The State Key Laboratory of Brain And Cognitive Sciences
脑与认知科学国家重点实验室

香港大學
The University of Hong Kong

Dec 14, 2022 PolyU CBS-RCLCN

Controlling Unwanted Memories & Adaptive Forgetting

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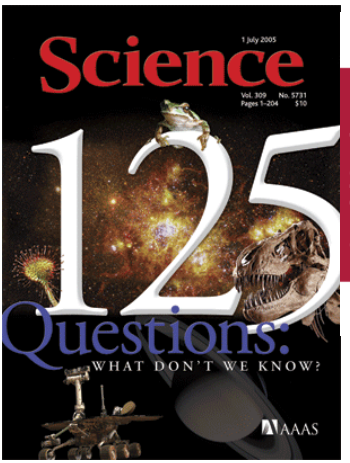
Department of Psychology,

The State Key Laboratory of Brain and Cognitive Sciences

The University of Hong Kong

Memory: Formation, change and loss



Special Section

WHAT DON'T WE KNOW?

How Are Memories Stored and Retrieved

Packed into the kilogram or so of neural wetware between the ears is everything we know: a compendium of useful and trivial facts about the world, the history of our lives, plus every skill we've ever learned, from riding a bike to persuading a loved one to take out the trash. Memories make each of us unique, and they give continuity to our lives. Memory is also the primary way we learn about the world. Learning is the process of acquiring memories, and remembering is the process of accessing them. Learning and remembering are the same as remembering what, as far as the brain is concerned.

Thanks to experiments on animals and the advent of human brain imaging, scientists now have a working knowledge of the various kinds of memory as well as which parts of the brain are involved in each. But persistent gaps remain. Although the MTL

150 nature

150 YEARS OF NATURE
Anniversary collection
go.nature.com/nature150

Memory editing from science fiction to clinical practice

Elizabeth A. Phelps & Stefan G. Hofmann

Annual Review of Psychology

Neuron

Perspective

The Biology of Forgetting—A Perspective

Ronald L. Davis[1,*] and Yi Zhong[2,*]
[1]Department of Neuroscience, The Scripps Research Institute Florida, Jupiter, FL, USA
[2]Tsinghua-Peking Center for Life Sciences, School for Life Sciences, Tsinghua University, Beijing, China
*Correspondence: rdavis@scripps.edu (R.L.D.), zhongyi@tsinghua.edu.cn (Y.Z.)
http://dx.doi.org/10.1016/j.neuron.2017.05.039

Active Forgetting: Adaptation of Memory by Prefrontal Control

Michael C. Anderson[1] and Justin C. Hulbert[2]

...s Unit, University of Cambridge.
...anderson@mrc-cbu.cam.ac.uk
...lson, New York 12504, USA

nature reviews neuroscience

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Perspective | Published: 13 January 2022

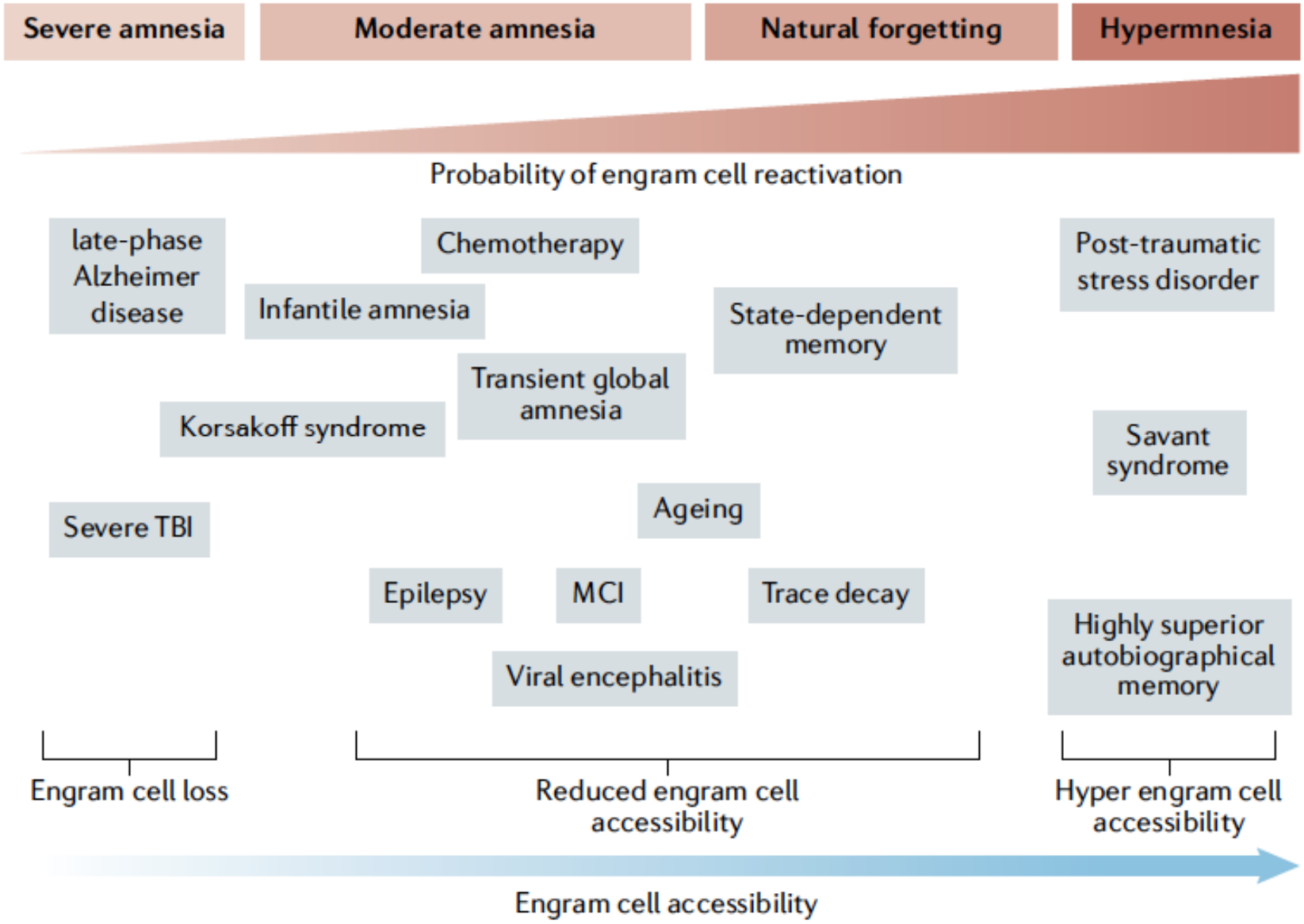
Forgetting as a form of adaptive engram cell plasticity

Tomás J. Ryan & Paul W. Frankland

Nature Reviews Neuroscience **23**, 173–186 (2022) | Cite this article

9878 Accesses | **7** Citations | **446** Altmetric | Metrics

The Gone Engrams



Ryan & Frankland, 2022, *Nat. Rev. Neurosci.*

Adaptive Forgetting and Memory Editing

Blessed are the forgetful:
for they get the better even for their blunders.
---- Friedrich Nietzsche

Unsuccessful

PTSD

Depression

Anxiety

Insomnia

Successful

Regulating emotion

Preserving self-image

Facilitating forgiveness

rumination, excessive worries,

flashbacks, intrusive thoughts

Hu et al., 2017. *Current Directions in Psy Sci*

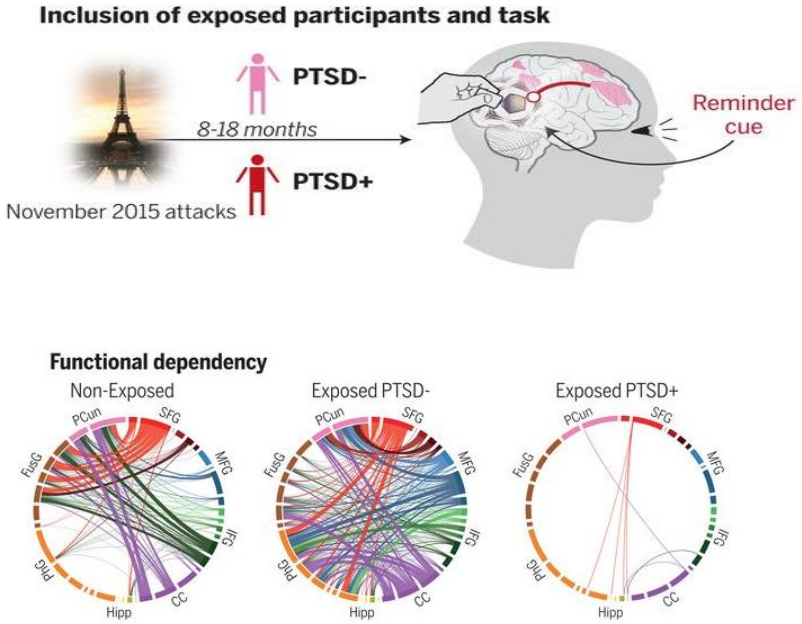
Adaptive Forgetting and Memory Editing

RESEARCH ARTICLE

NEUROSCIENCE

Resilience after trauma: The role of memory suppression

Alison Mary[1], Jacques Dayan[1,2], Giovanni Leone[1], Charlotte Postel[1], Florence Fraisse[1], Carine Malle[1], Thomas Vallée[1], Carine Klein-Peschanski[3], Fausto Viader[1], Vincent de la Sayette[1], Denis Peschanski[3], Francis Eustache[1], Pierre Gagnepain[1]*

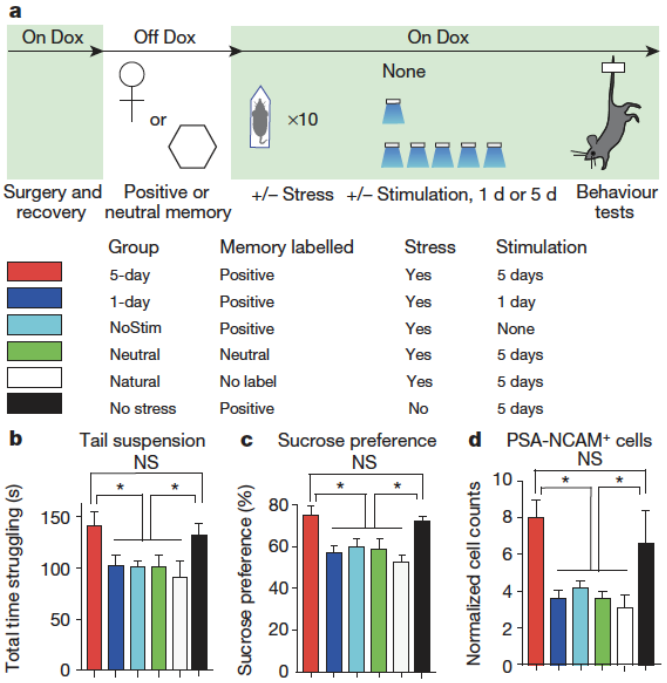


LETTER

doi:10.1038/nature14514

Activating positive memory engrams suppresses depression-like behaviour

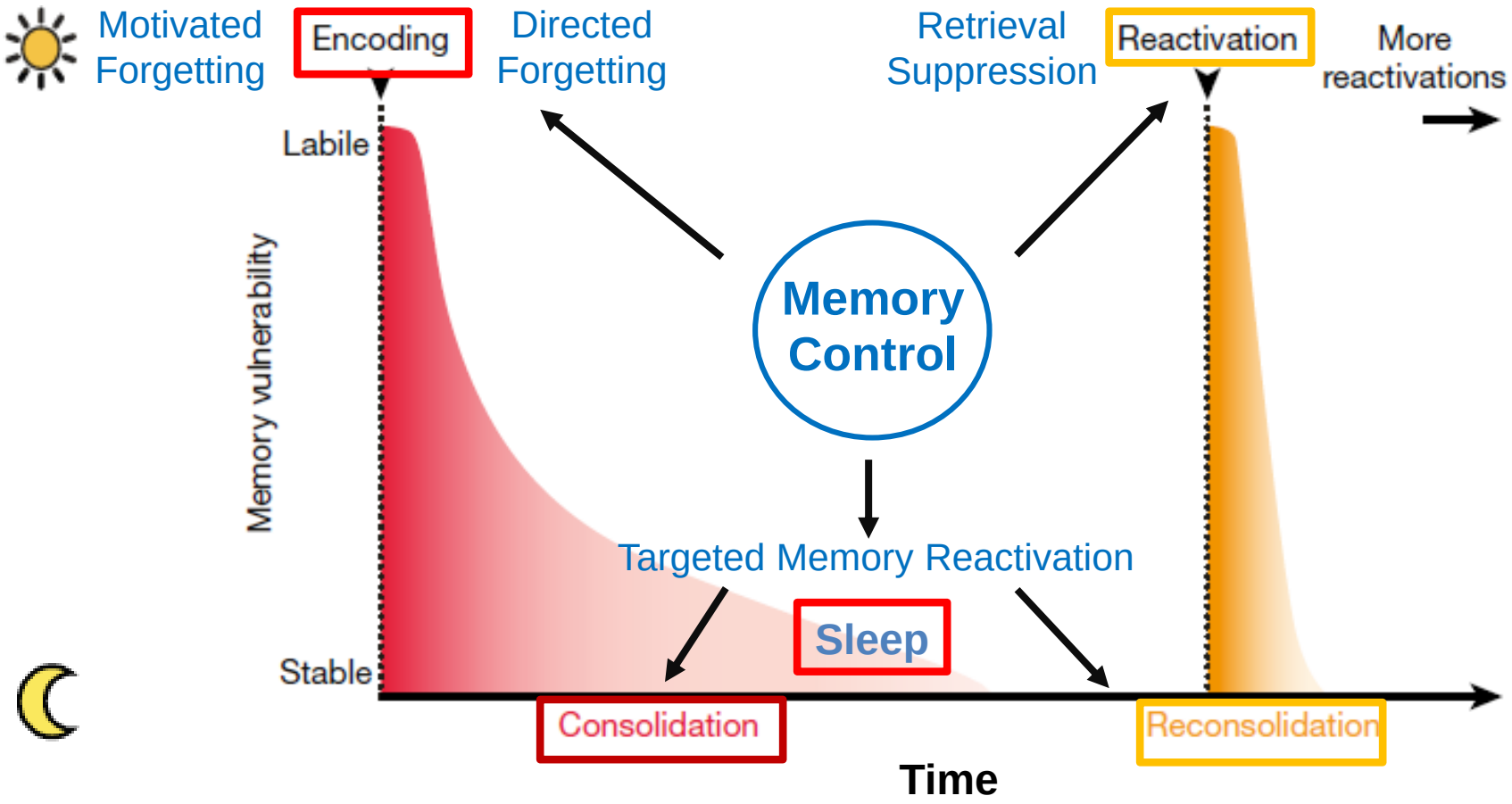
Steve Ramirez[1], Xu Liu‡, Christopher J. MacDonald[1], Anthony Moffa[1], Joanne Zhou[1], Roger L. Redondo[1,2] & Susumu Tonegawa[1,2]



Mary et al., 2020, *Science;* Ramirez et al., 2015, *Nature*

Memory Editing: Timepoints

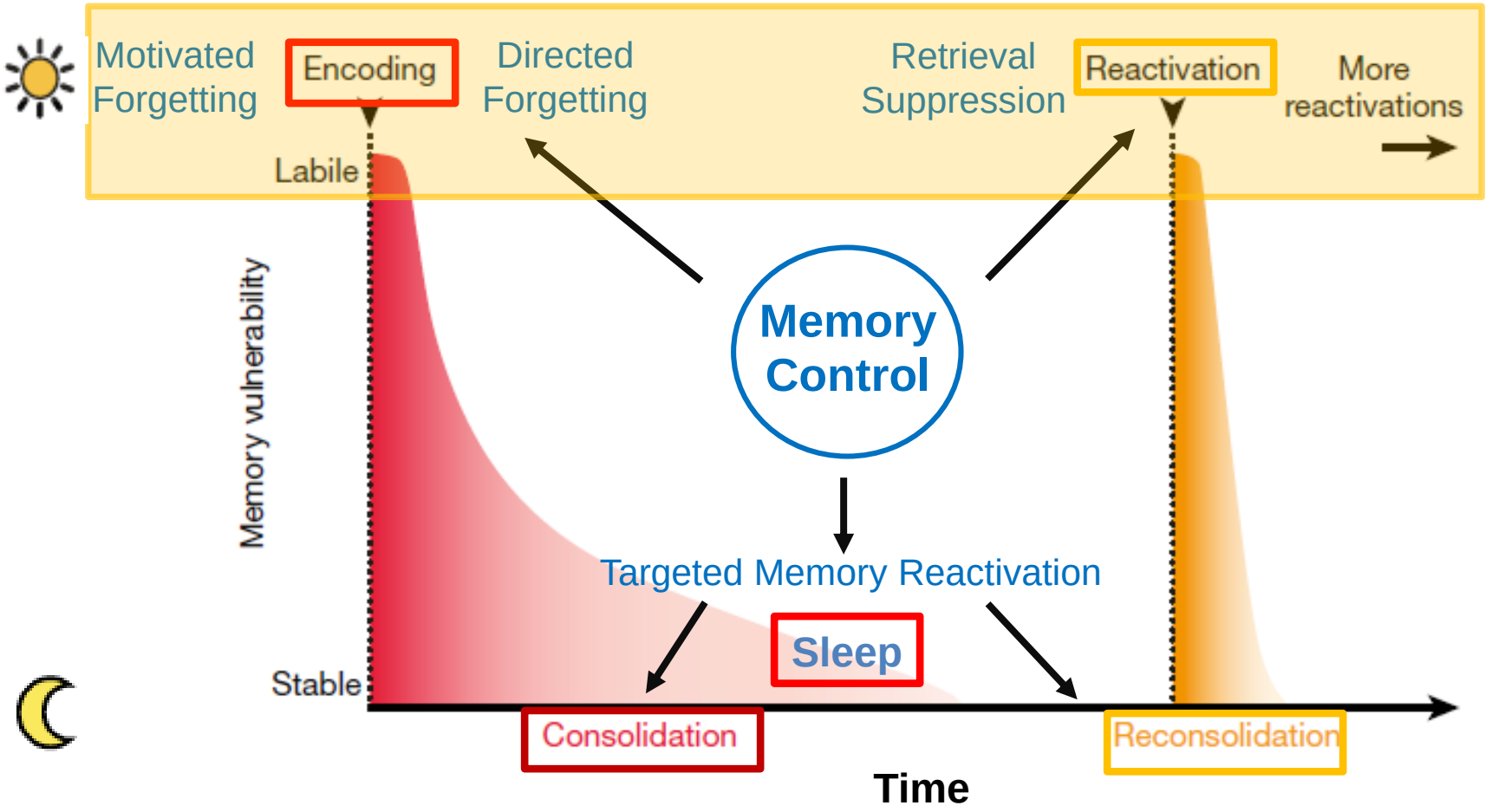
Memory: The Restless Engram



Phelps & Hoffman, 2019. *Nature*

Memory Editing: Wake

Memory: The Restless Engram



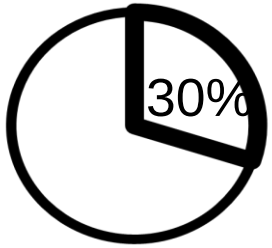
Hu et al., 2015; Hu et al., 2017; Xie et al., 2020; Xie et al., 2022; Yao et al., 2021;

Motivated Forgetting

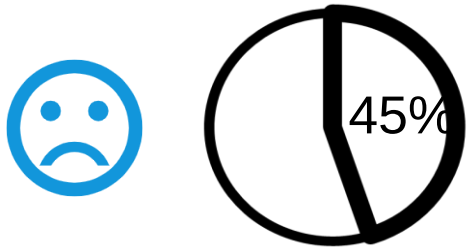
YAO Ziqing
姚子青

Optimistic Amnesia

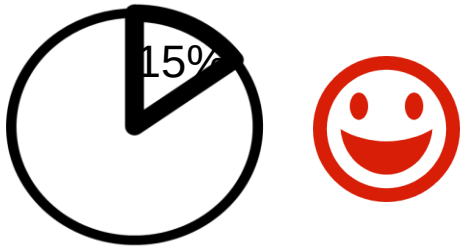
How likely will you get cancer when you reach 60?



The actual probability is



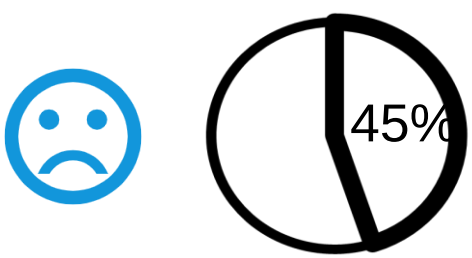
Bad news!



Good news!

Yao et al. 2021, *Soc Cogn Affect Neurosci.*

Motivated Forgetting



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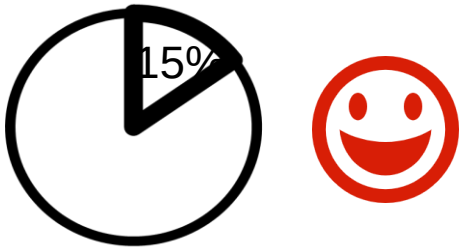

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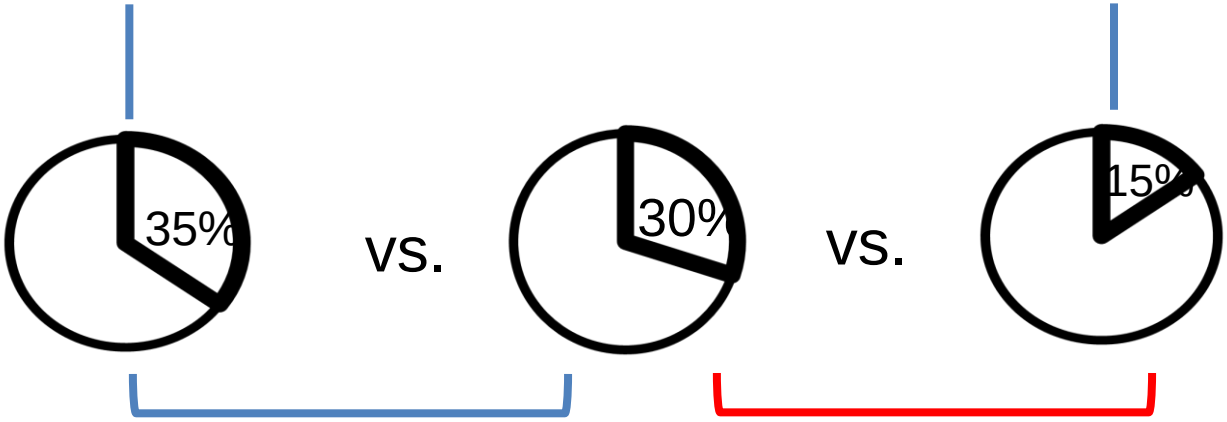


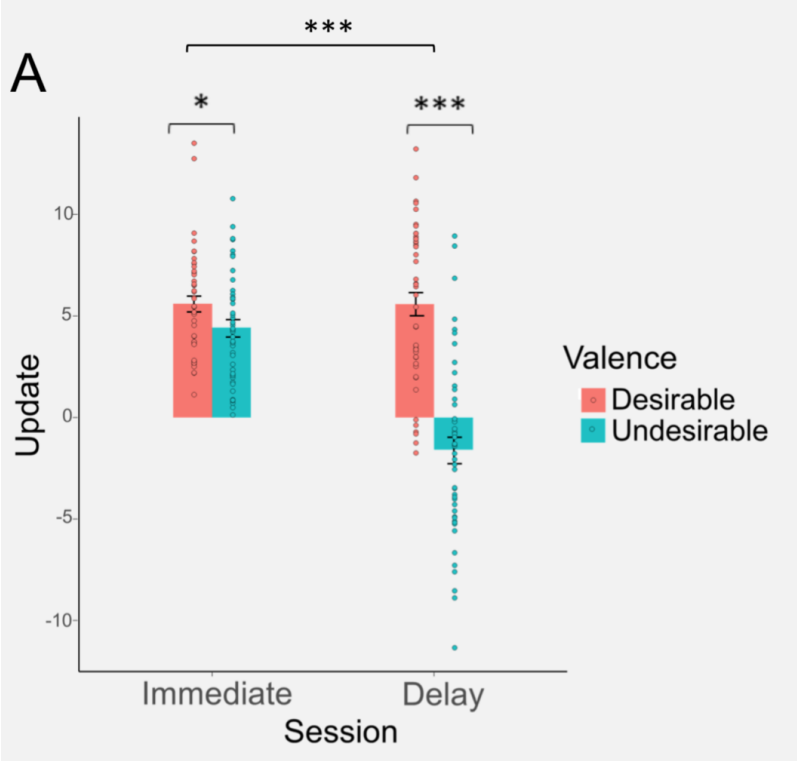
5% vs. **15%**

Optimistic Bias in Belief Updating

Yao et al. 2021, *Soc Cogn Affect Neurosci.*

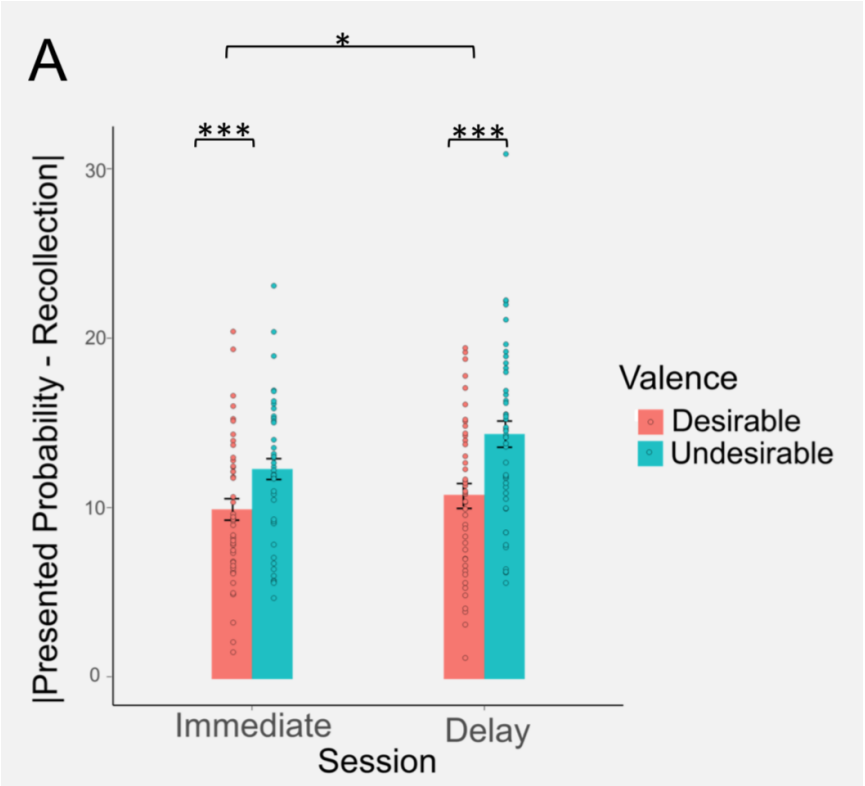
Motivated Forgetting

Optimistic Belief Updating



People are more likely to update their beliefs for desirable feedback

Optimistic Amnesia



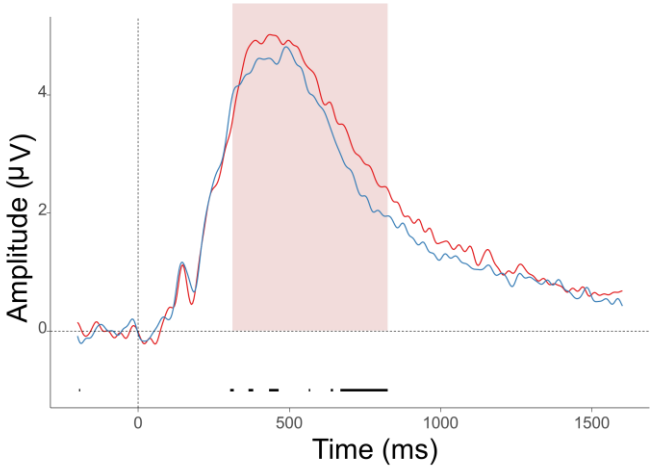
People are more likely to forget undesirable feedbacks

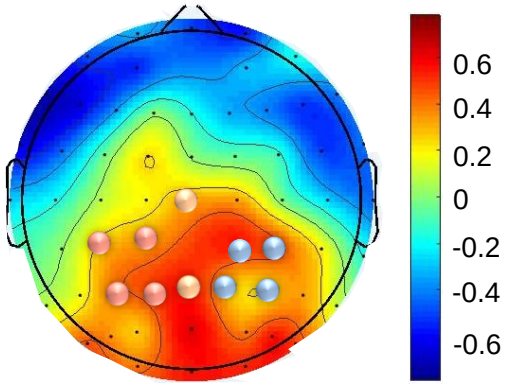
Yao et al. 2021, *Soc Cogn Affect Neurosci.*

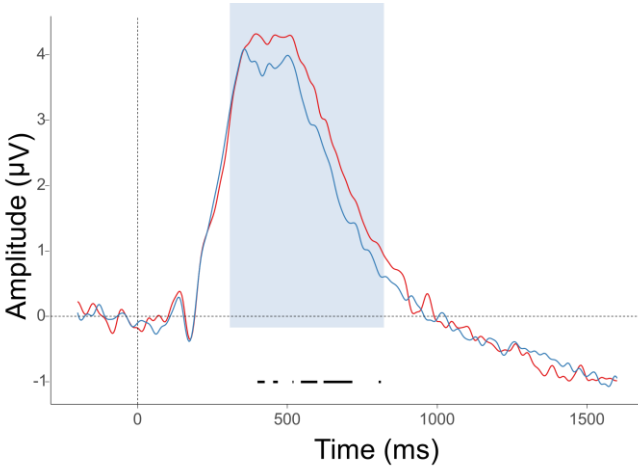
Motivated Forgetting

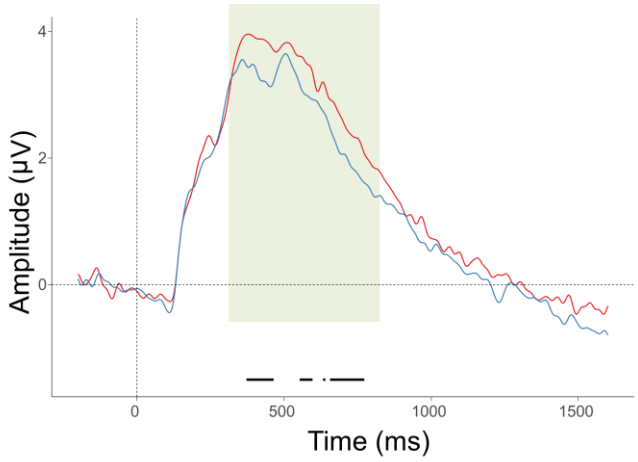
Shallower encoding depth of undesirable feedback

Desirable – Undesirable
Parietal P300



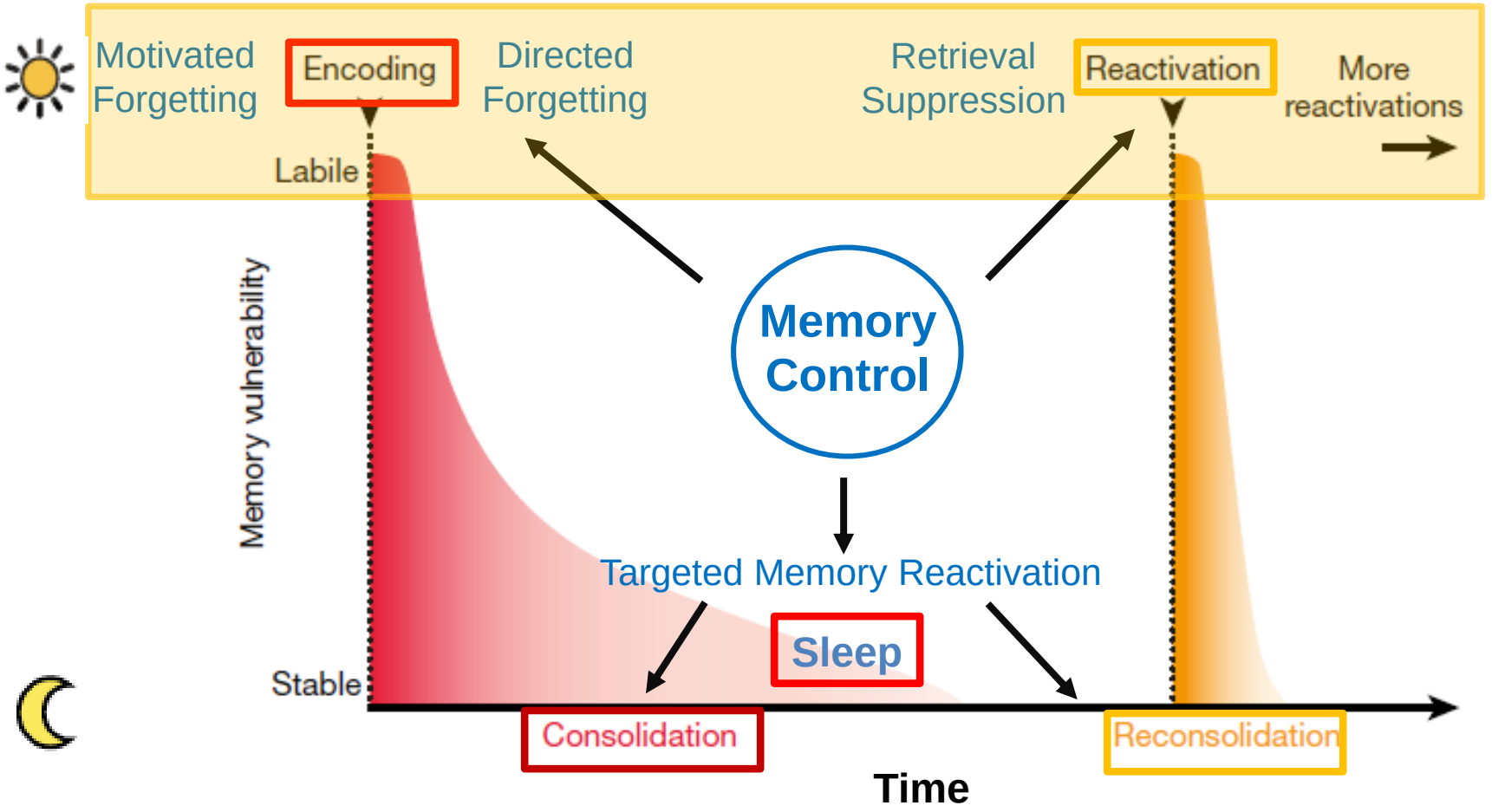






Memory Editing: Wake

Memory: The Restless Engram



Hu et al., 2015; Hu et al., 2017; Xie et al., 2020; Xie et al., 2022; Yao et al., 2021;

Memory Editing: Encoding

XIE Hui 谢慧

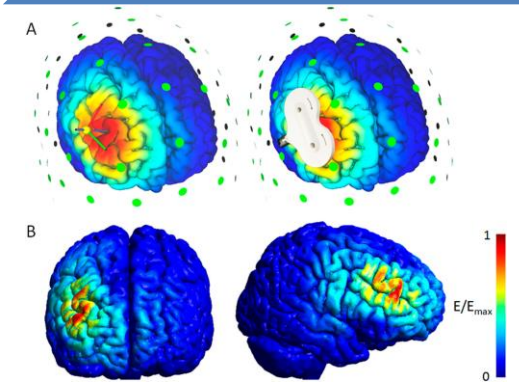
rTMS over right DLPFC impair voluntary forgetting

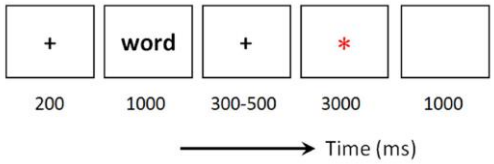
ZHANG Dandan
张丹丹教授

Offline low frequency (1HZ) rTMS over the right DLPFC

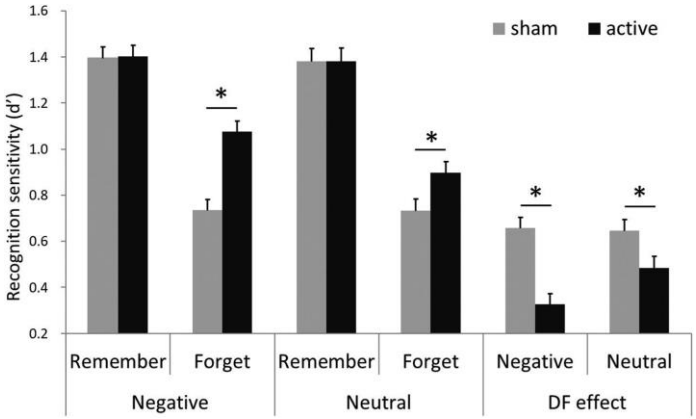
Directed forgetting task
(item-method)

Memory tests
1. Word completion (implicit)
2. Recognition





Word: negative vs. neutral
Cue: * Remember * Forget

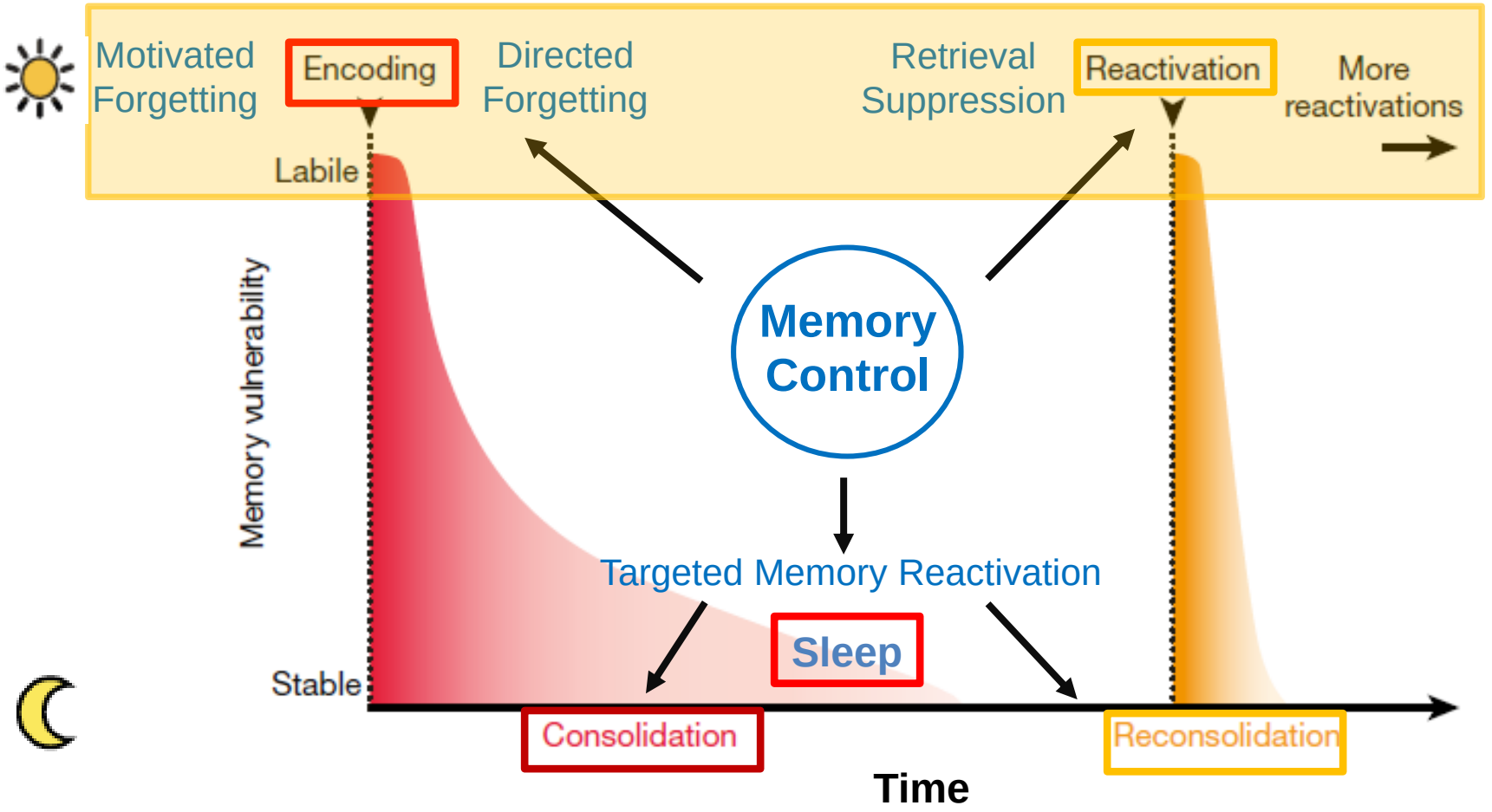


Highlighting the critical role of right DLPFC in voluntary forgetting

Xie et al., 2020 *Memory*

Memory Editing: From Wake to Sleep

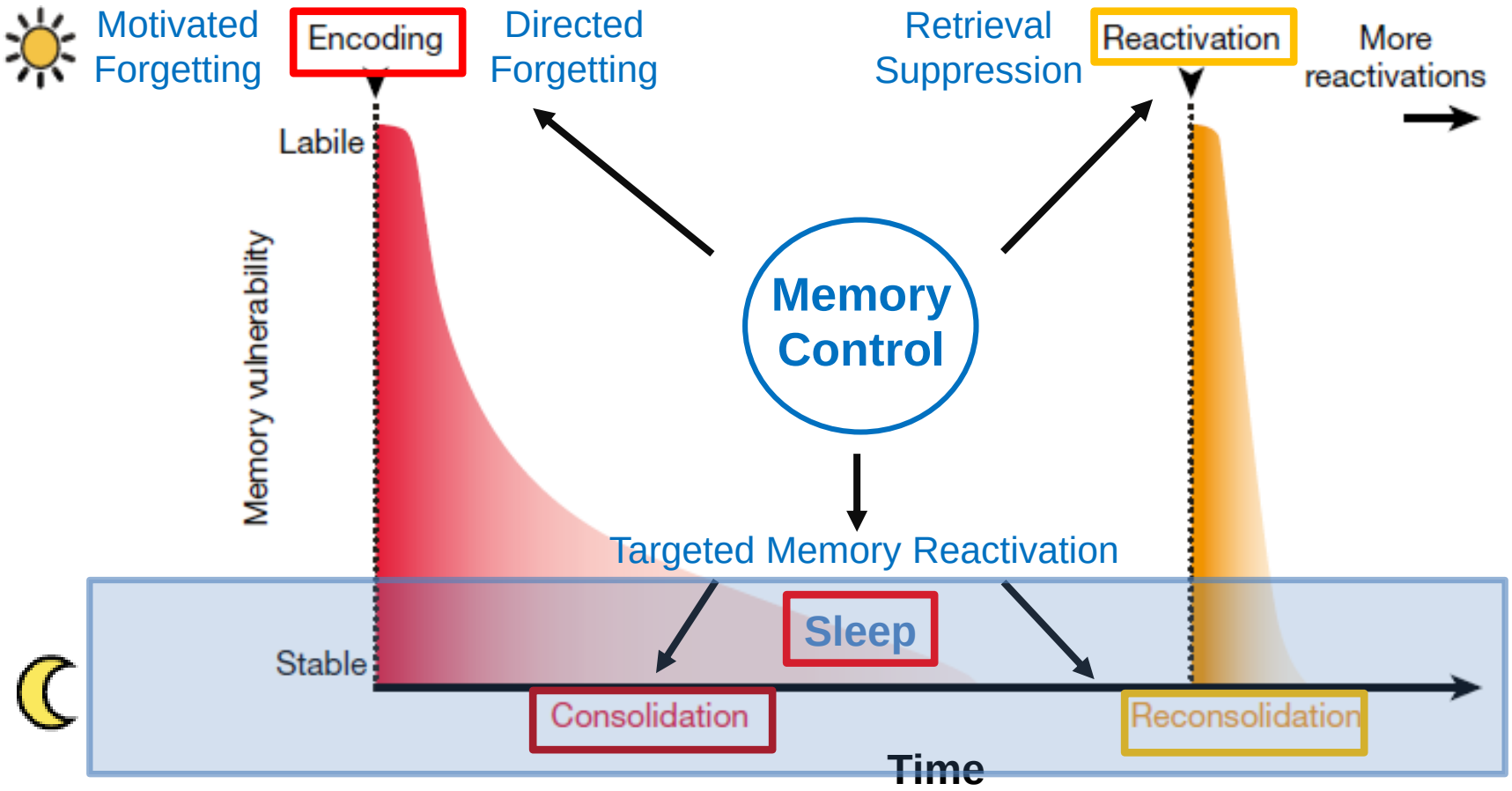
Memory: The Restless Engram



Hu et al., 2015; Hu et al., 2017; Xie et al., 2020; Xie et al., 2022; Yao et al., 2021;

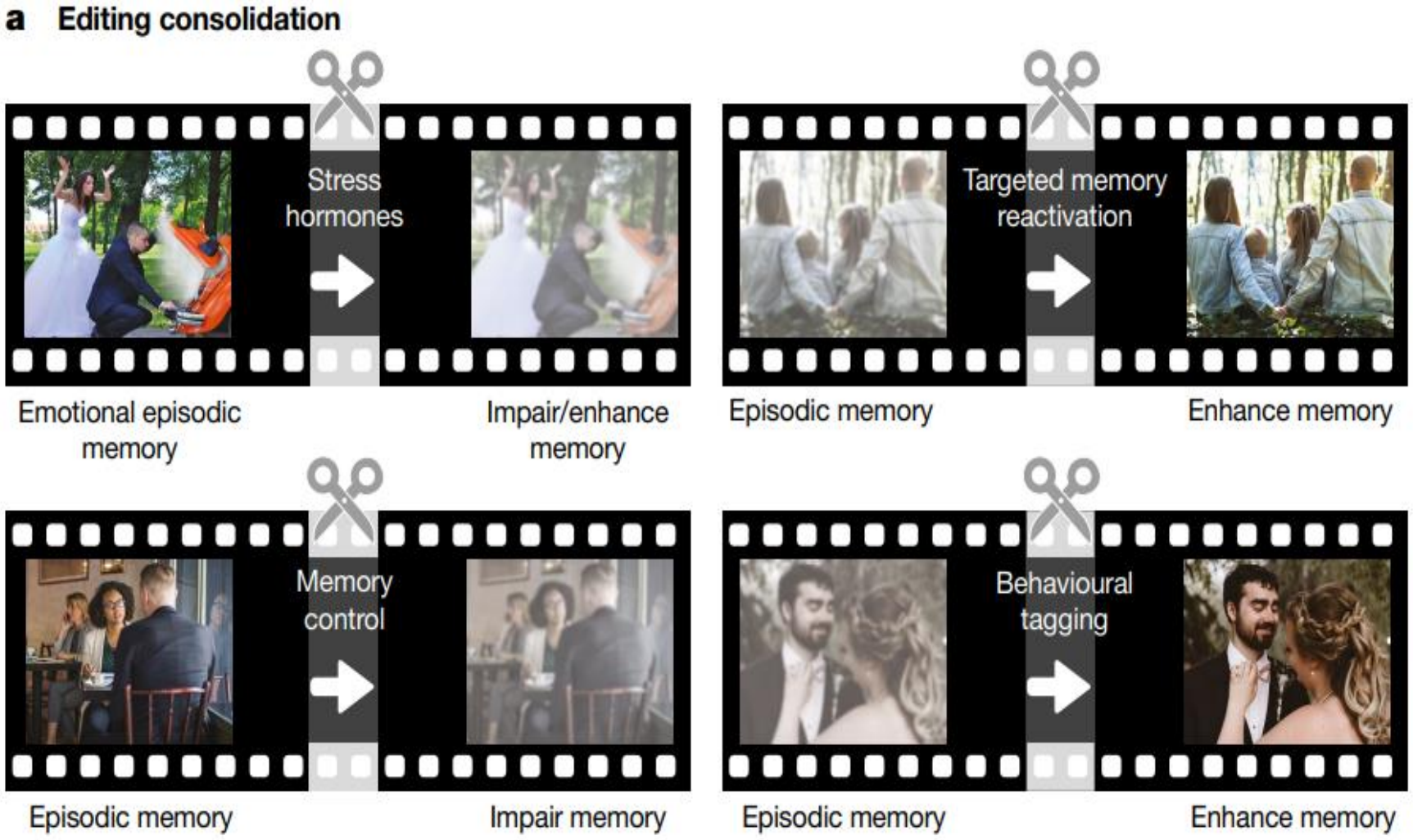
Memory Editing: Sleep

Memory: The Restless Engram



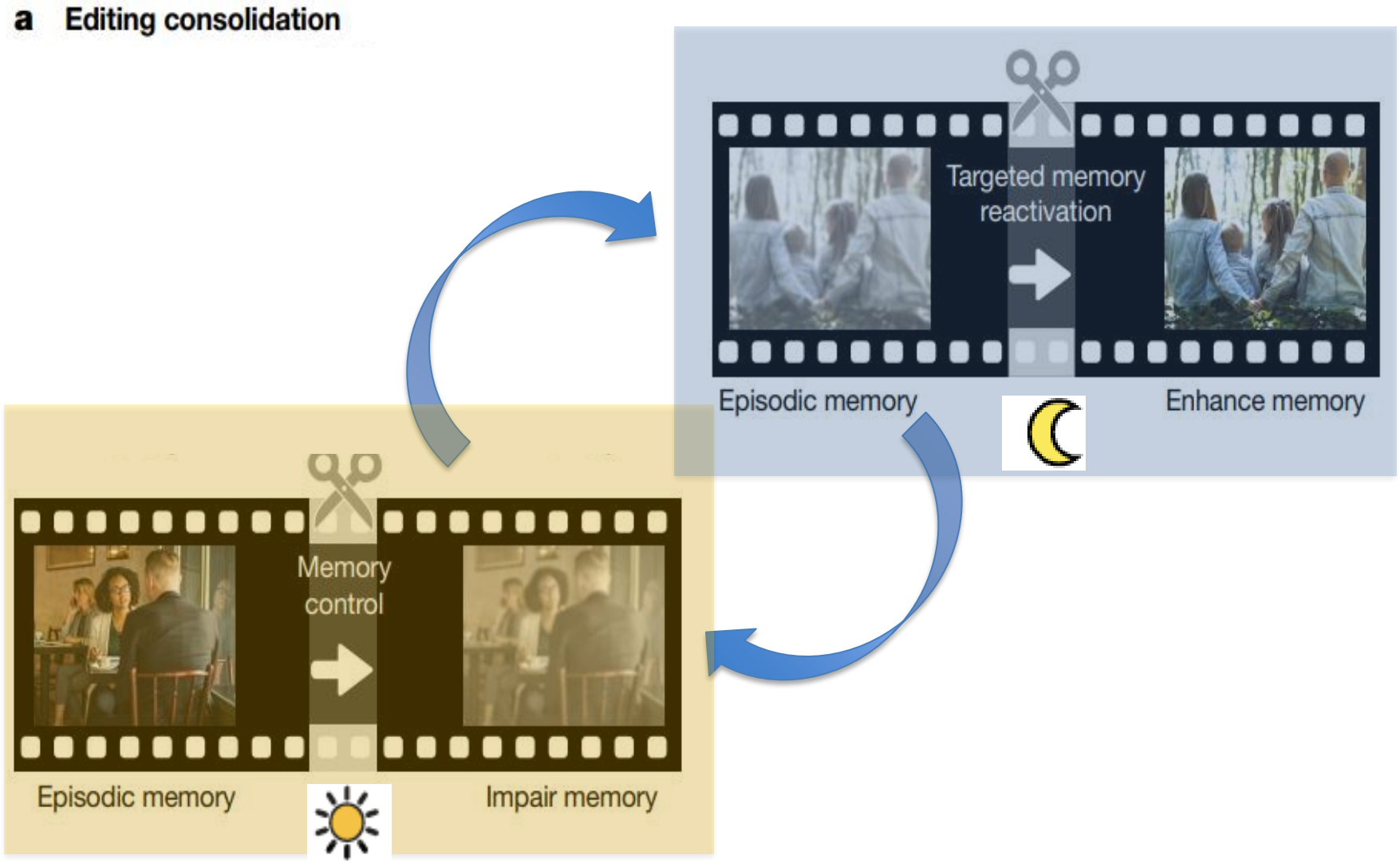
Hu et al., 2015; Hu et al., 2020; Zeng et al., 2021; Zeng, Lin et al., 2021; Xia et al., 2022; Xia et al., 2023

Memory Editing: Techniques



Phelps & Hoffman, 2019. *Nature*

Memory Editing: Wake and Sleep



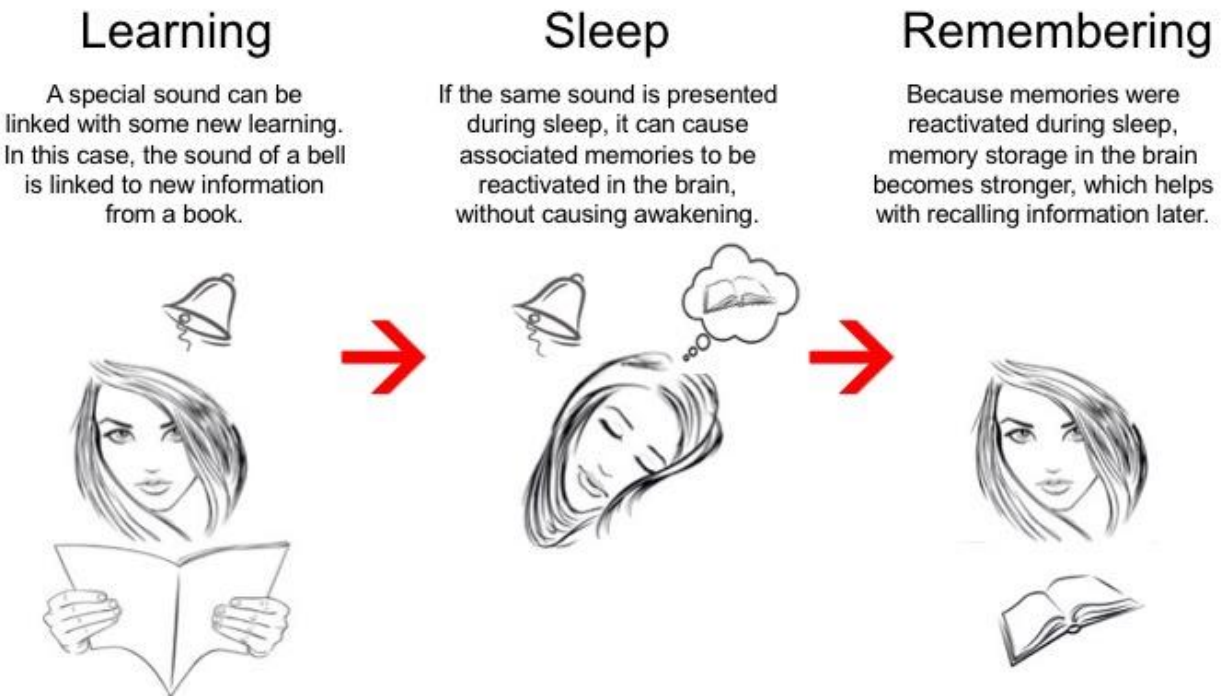
Phelps & Hoffman, 2019. *Nature*

From Science Fiction to Lab

Targeted Memory Reactivation

Targeted Memory Reactivation TMR

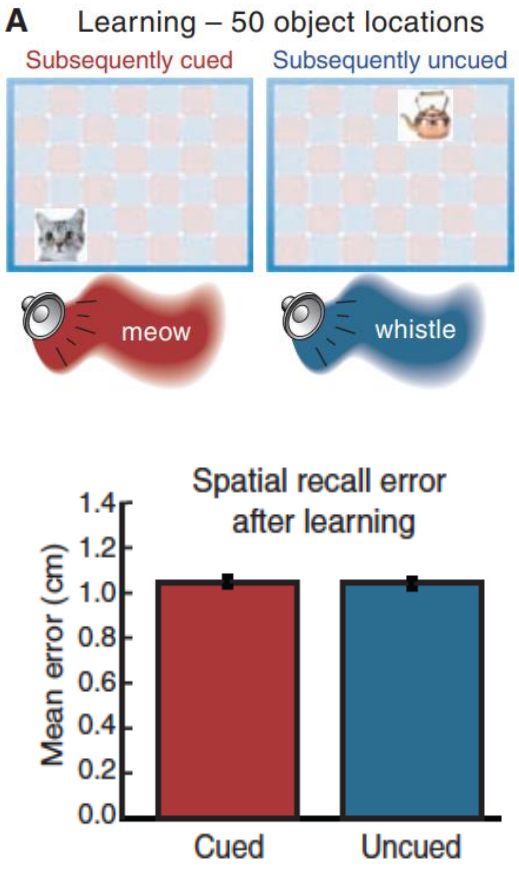
Employing sensory cues to guide covert memory reactivation during sleep

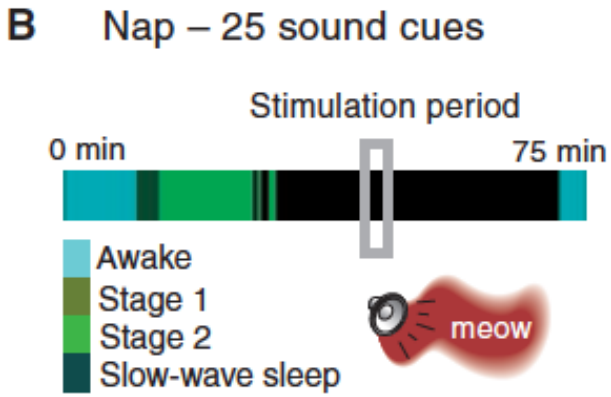


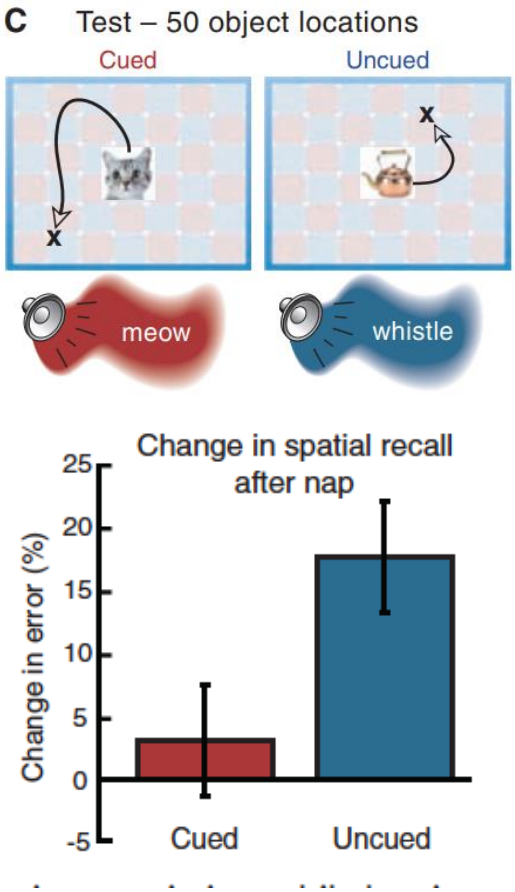
Rasch et al., 2007, *Science*; Rudoy et al., 2009, *Science*; Hu et al., 2015, *Science*; Hu et al., 2020, *Psychol Bull*

Targeted Memory Reactivation

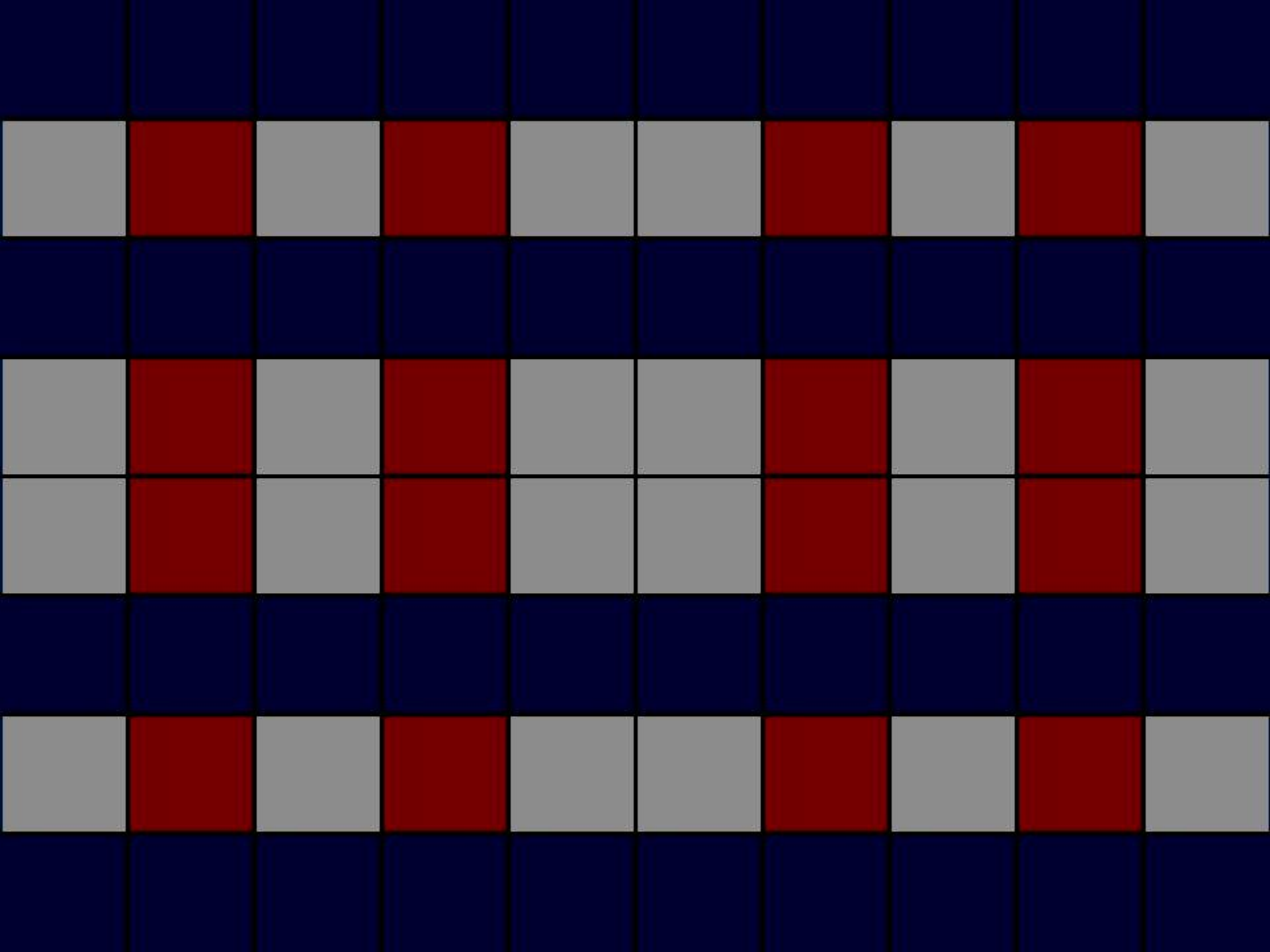
TMR promotes Spatial Learning

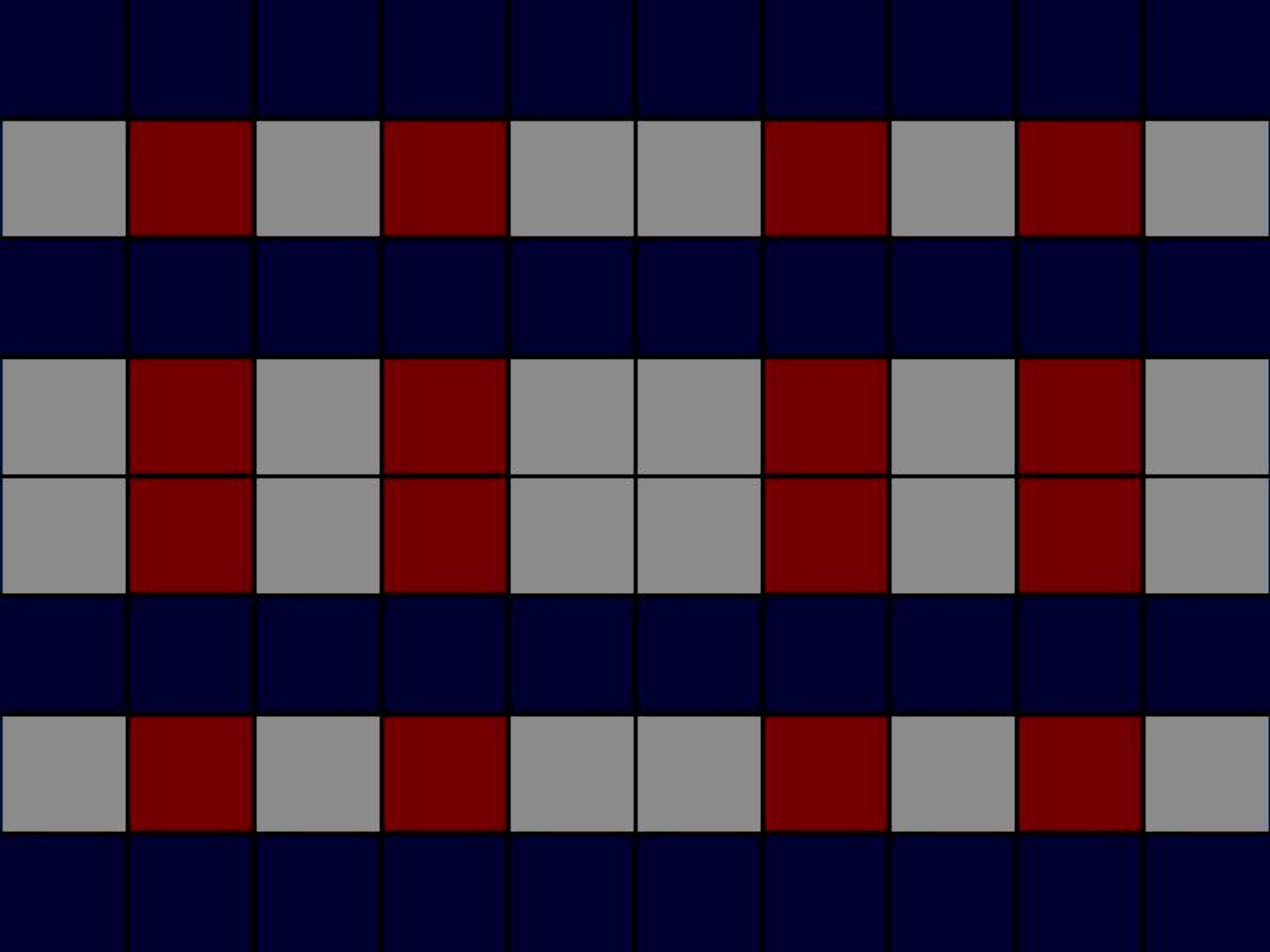




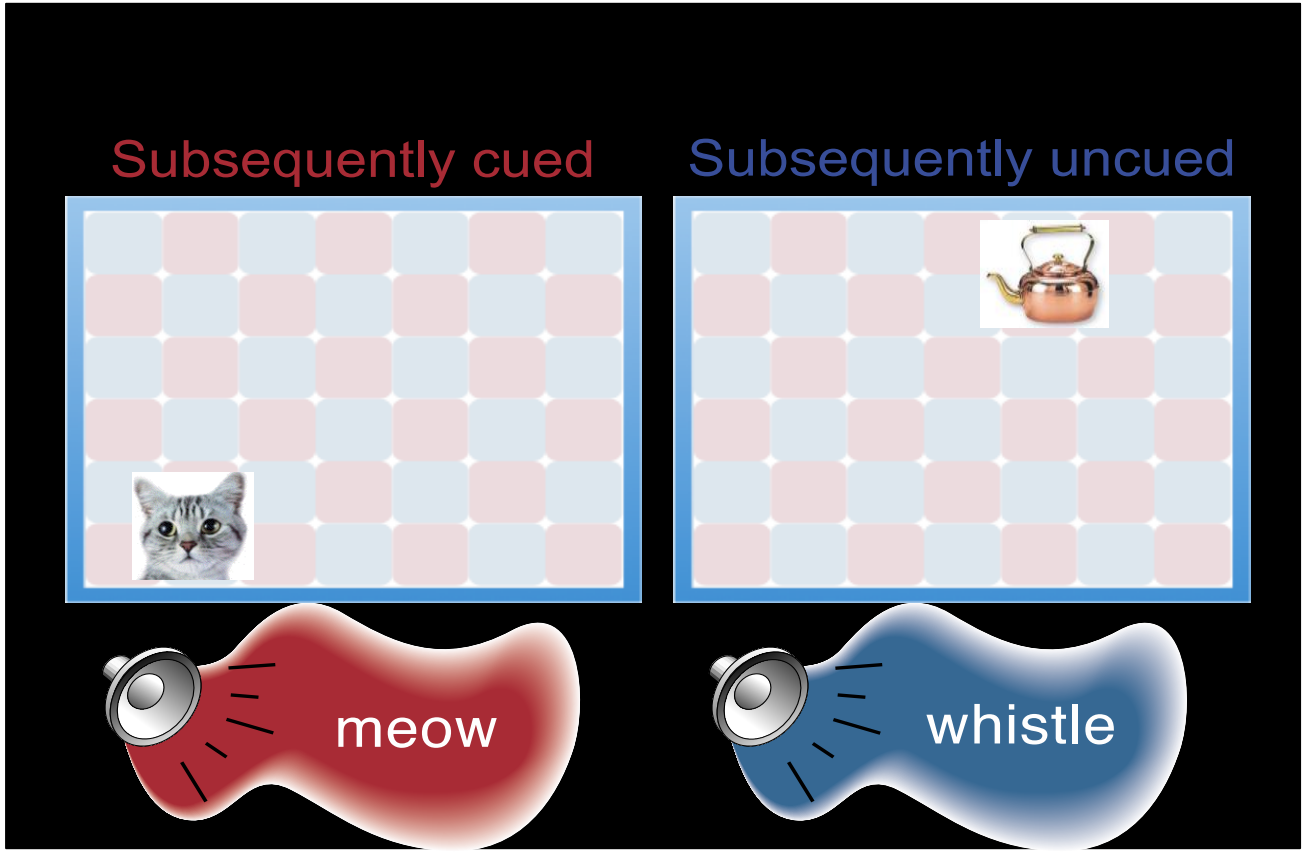


Rudoy et al. 2009, *Science*

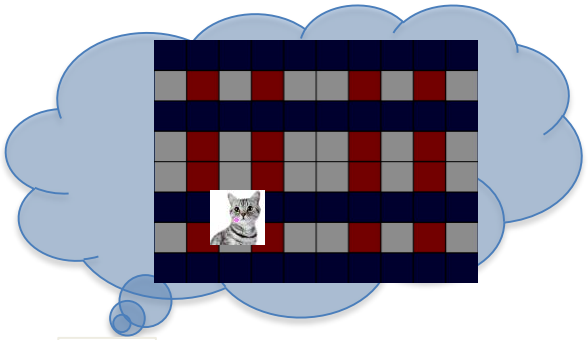




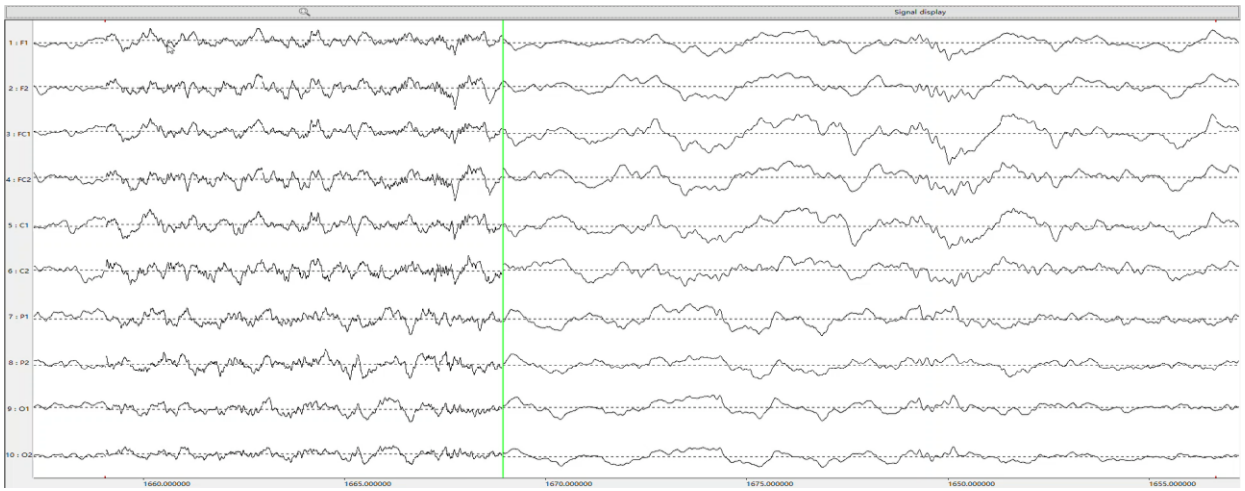
Targeted Memory Reactivation



Targeted Memory Reactivation



EEG Sleep Research



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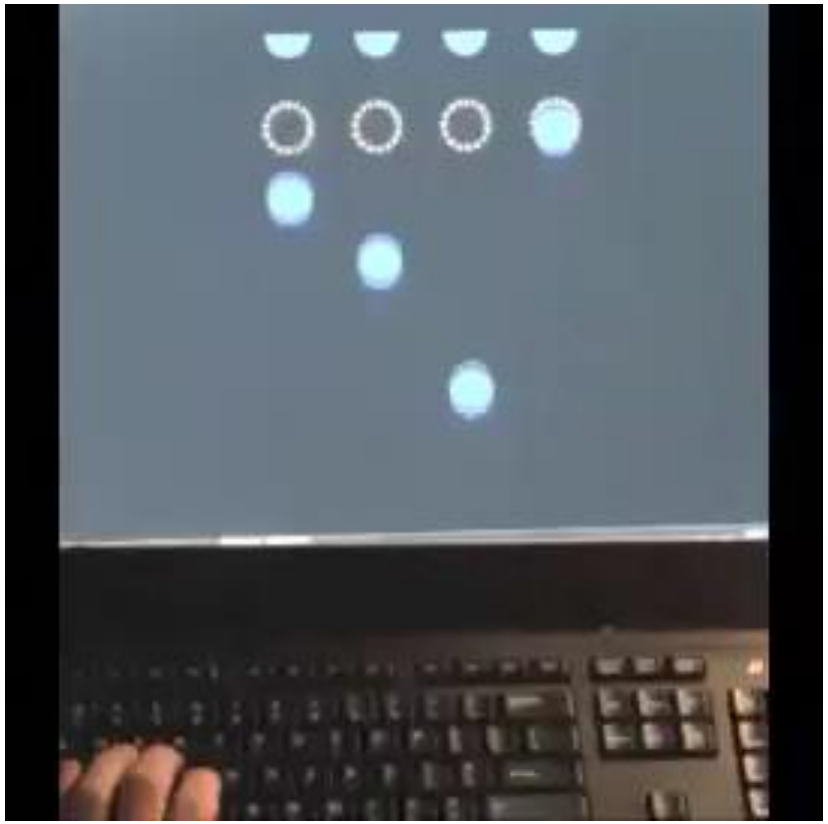
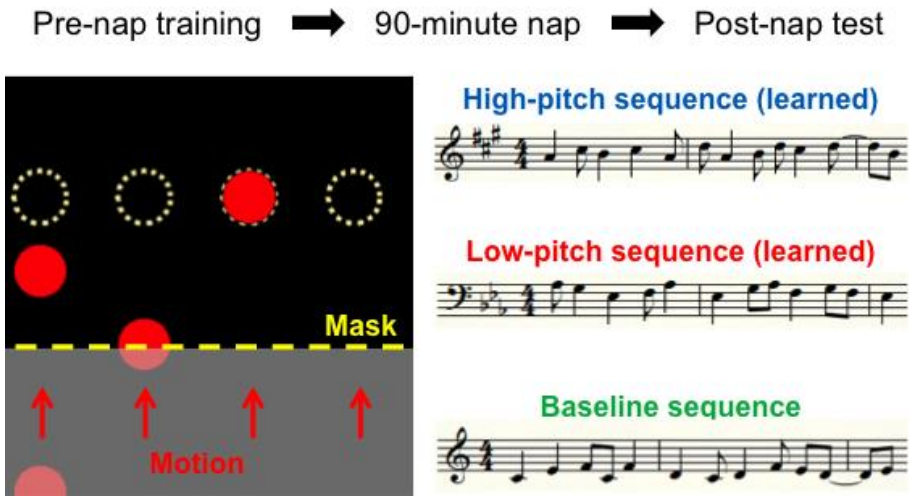
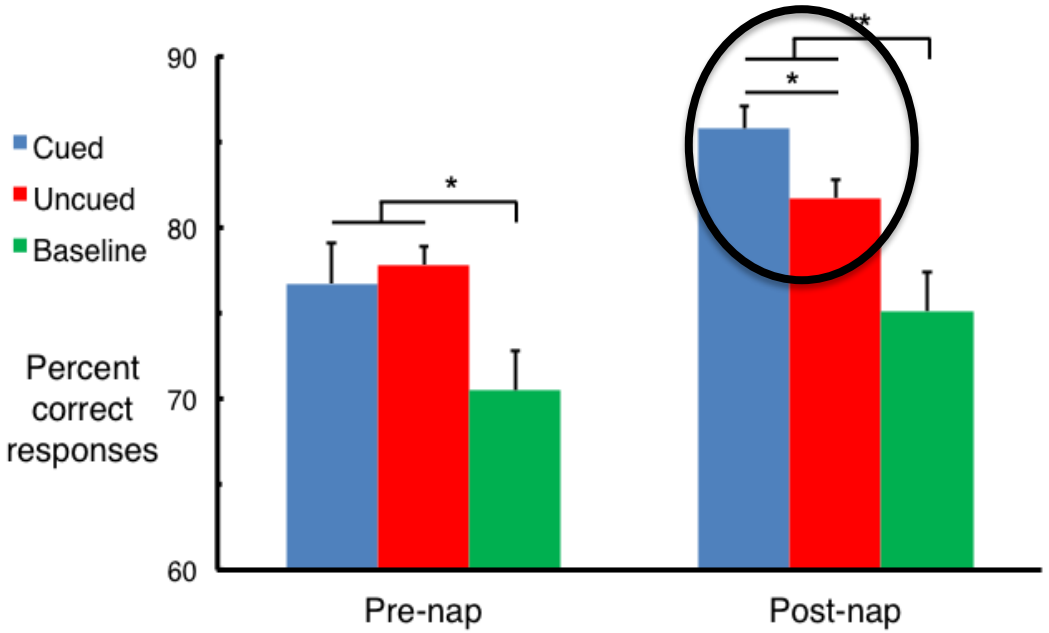
TMR improves Skill Learning

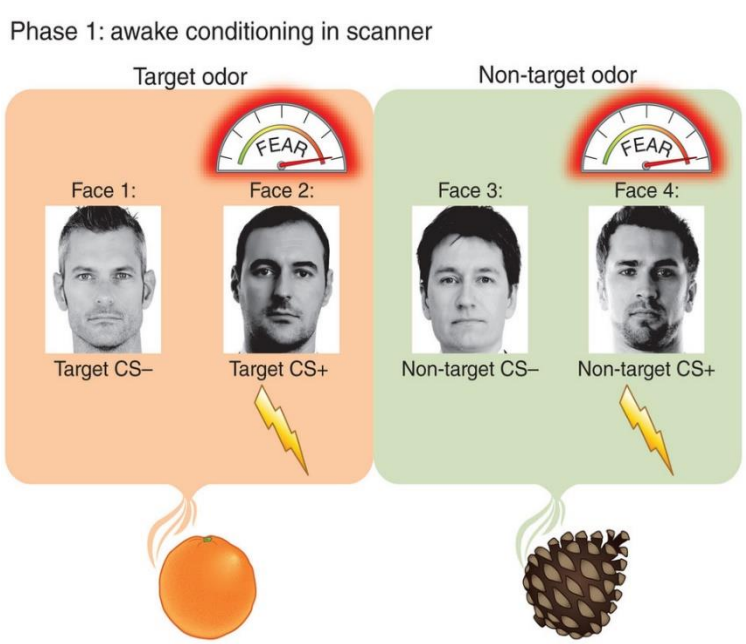


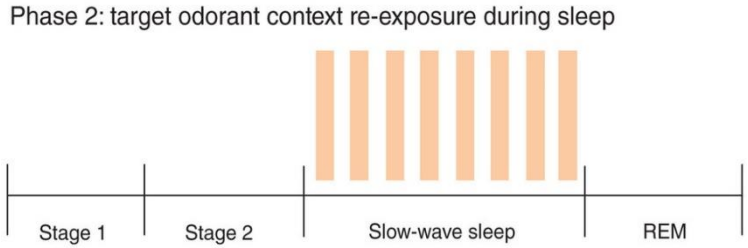


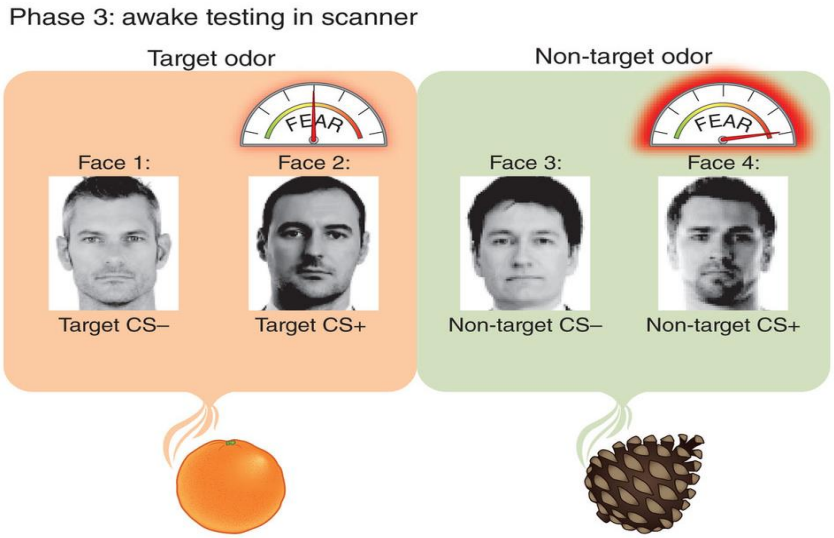


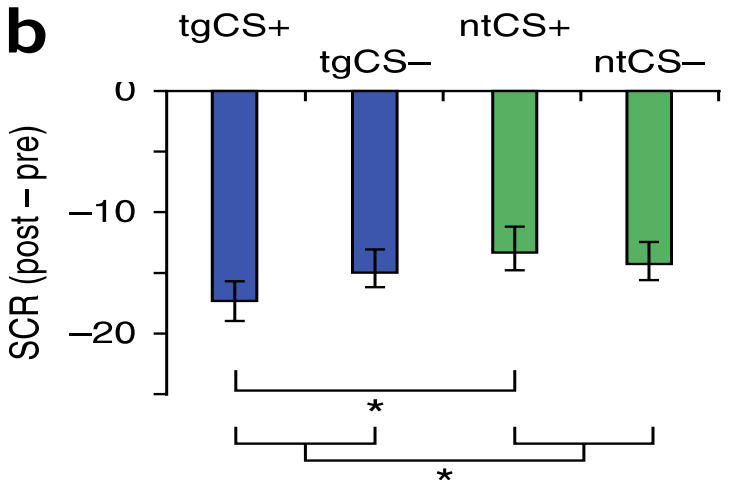
Antony et al., 2012, *Nat Neurosci.*

TMR induces Fear Extinction









Hauner et al., 2013, *Nat Neurosci.*

TMR induces Fear Extinction

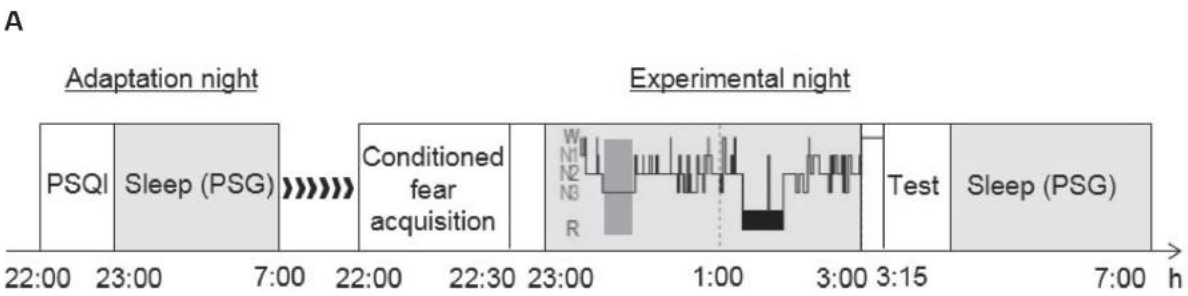
pii: sp-00026-14 http://dx.doi.org/10.5665/sleep.4502

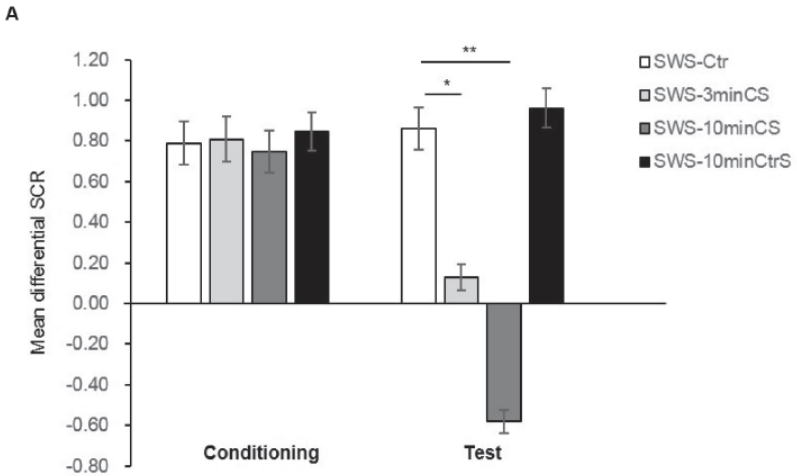
SLOW WAVE SLEEP AND FEAR MEMORY EXTINCTION IN HUMANS

Effect of Conditioned Stimulus Exposure during Slow Wave Sleep on Fear Memory Extinction in Humans

Jia He (Postgraduate Student)[1,2]; Hong-Qiang Sun, MD, PhD[1]; Su-Xia Li, MD, PhD[2]; Wei-Hua Zhang, MD[1]; Jie Shi, MD, PhD[2]; Si-Zhi Ai (Postgraduate Student)[2]; Yun Li, MD[3]; Xiao-Jun Li, MD[1]; Xiang-Dong Tang, MD, PhD[3]; Lin Lu, MD, PhD[1,2,4]

[1]Pekin ... ence, Pekin ... hengdu, Chin...

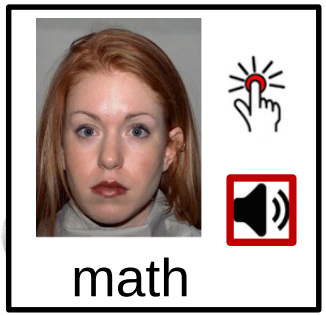




He et al., 2015, *SLEEP*

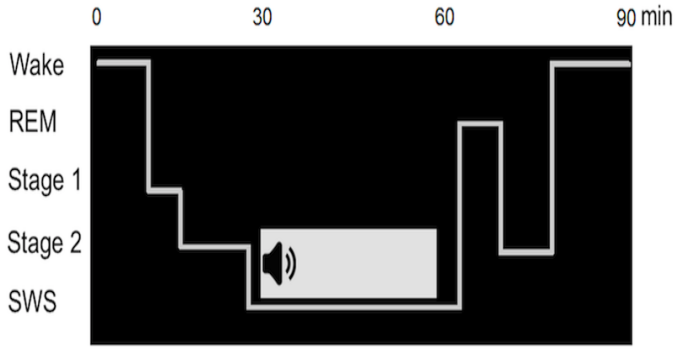
TMR induced Forgetting

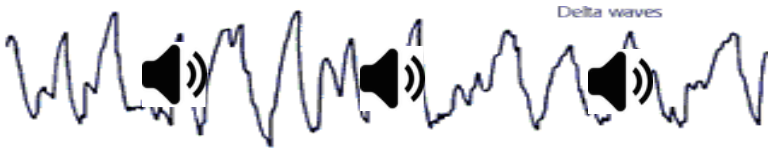
Counter-Bias Training + TMR

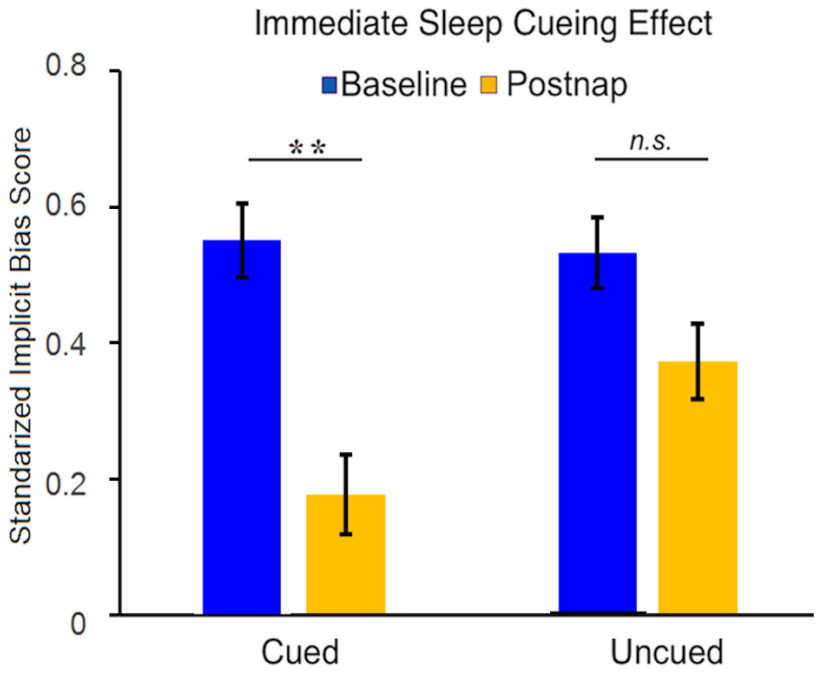


Gender Bias

Racial Bias







Hu et al., 2015, *Science*

TMR: A Meta

American Psychological Association

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Promoting Memory Consolidation During Sleep: A Meta-Analysis of Targeted Memory Reactivation

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Larry Y. Cheng
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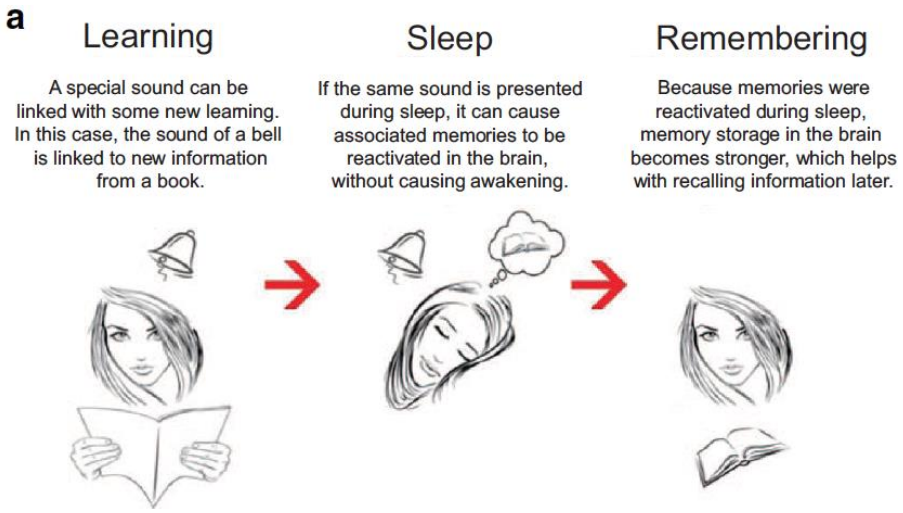
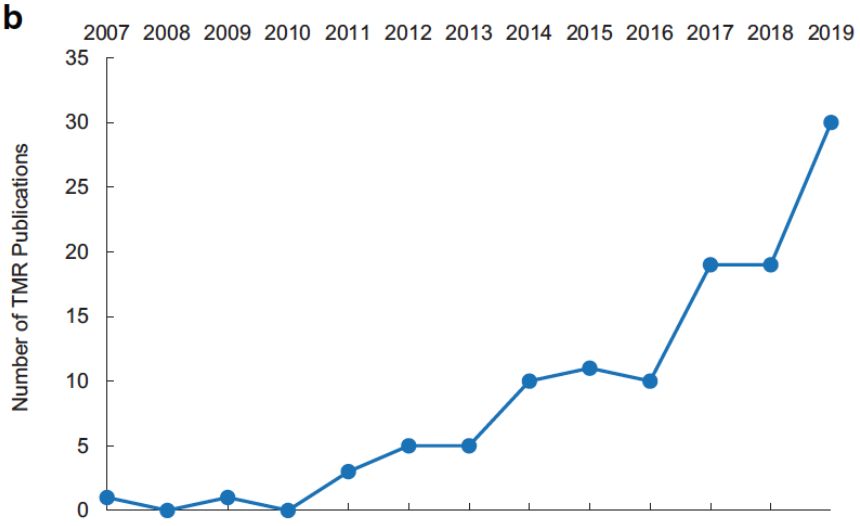
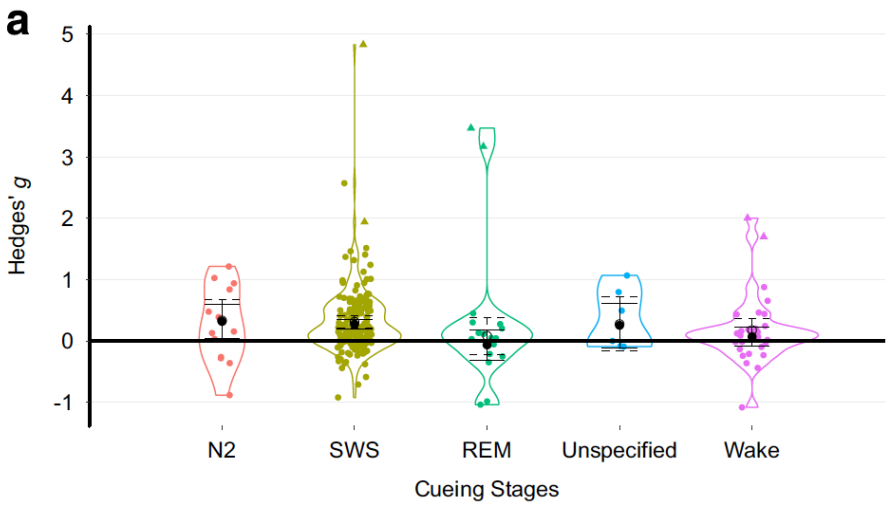




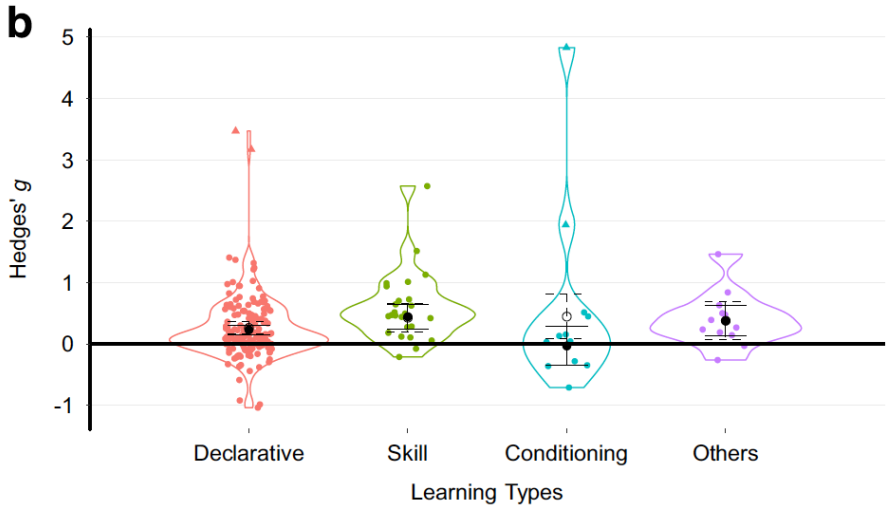
Hu et al., 2020, *Psychol Bull*

TMR: A Meta

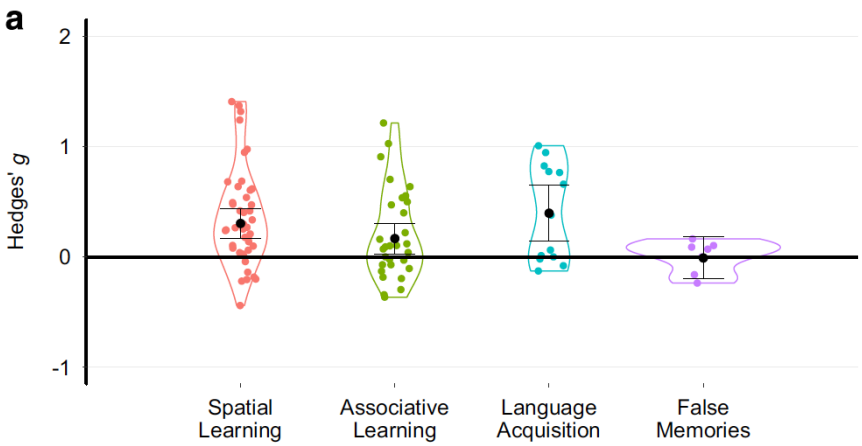
Cueing stages

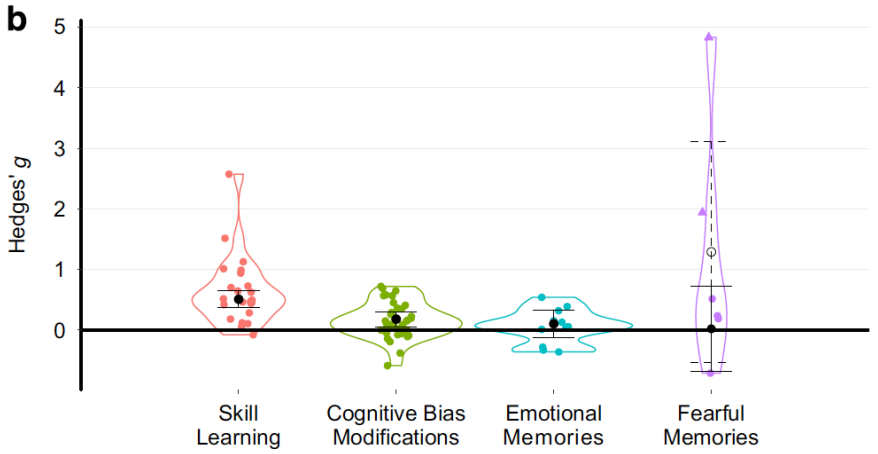


Learning tasks



Focal Analyses





Hu et al., 2020, *Psychol Bull*

TMR: from lab to real-world

aps
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Sleeping in
Opportunit
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Targeted M

Ken A. Paller
Department of Psychology,

Table 1. Framework for Applied Research on Enhancing the Influence of Sleep on Memory via Different Applications

Population and application	Sleep hygiene	Targeted memory reactivation	Brain stimulation	Hypnosis
Healthy subjects				
Neuroenhancement	+++	+++	++	+
Clinical subjects				
Rehabilitation	++	+++	++	+
Psychotherapy	++	+	++	+
Aging/dementia	+++	+	++	+
Health behavior	0	+++	+	0

Note: Rows show different application targets, and columns show different methods. Symbols indicate potential effectiveness: very high (+++), high (++), medium (+), and low (0). These ratings represent the authors' personal perspectives, which are based on varying degrees of evidence and should not be interpreted quantitatively. Rather, these ratings are intended as a guide for the most promising areas for future applied research.

ow Sleep
e the
Better

Ken A. Paller, Jessica D. Creery, and Eitan Schechtman

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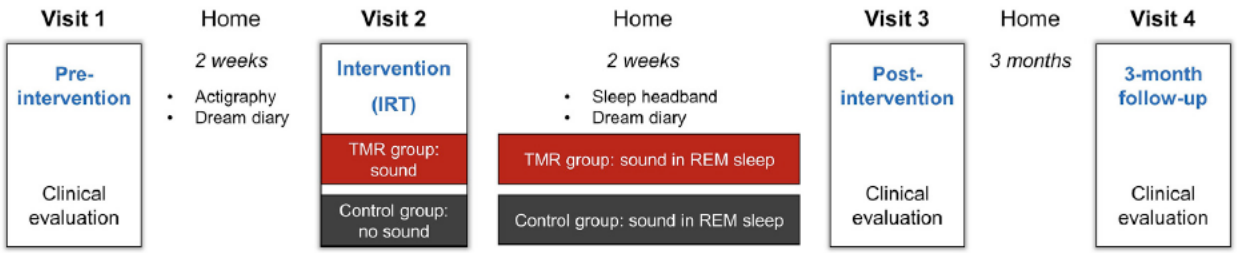
Feld & Diekelmann, 2020, *Curr Dir Psychol Sci.*
Paller 2017, *Curr Dir Psychol Sci.*
Paller et al., 2021, *Annu Rev Psychol*

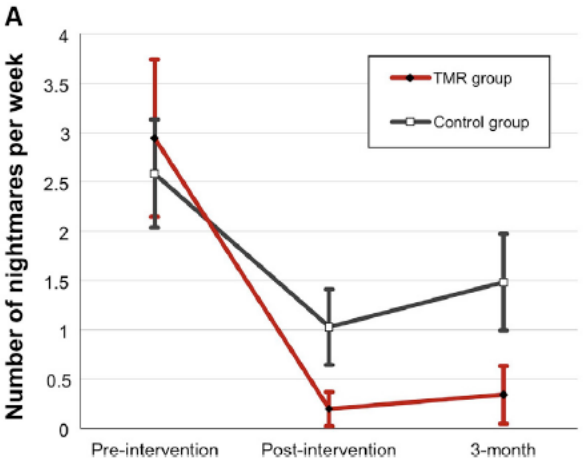
TMR: from lab to real-world

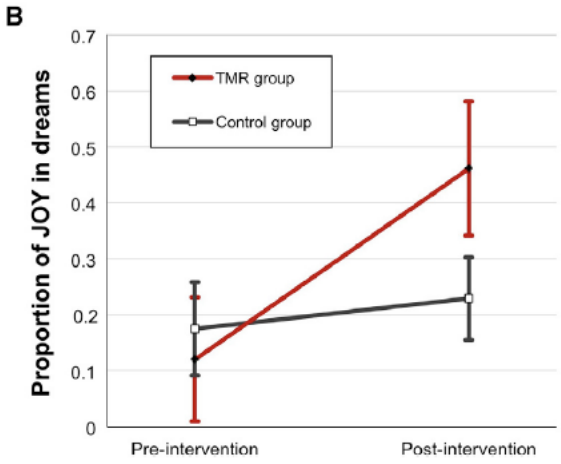
Article

Current Biology

Enhancing imagery rehearsal therapy for nightmares with targeted memory reactivation

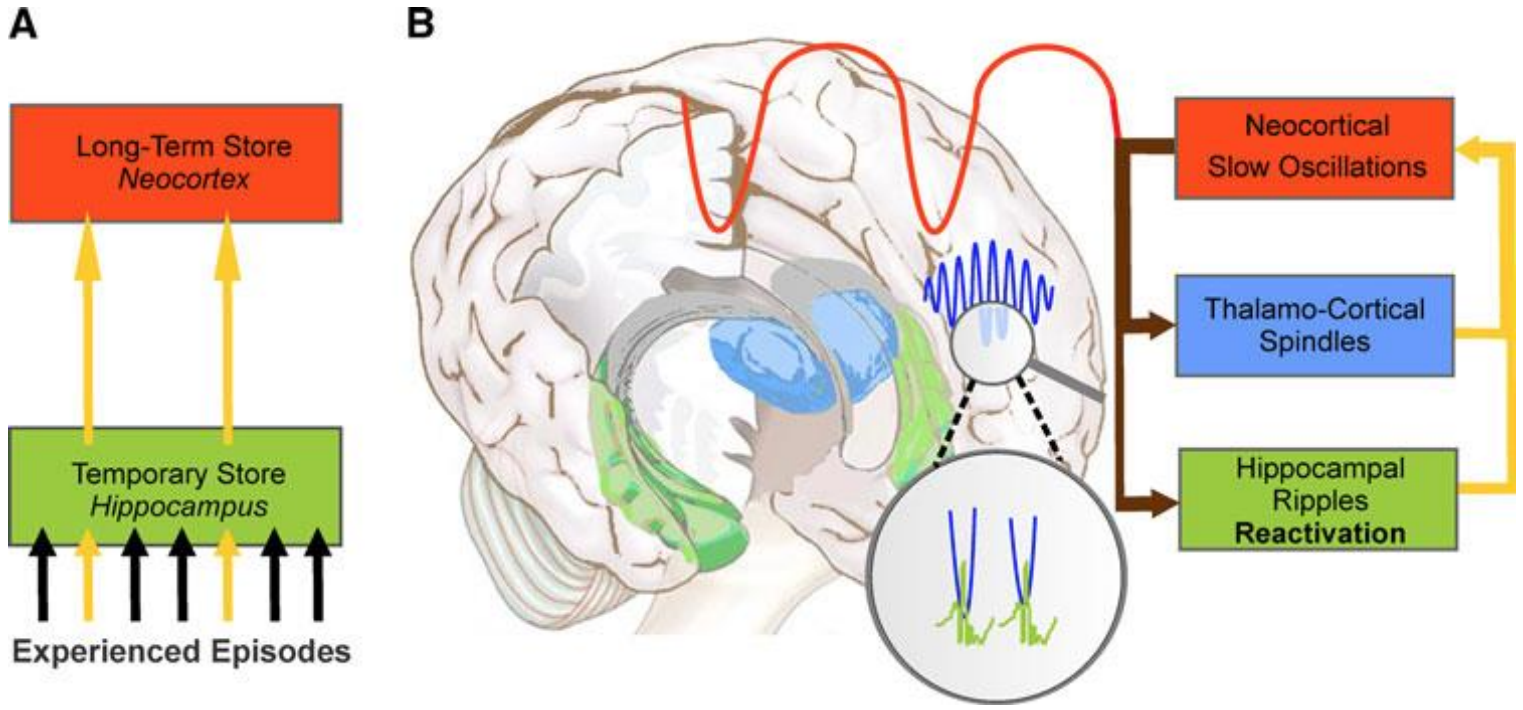






Schwartz et al., 2022, *Curr Biol.*

TMR: Mechanisms



Cross-regional, hierarchical coupling between

Slow oscillations (<1.5 Hz, frontal cortex)

Spindles (12-16Hz, thalamus)

Ripples (>100 Hz, hippocampus)

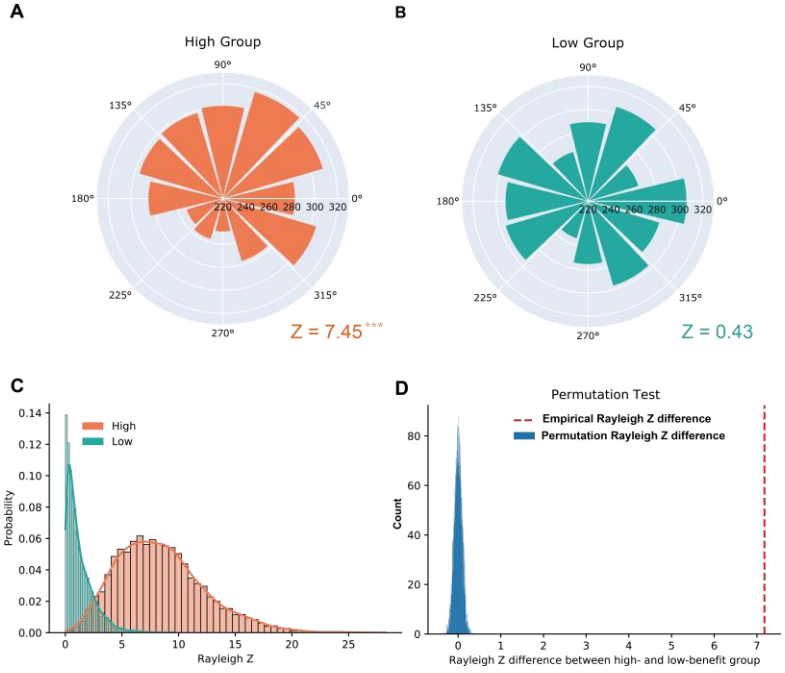
Born & Wilhelm, 2012, *Psychol. Res.*

TMR: Mechanisms

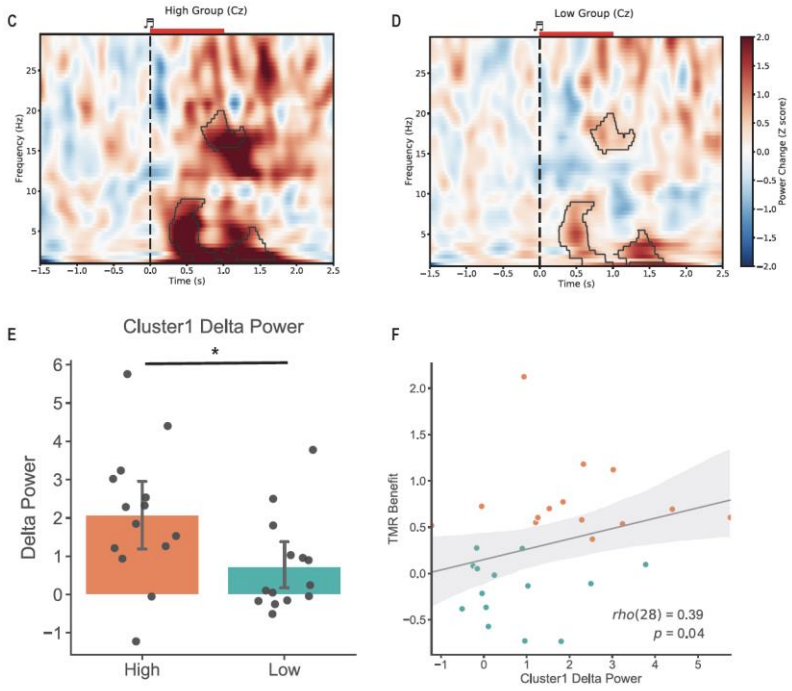
XIA Tao 夏濤

Cueing is most effective when delivered during SO up-phases, and elicited stronger Delta/Theta power

SO phases



1-4 Hz Delta Power

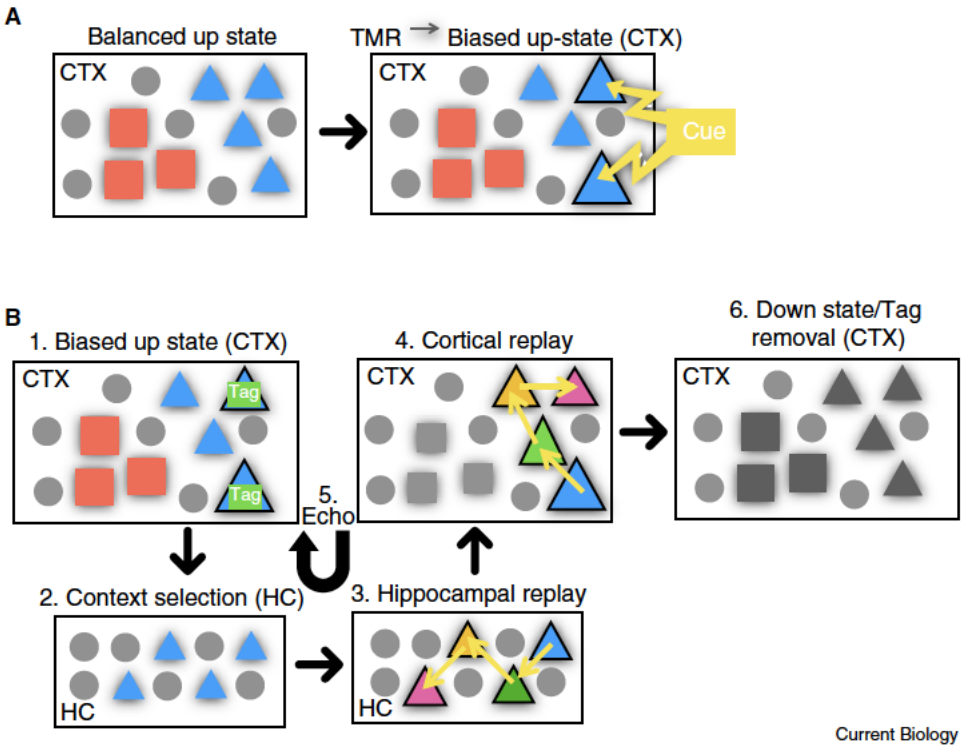


Xia et al., 2023 *Psychophysiology*

TMR: Mechanisms

How Targeted Memory Reactivation Promotes the Selective Strengthening of Memories in Sleep

Penelope A. Lewis[1,*] and Daniel Bendor[2]
[1]Psychology Department, Cardiff University, Cardiff, UK
[2]Department of Experimental Psychology, University College London, London, UK
*Correspondence: LewisP8@cardiff.ac.uk
https://doi.org/10.1016/j.cub.2019.08.019

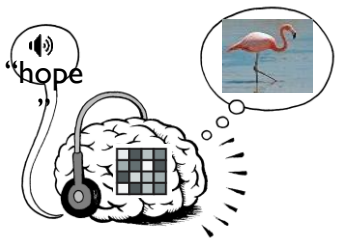


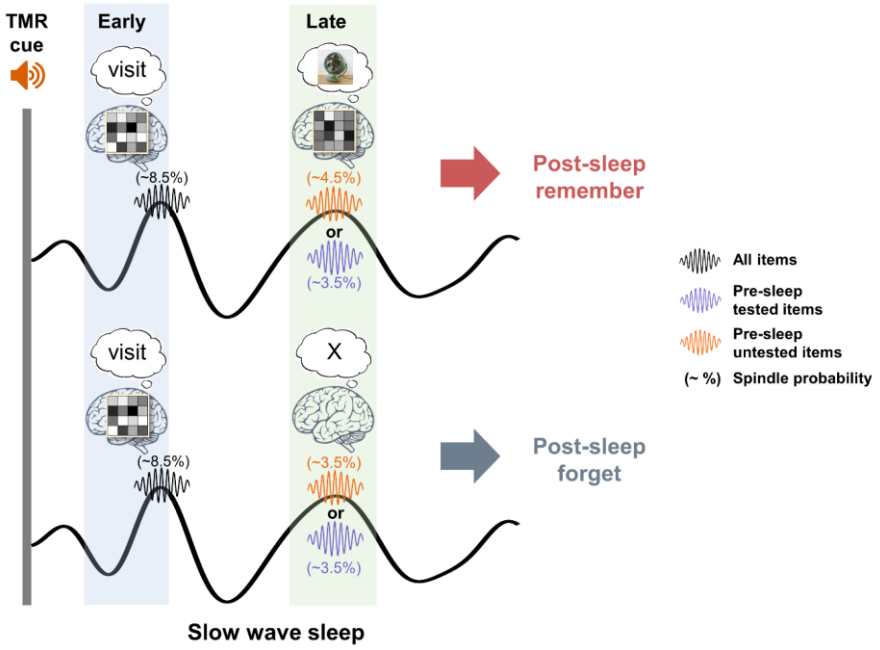
Lewis & Bendor, 2019, *Curr Biol.*

TMR: Mechanisms

LIU Jing 劉婧

Item-specific Representations during Sleep is temporally orchestrated via slow oscillations





V

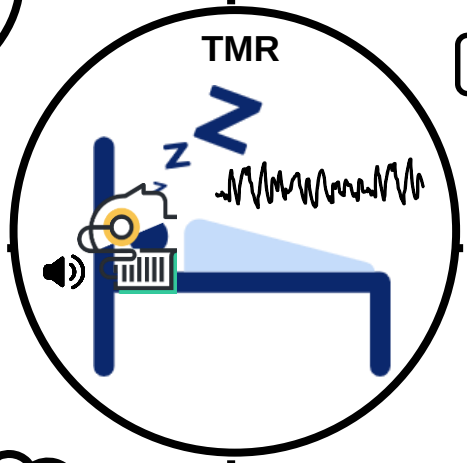
Liu et al., in prepraration

TMR and Memory Editing during Sleep

Yao Ziqing

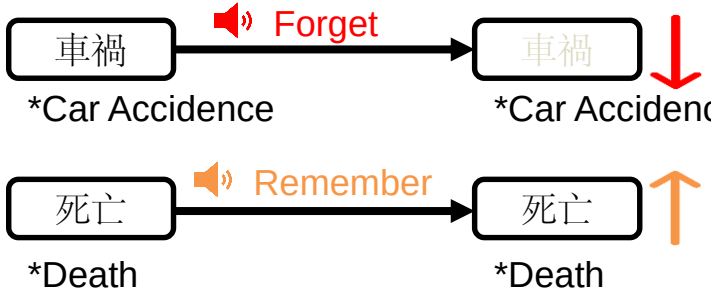
Self-evaluations

TMR



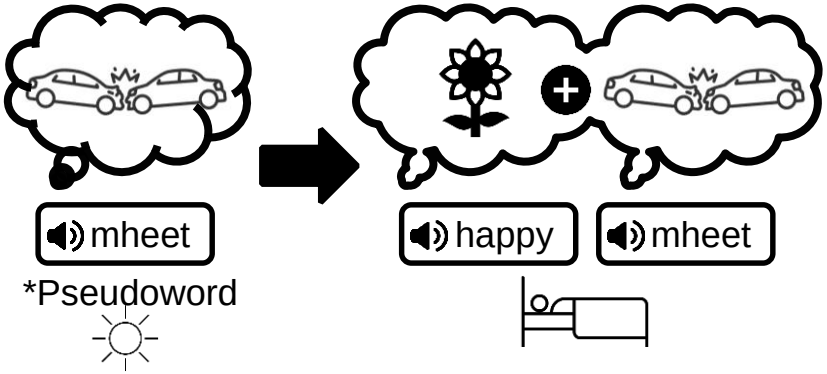
Voluntary Forgetting

Lin Xuany



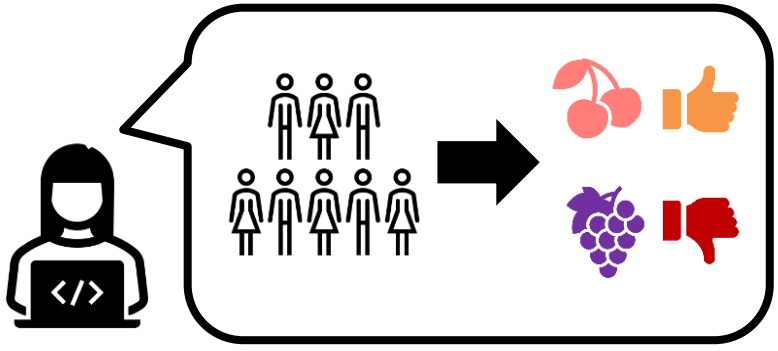
Xia Tao

Affective Updating



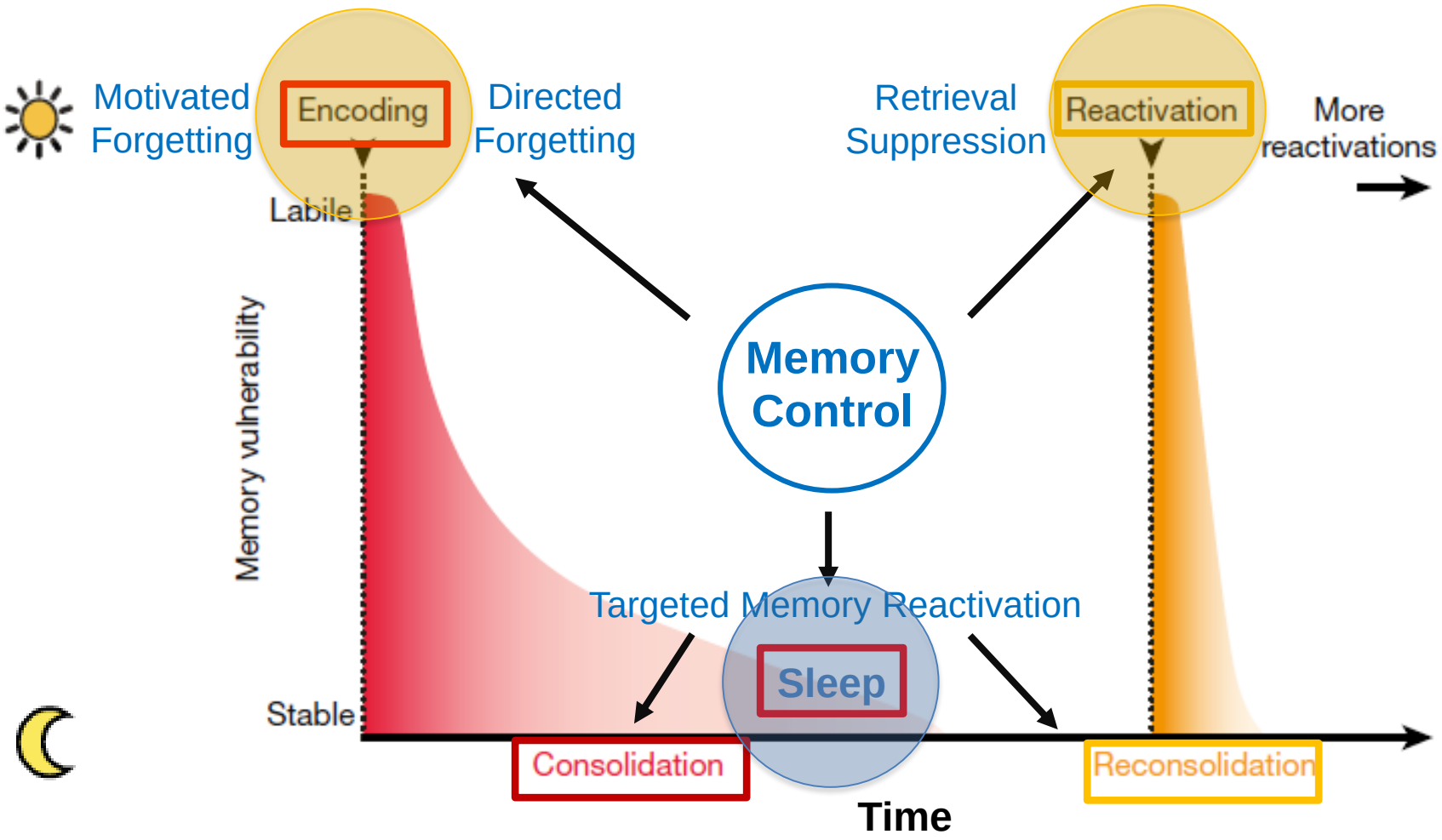
Social Norms Learning

Chen Danni



Memory Editing

Memory: The Restless Engram



Hu et al., 2015; Hu et al., 2017; Xie et al., 2020; Xie et al., 2022; Yao et al., 2021; Hu et al., 2015; Hu et al., 2020; Zeng et al., 2021; Zeng, Lin et al., 2021; Xia et al., 2022

Sleep: Mechanisms to Behavior to Health

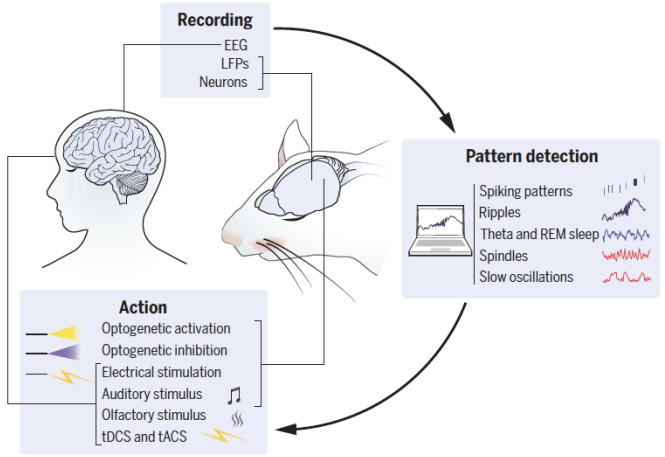
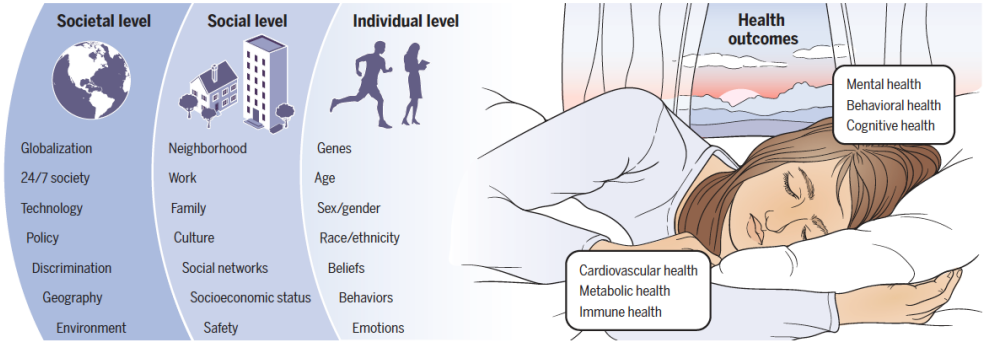


Fig. 2. Closed-loop experiments allow for the modulation of ongoing brain patterns in real time. Recorded brain signals are processed in real time to detect sleep patterns. The detection of a given pattern automatically triggers an action using invasive or noninvasive methods that affect the neural networks in real time to test whether the manipulation boosts or impairs memory consolidation. The effect on memory is assessed during a recall session after the modified sleep period. tDCS, transcranial direct current stimulation; tACS, transcranial alternating current stimulation.

Sleep health in context

There are several dimensions to sleep health, such as regularity, satisfaction, alertness, timing, efficiency, and duration. Alone and in combination, these dimensions interact with many aspects of our general health, including cardiovascular, metabolic, immune, mental, behavioral, and cognitive health. Interactions between sleep and health are further shaped by individual- and social-level factors operating within larger societal factors. All occur in the context of the day-night cycle.



WHY WE SLEEP 2021 *Science*

人最大的煩惱就是記性太好
The root of Man's problems is memory

Acknowledgements

Department of Psychology
The University of Hong Kong
香港大學心理學系

SOCIAL AND COGNITIVE NEUROSCIENCE LAB

PI: XIAOQING HU, PH.D.

Memory plays a central role in almost all aspects of our mental lives: it shapes our preferences and beliefs, guides our judgments and behaviors, and defines who we are.

Our research aims to elucidate how motivational, emotional and cognitive processes may influence memory dynamics.

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