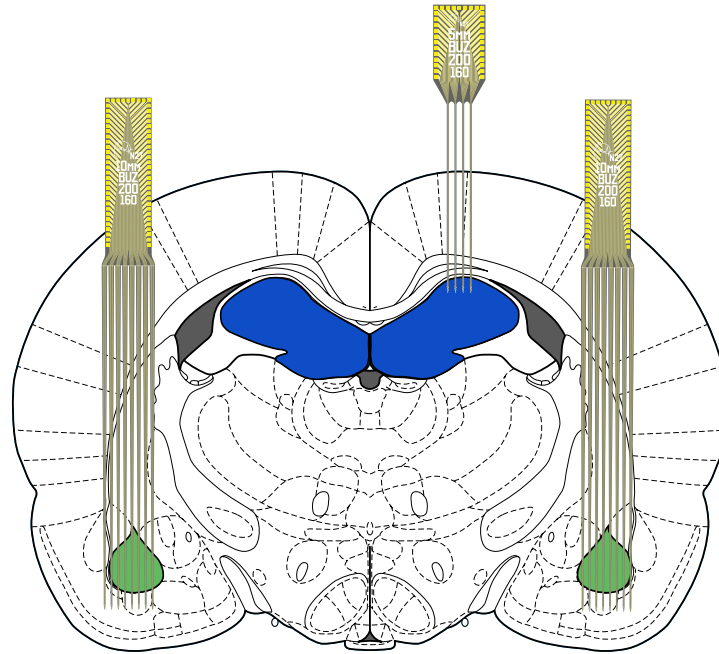
Hippocampus

Contextual fear conditioning



Amygdala

Hippocampus-amygdala dialogue (correlation study)



Dorsal hippocampus
Basolateral amygdala

Structure	# cells
Hippocampus	1210
Basolateral Amygdala (BLA)	2038

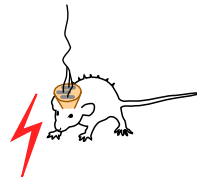
(in 4 animals)

Open dataset (crcns.org)

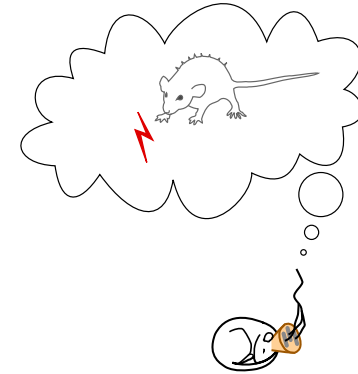
Hippocampus-amygdala dialogue (correlation study)



Pre-training sleep



Aversive training

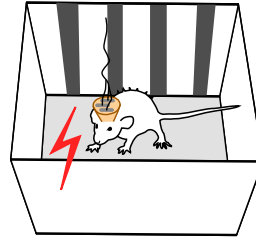


Post-training sleep

Hippocampus-amygdala dialogue (correlation study)

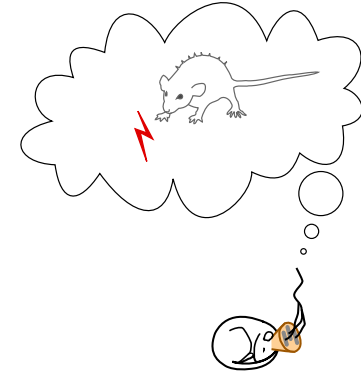


Pre-training sleep



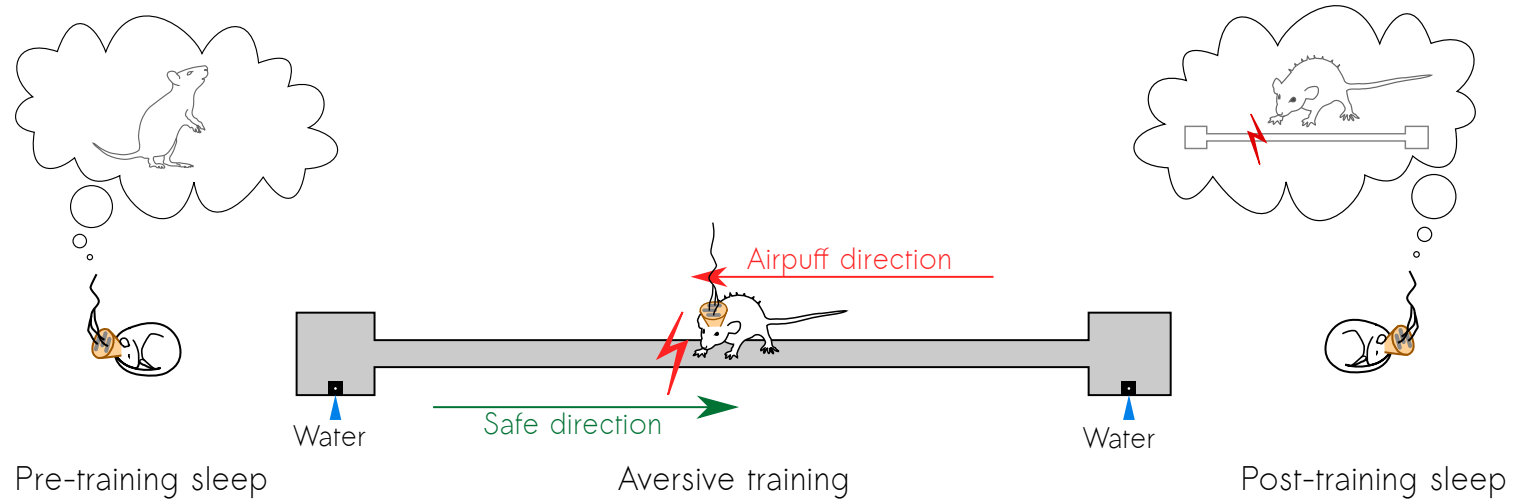
Aversive training
Contextual Fear Conditioning

- Small enclosure
- Freezing
- One-shot

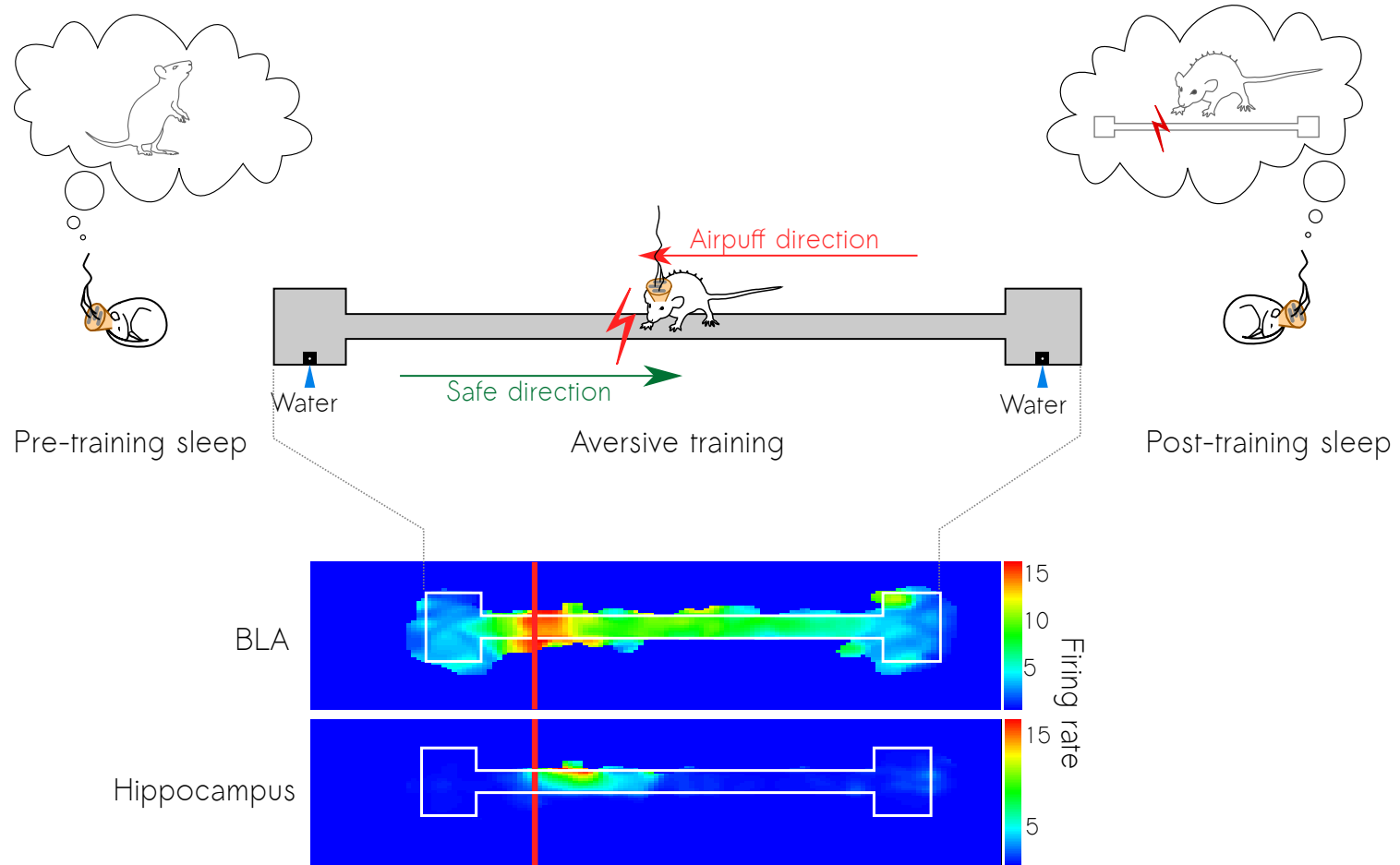


Post-training sleep

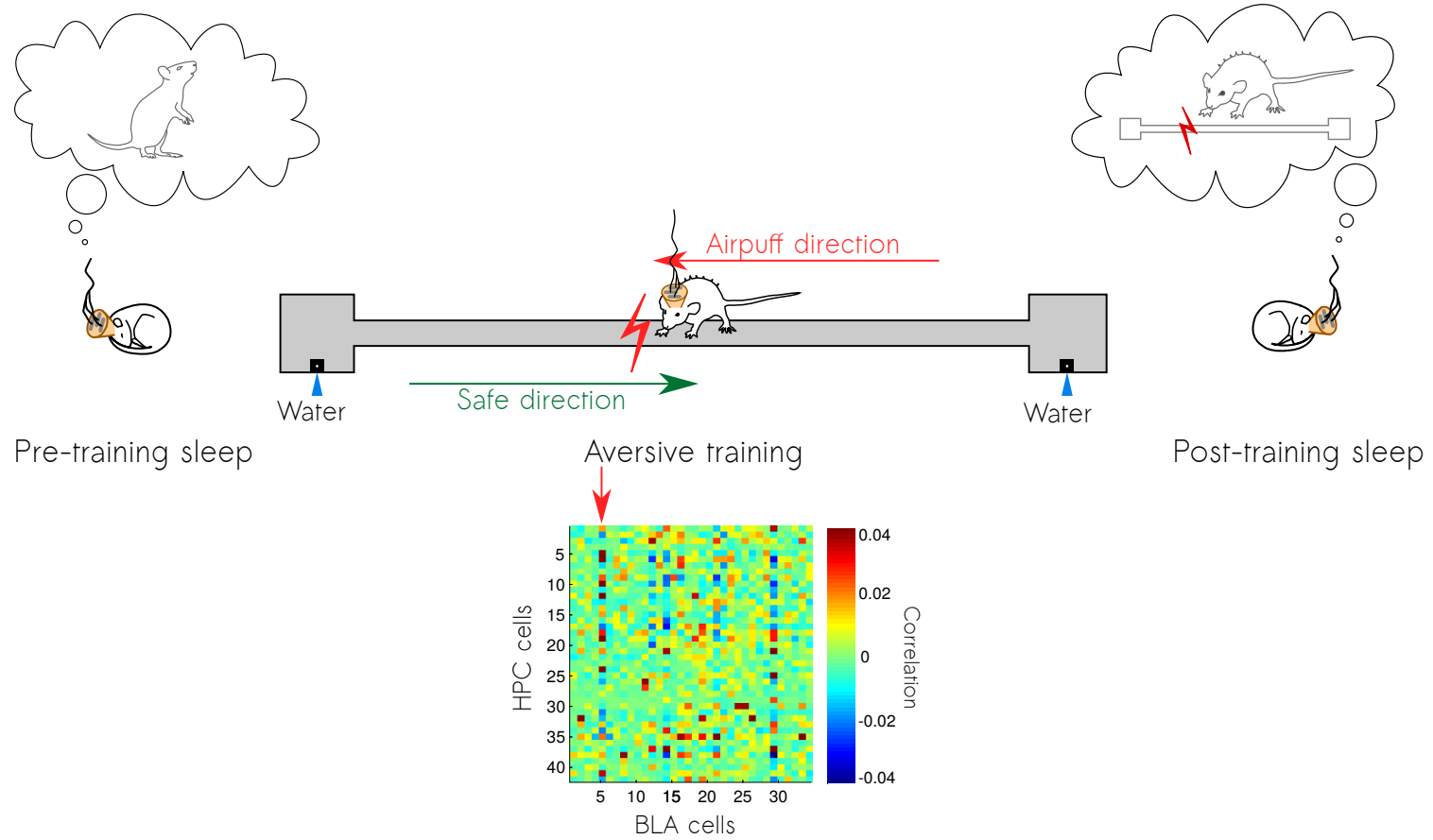
Hippocampus-amygdala dialogue (correlation study)



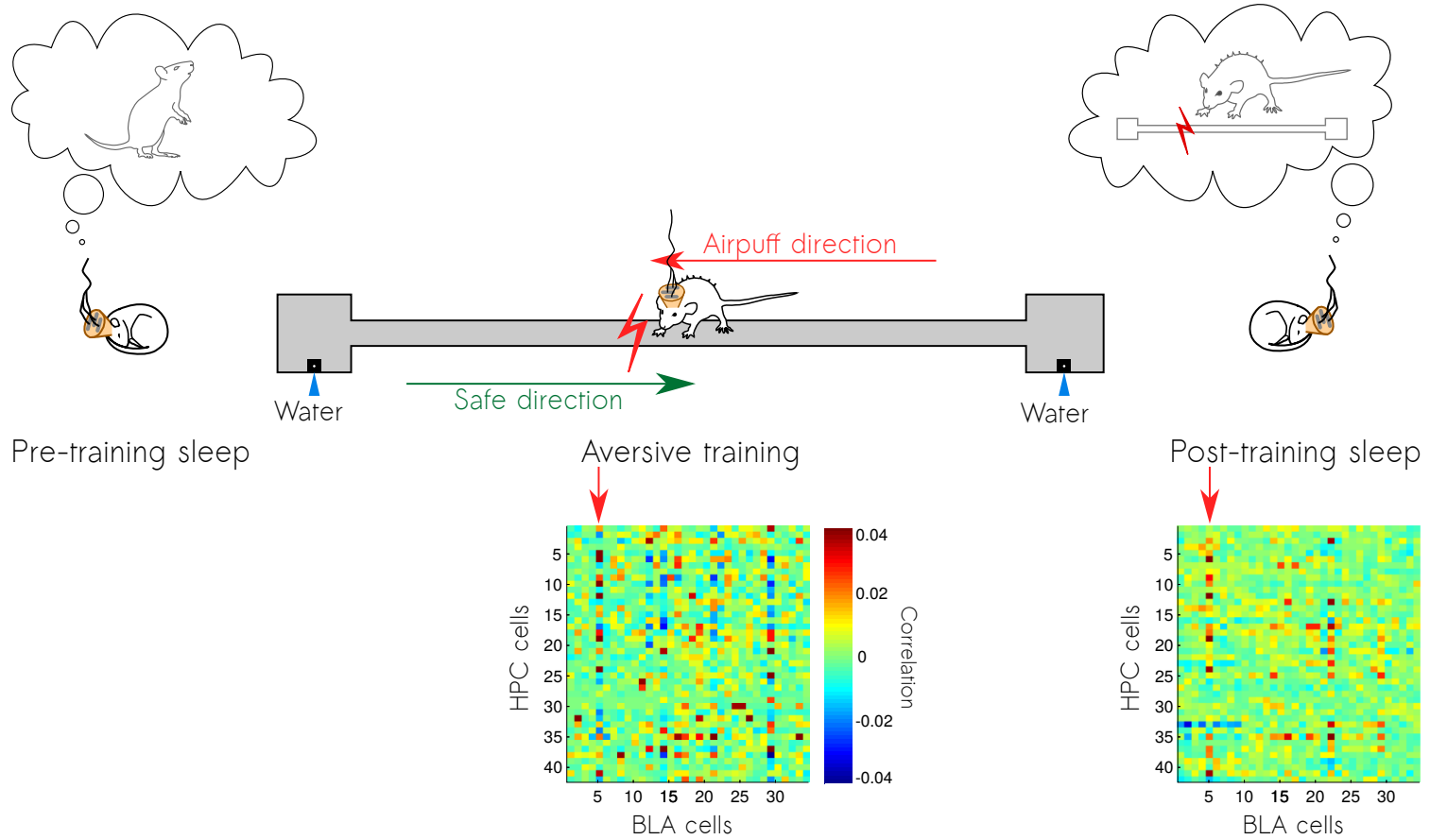
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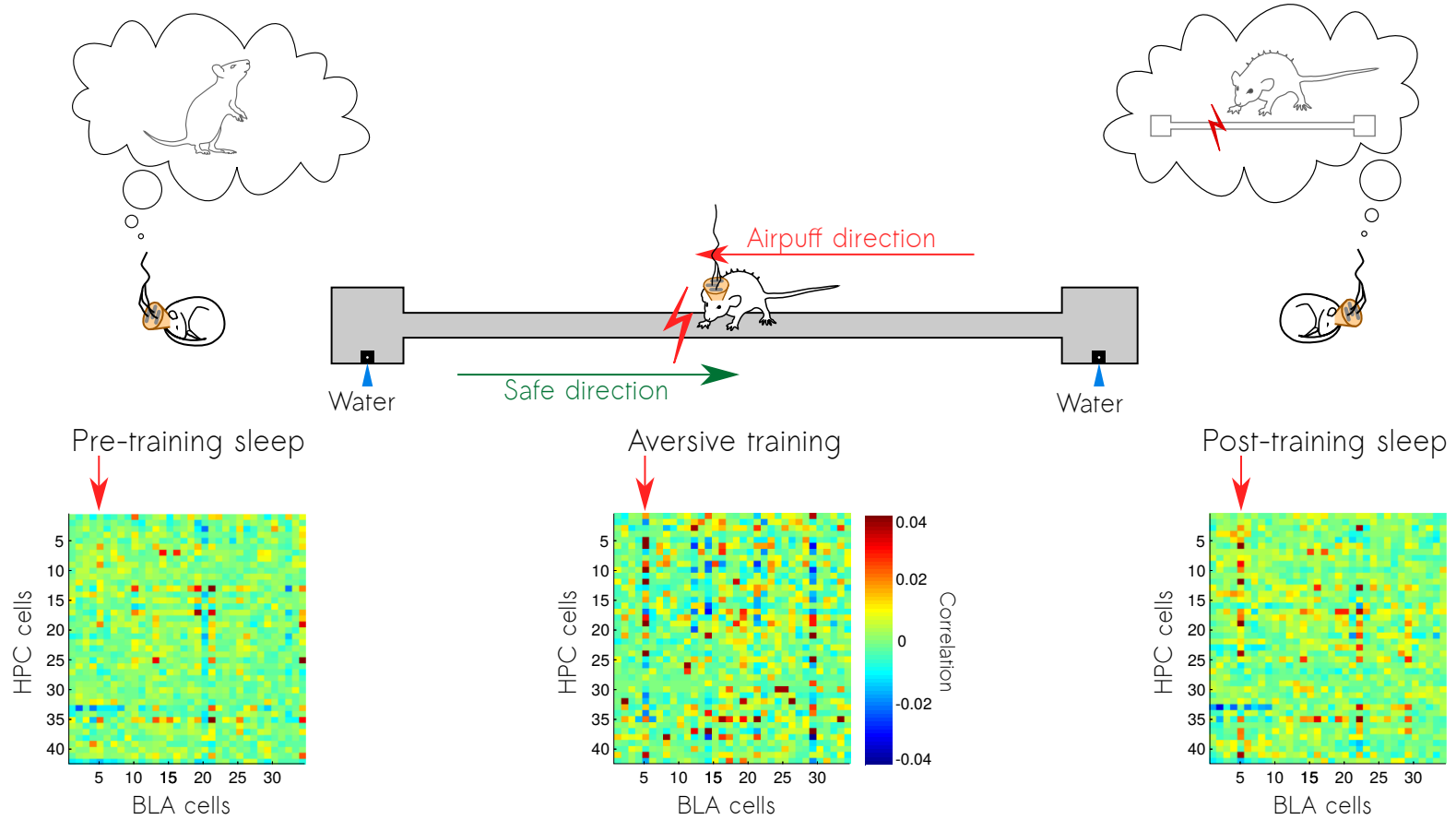
Hippocampus-amygdala dialogue (correlation study)



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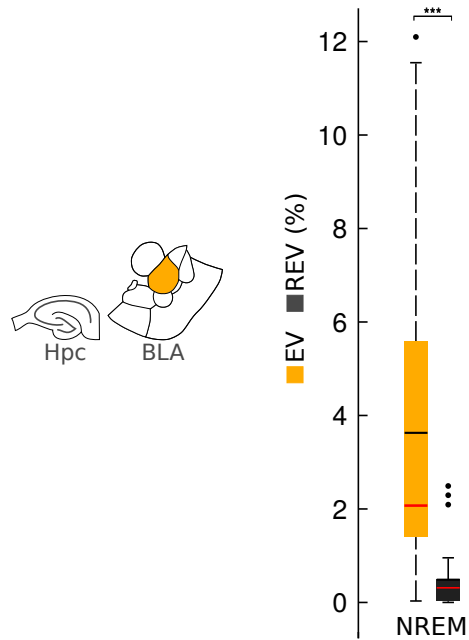


Hippocampus-amygdala dialogue (correlation study)



$$EV \text{ (Explained variance)} = \left(\frac{r_{tr,post} - r_{tr,pre} \times r_{post,pre}}{\sqrt{(1-r_{tr,pre}^2)(1-r_{post,pre}^2)}} \right)^2$$

Hippocampus-amygdala dialogue (correlation study)



n = 3 rats, 25 sessions

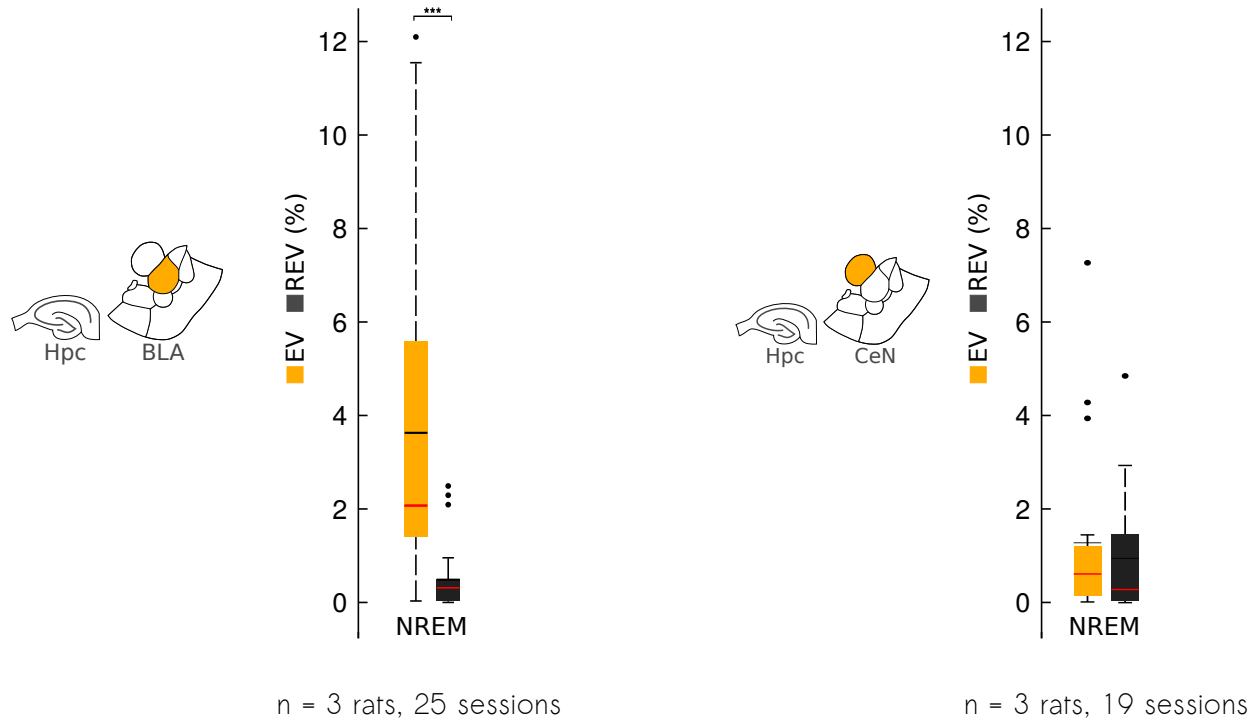
Wilcoxon signed rank tests

* p<0.05

** p<0.01

*** p<0.001

Hippocampus-amygdala dialogue (correlation study)



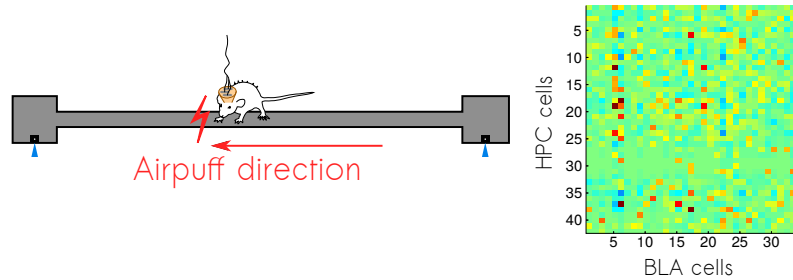
Wilcoxon signed rank tests

* $p < 0.05$

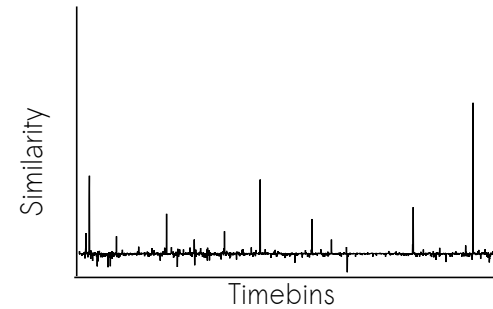
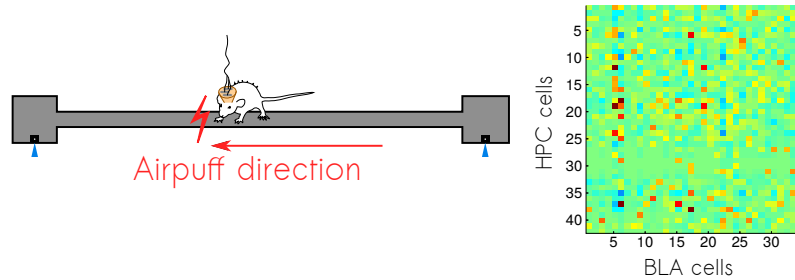
** $p < 0.01$

*** $p < 0.001$

Hippocampus-amygdala dialogue (correlation study)

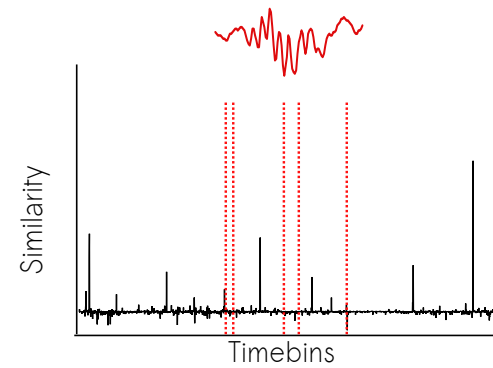
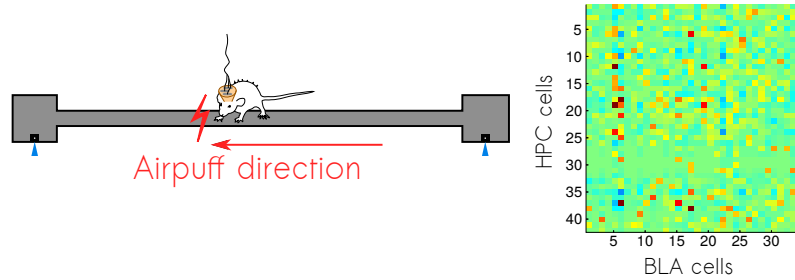


Hippocampus-amygdala dialogue (correlation study)



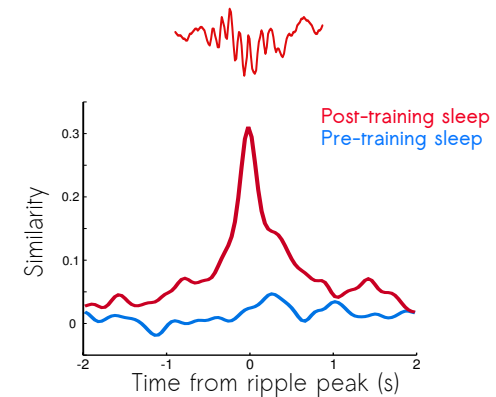
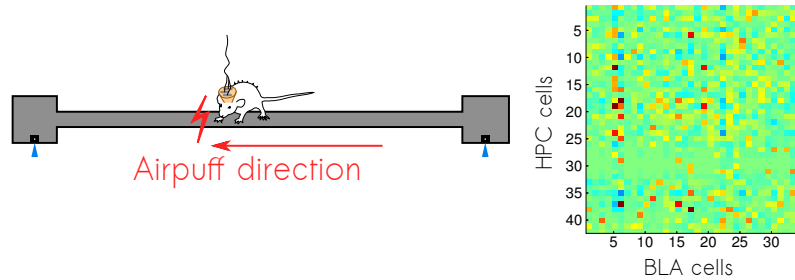
Similarity between training pattern and instantaneous pre or post-sleep patterns

Hippocampus-amygdala dialogue (correlation study)



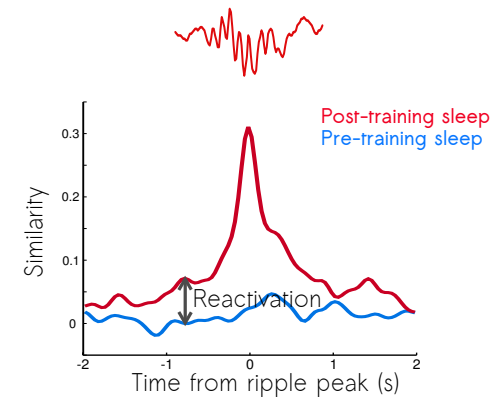
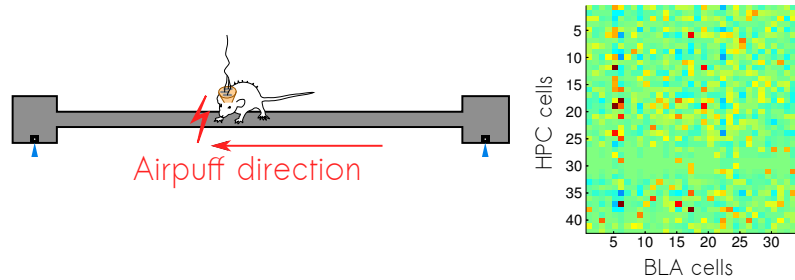
Similarity between training pattern and instantaneous pre or post-sleep patterns

Hippocampus-amygdala dialogue (correlation study)



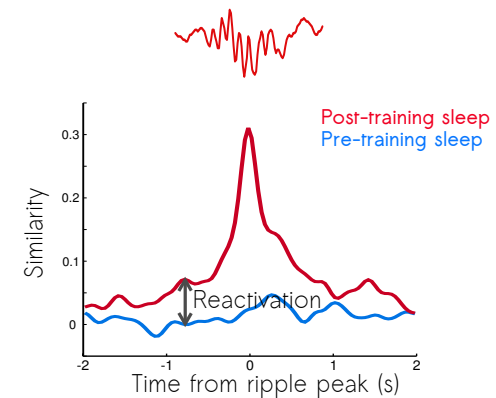
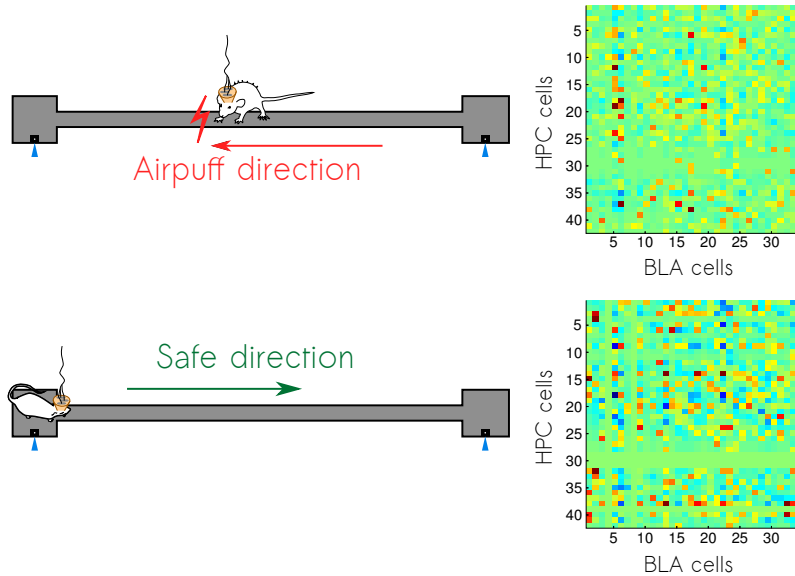
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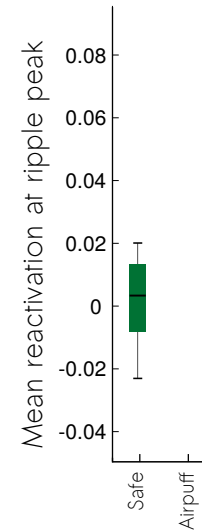
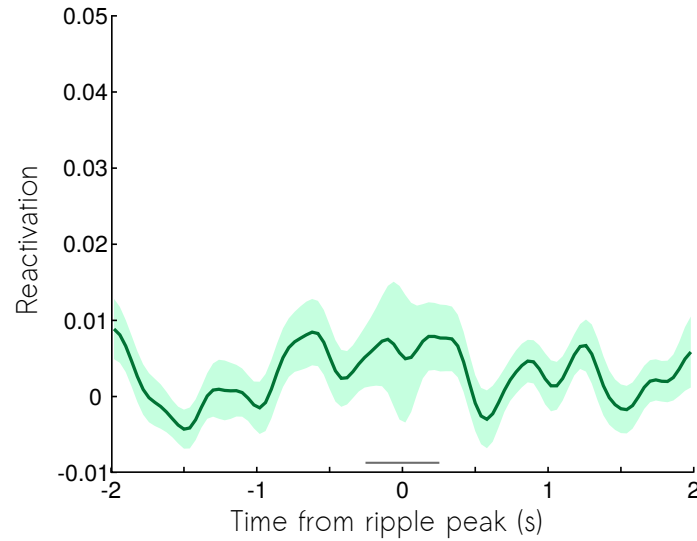
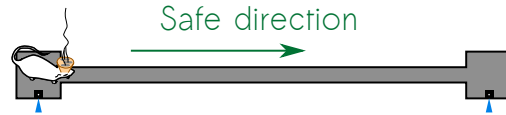
Similarity between training pattern and instantaneous pre or post-sleep patterns

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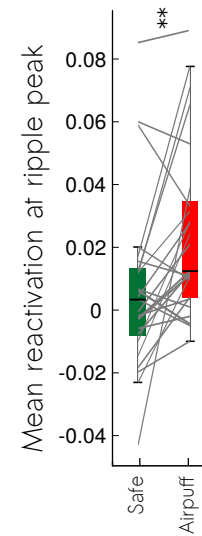
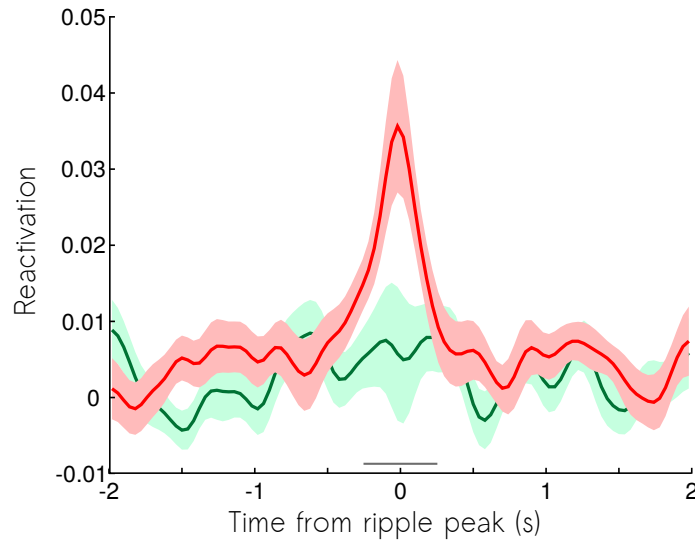
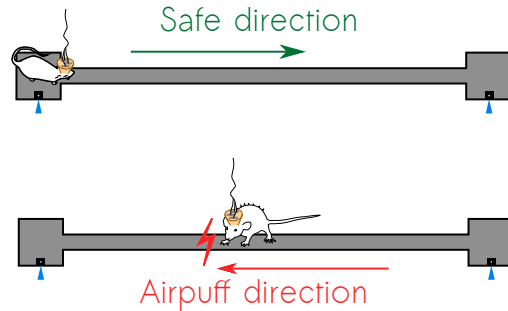


Similarity between training pattern and instantaneous pre or post-sleep patterns

Hippocampus-amygdala dialogue (correlation study)



Hippocampus-amygdala dialogue (correlation study)



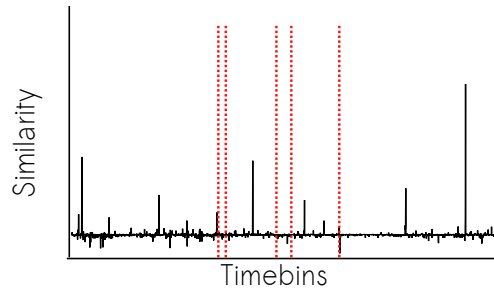
Notes on methods

> *Philos Trans R Soc Lond B Biol Sci.* 2020 May 25;375(1799):20190231. doi: 10.1098/rstb.2019.0231.

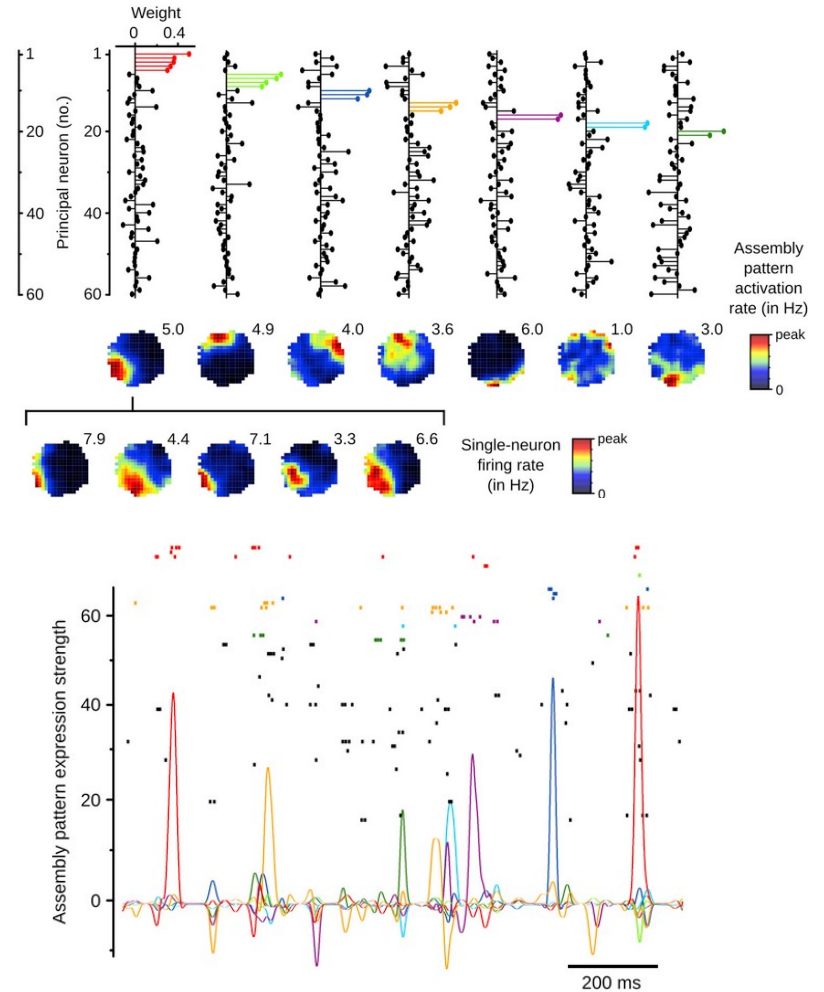
Epub 2020 Apr 6.

On the methods for reactivation and replay analysis

David Tingley¹, Adrien Peyrache²



PCA/ICA
Neuronal assembly tracking



Take-home messages

- Be a control freak (in science)
- Hippocampal Non-REM sleep ripples and replay sustain contextual memory consolidation.
- Ripples mediate a dialogue between the hippocampus and other cortical and subcortical areas
- REM-sleep and theta : not so clear.
- Closed-loop systems and optogenetics allow for more and more precise targetting of neural mechanisms in **1)** time and **2)** space (specific neural networks, engrams, holographic stimulations)
- Complementarity of correlation and causal studies
- Be familiar with a few canonical behavioral test for hippocampus-dependent memory (one-shot, gradual learning, rule + daily learning...) and understand the parameters to be taken in account.
- Use pubmed search and read the titles, sometimes the abstracts to get a broad, initial overview of the state of research in a given topic. Then read reviews, get down the rabbithole (references) and select a few result papers to read more thoroughly.