

New Treatment Strategies Based on Modifying Cognition During Sleep: Insomnia, Sleep Apnea, and Nightmares

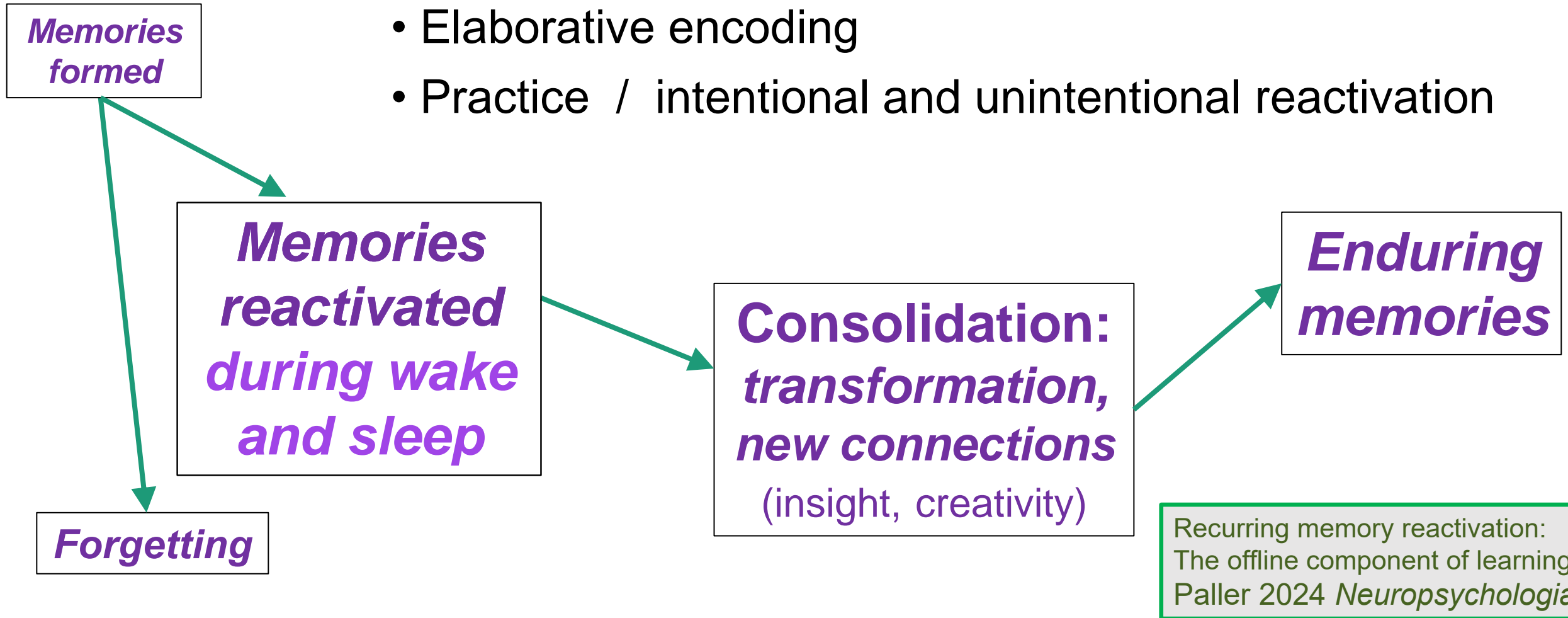
Ken Paller, Erika Yamazaki, Jennifer Mundt
Northwestern University

Society for Behavioral Sleep Medicine
9-14-2024

- 1) Countless memories are created each day
- 2) As days pass, they become more difficult to recall

What determines which memories endure?

- Elaborative encoding
- Practice / intentional and unintentional reactivation

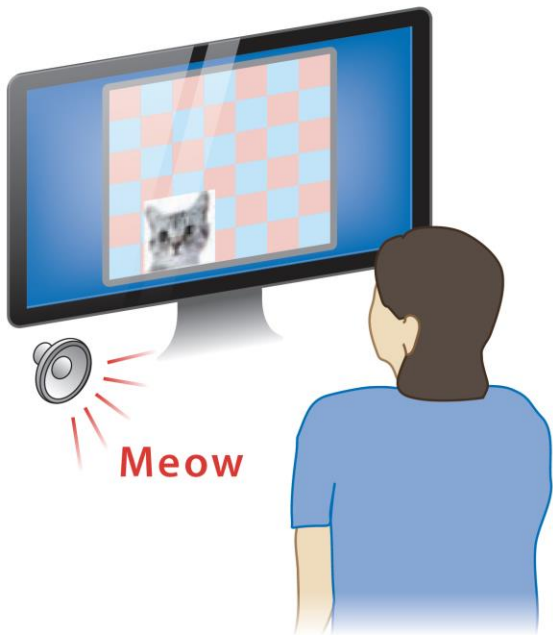


Targeted Memory Reactivation (TMR) → memory reactivation during sleep changes memory storage

Pre-sleep

Participants learn new information linked with a specific stimulus.

50 object-location associations



Sleep

The same stimulus during sleep causes associated memories to be reactivated, without disrupting sleep.

0 min 90 min

Awake

Stage 1

Stage 2

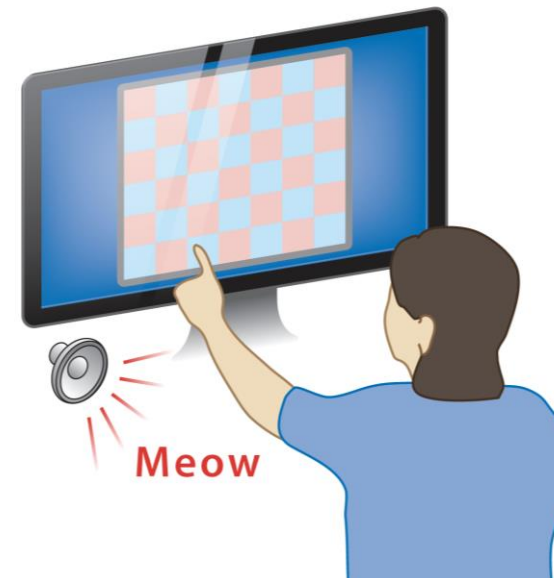
Slow-wave sleep

REM

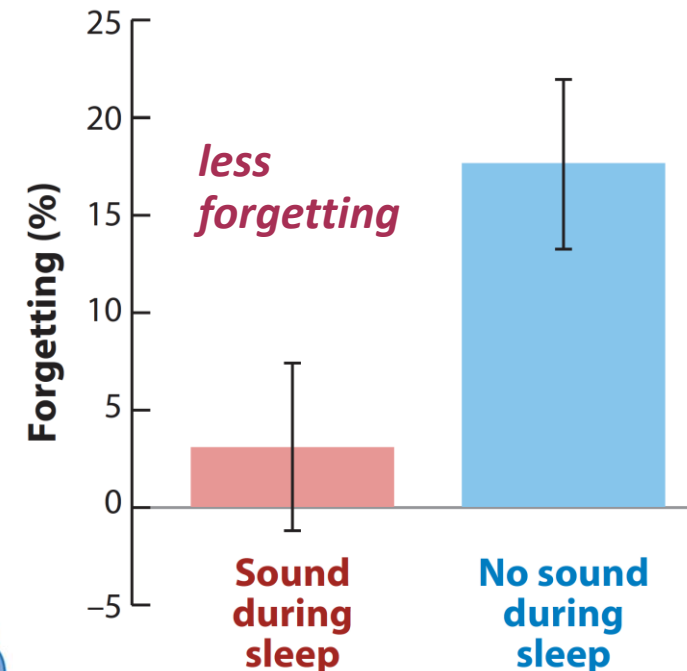


Post-sleep

Memory testing shows that retrieval is improved for memories that were reactivated during sleep.



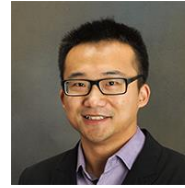
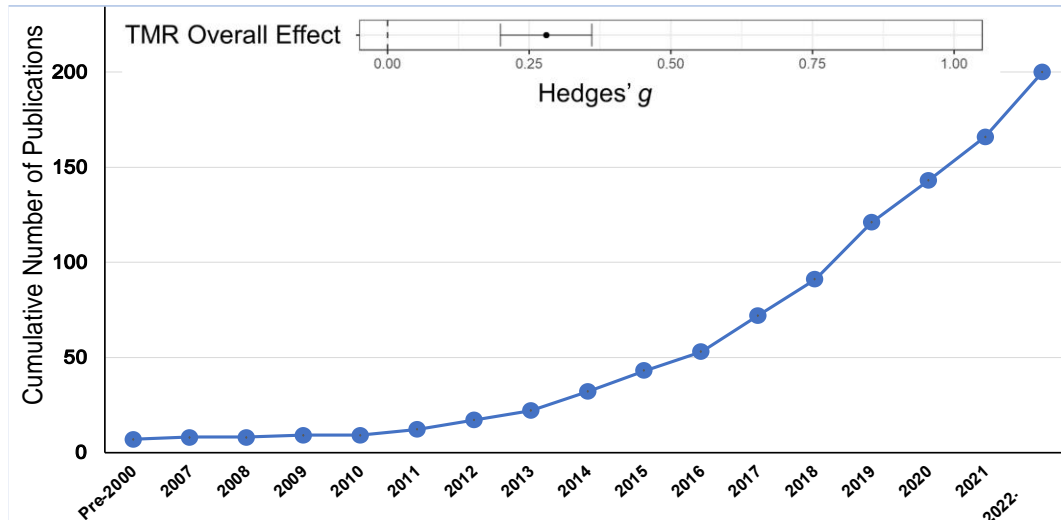
strong evidence now favors the notion of sleep-based memory consolidation



Paller, Creery, & Schechtman 2021
Annual Review of Psychology (illustration)

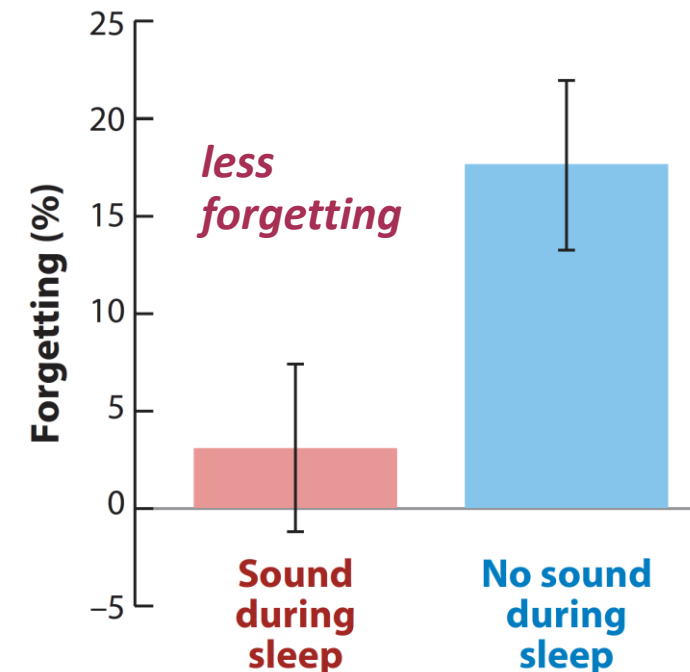
Rudoy, Voss, Westerberg, & Paller 2009 *Science*

Targeted Memory Reactivation (TMR) → memory reactivation during sleep changes memory storage



meta-analysis
Xiaoqing Hu et al.
2020 *Psych Bulletin*

- TMR benefits for memory are replicable
- Multi-lab replication study in progress (Gordon Feld et al. funded by DFG)
- Found for many types of memory
- TMR stimuli can avoid disrupting sleep (if not, additional forgetting)

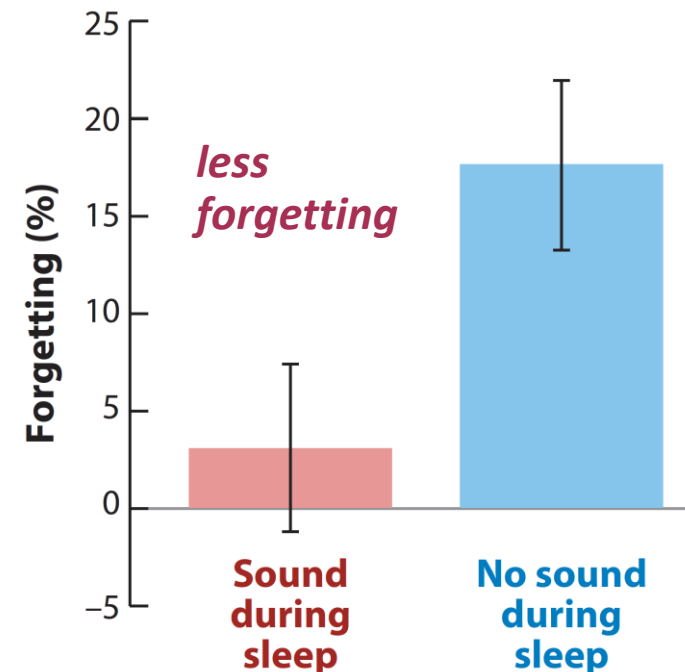
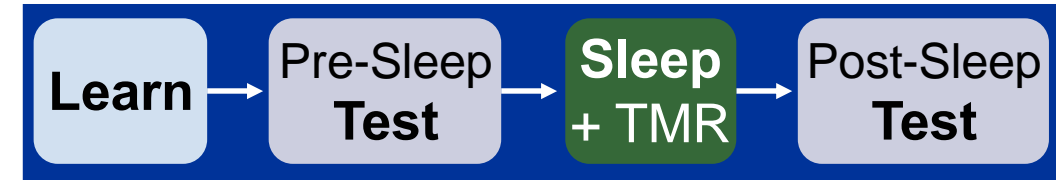


Rudoy, Voss, Westerberg, & Paller 2009 *Science*

Targeted Memory Reactivation (TMR) → memory reactivation during sleep changes memory storage

3 conceptual issues underlying the TMR literature:

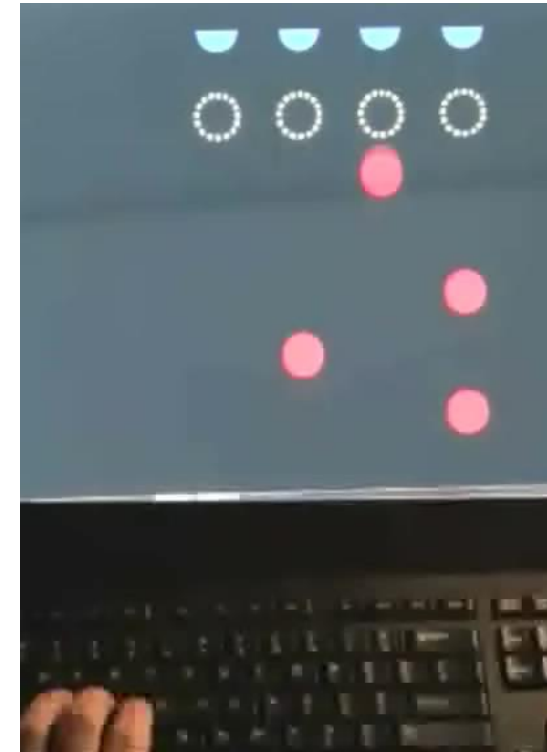
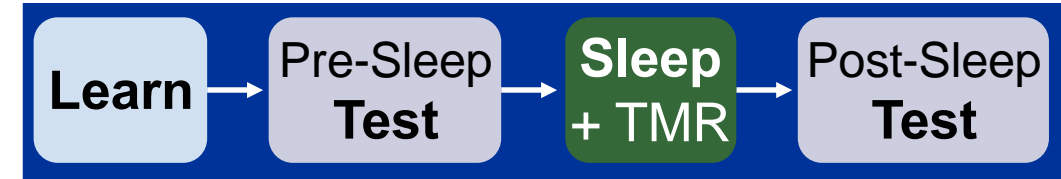
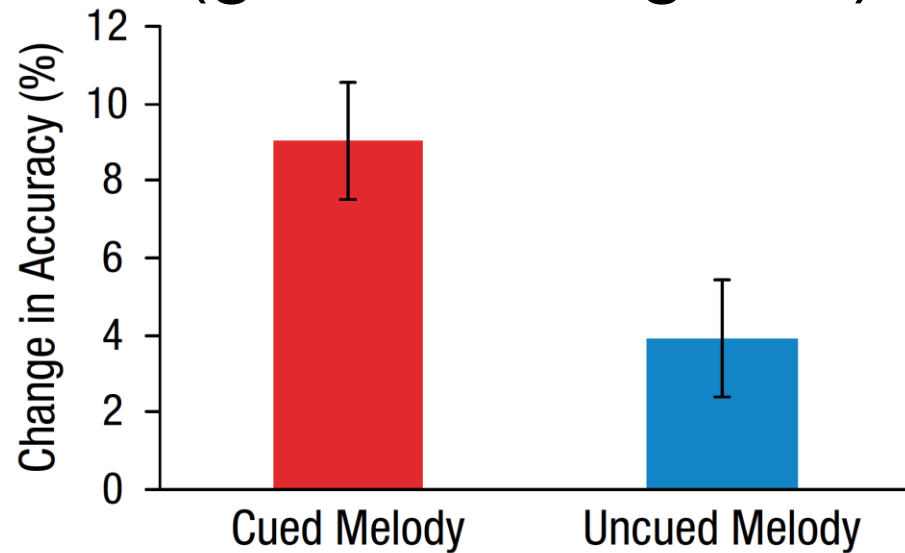
- 1) Building on awake learning, not learning new things during sleep
- 2) Escaping the dogma that almost all sensory information is blocked during sleep
- 3) Focusing on slow-wave sleep



Rudoy, Voss, Westerberg, & Paller 2009 *Science*

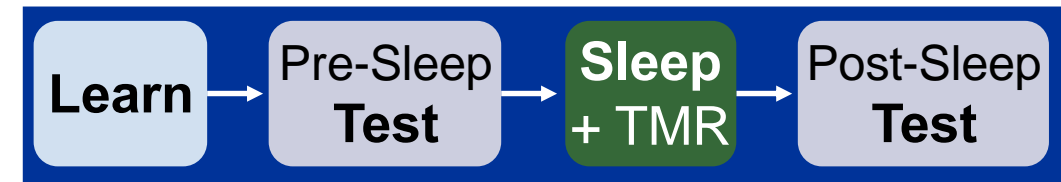
Targeted Memory Reactivation (TMR) with Skills and Habits

Learning to play a
melody on a keyboard
(guitar hero game)

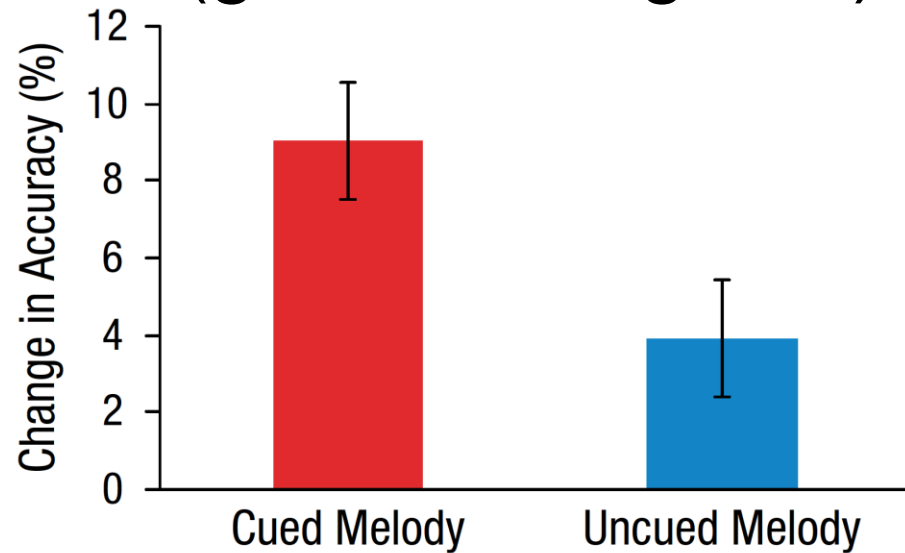


James Antony, Gobel, O'Hare, Reber,
& Paller 2012 *Nature Neuroscience*
- contralateral spindles; real-time detection

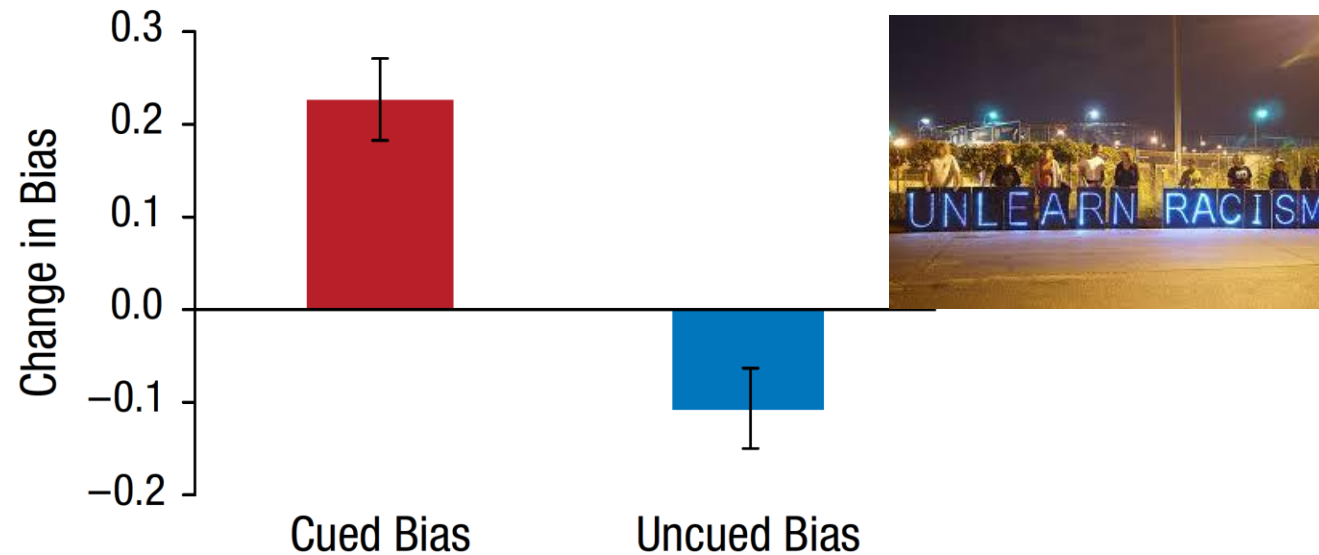
Targeted Memory Reactivation (TMR) with Skills and Habits



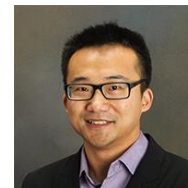
Learning to play a
melody on a keyboard
(guitar hero game)



Training to reduce
implicit social bias based
on gender or race



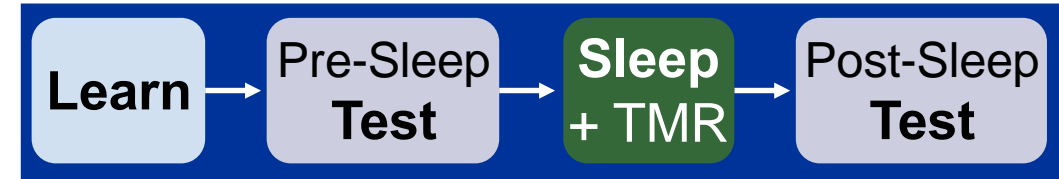
James Antony, Gobel, O'Hare, Reber,
& Paller 2012 *Nature Neuroscience*
- contralateral spindles; real-time detection



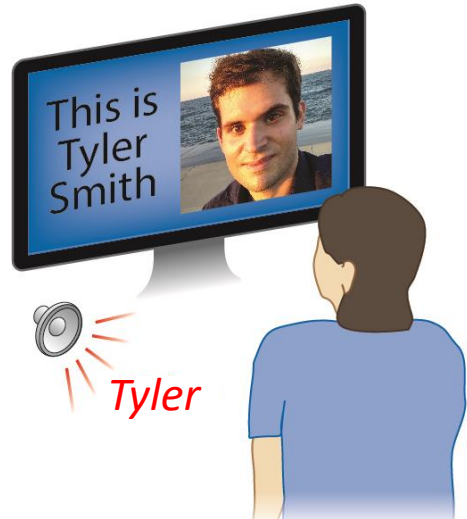
Xiaoqing Hu, Antony, Creery, Vargas,
Bodenhausen, & Paller 2015 *Science*

TMR Improved Face-Name Learning

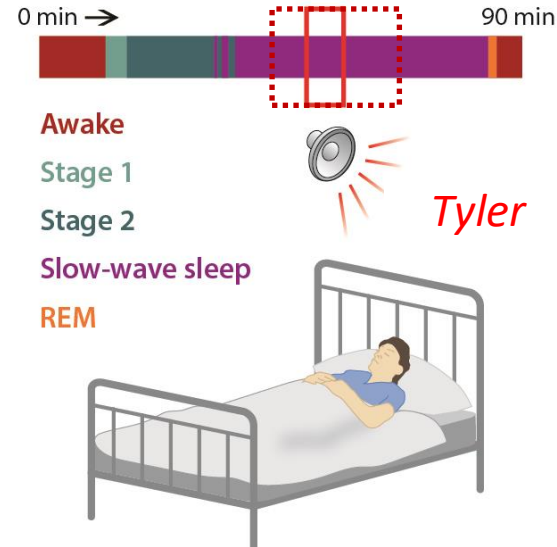
Nathan Whitmore et al 2022 *npj Sci Learning*



Participants try to learn the names of 80 people



Some names presented during sleep



Remembering is better for those names and faces

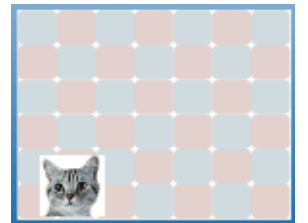


Whereas TMR improved recall, **reactivation with sleep disruption from the sounds was detrimental**

TMR with sounds intentionally too loud → impaired memory for 1-hour-old memories but not 1-week-old memories

Whitmore et al 2023 *Learning & Memory*

Whitmore, Yamazaki, & Paller, under review



TMR to change unwanted memories

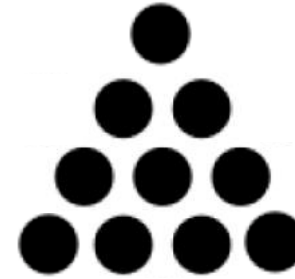
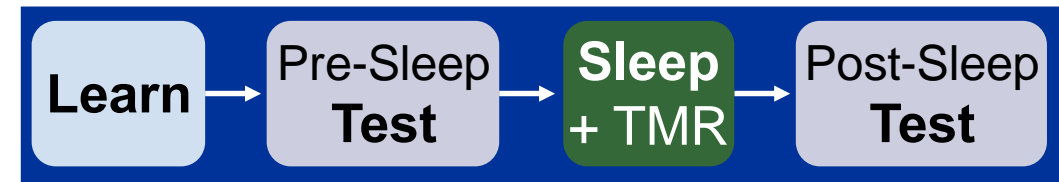
Xia et al 2023 *Current Biology*

Xia et al 2024 *PNAS*

TMR for Creative Problem-Solving



Kristin Sanders, Osburn, Paller, & Beeman
2019 *Psychological Science*



Slept at home with
wireless EEG
to monitor sleep
2 nights, $N = 57$



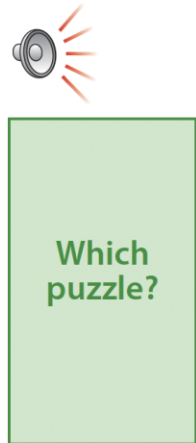
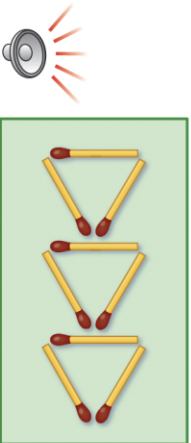
Pre-sleep

Participants fail to solve six puzzles,
each linked with a unique music track.

Evening session

Puzzles
presented
for solving

Sound-
puzzle
recall



2 min each

Three rounds
with feedback

Sleep

Music tracks during sleep cause
associated problems to receive
additional processing.

Overnight



Half of the sounds
play during SWS

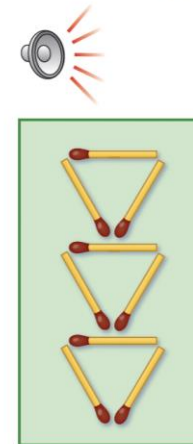
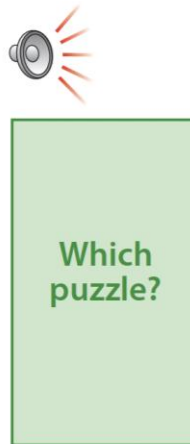
Post-sleep

Solutions are reached more often
for puzzles that were reactivated
during sleep.

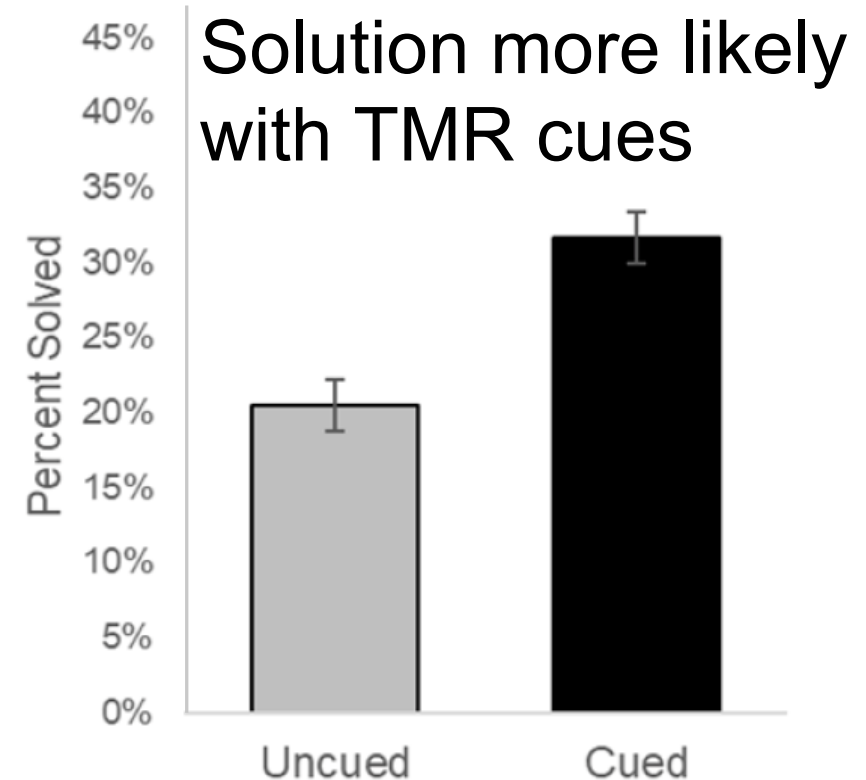
Morning session

Sound-
puzzle
recall

Puzzles
presented
for solving



4 min each

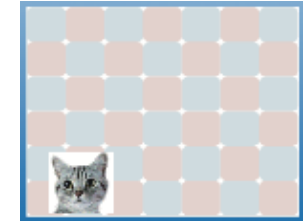


At-home TMR Procedures via Wearable Sleep Technology

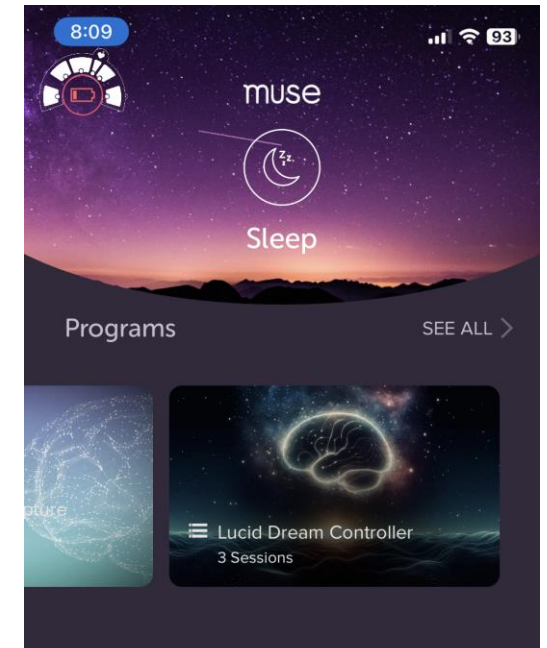
Automated at-home TMR improved spatial recall

- fitbit+smartphone with our own SWS algorithm
- verified with headband EEG

Whitmore et al 2022 J Sleep Research



Muse-S headband
Samsung Galaxy watch
Additional options...



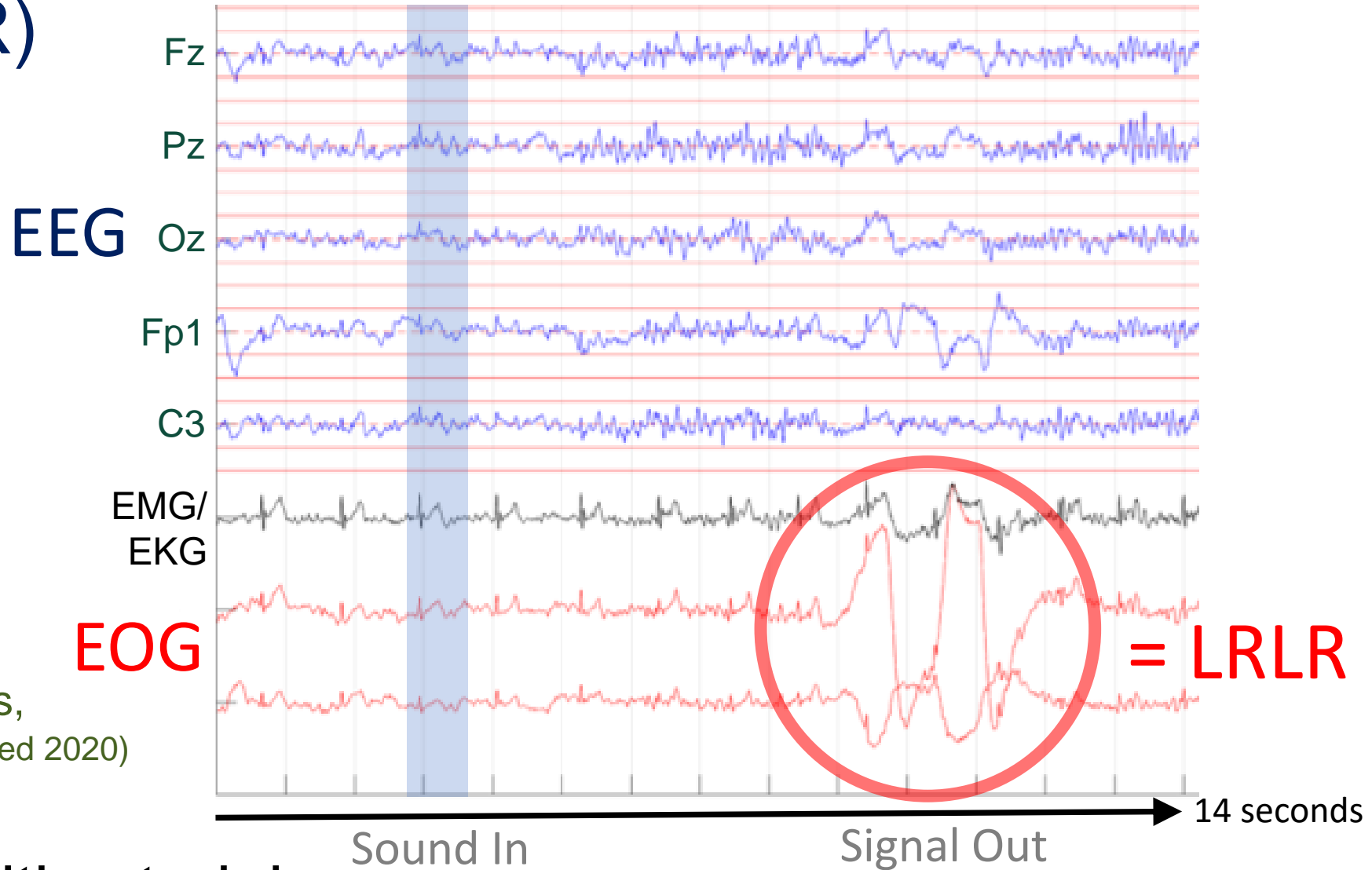
Targeted Lucidity Reactivation (TLR)

**Pre-sleep
training**
beeps → lucid

REM cues
soft beeps

- Carr, Konkoly, Mallett, Edwards, Appel, & Blagrove 2023 (accepted 2020)
- Konkoly et al. 2021

TMR to Provoke a Lucid Dream



Both pre-sleep cognitive training
and the same sounds during sleep

Real-Time Two-Way Communication during REM Sleep

Targeted
Lucidity
Reactivation

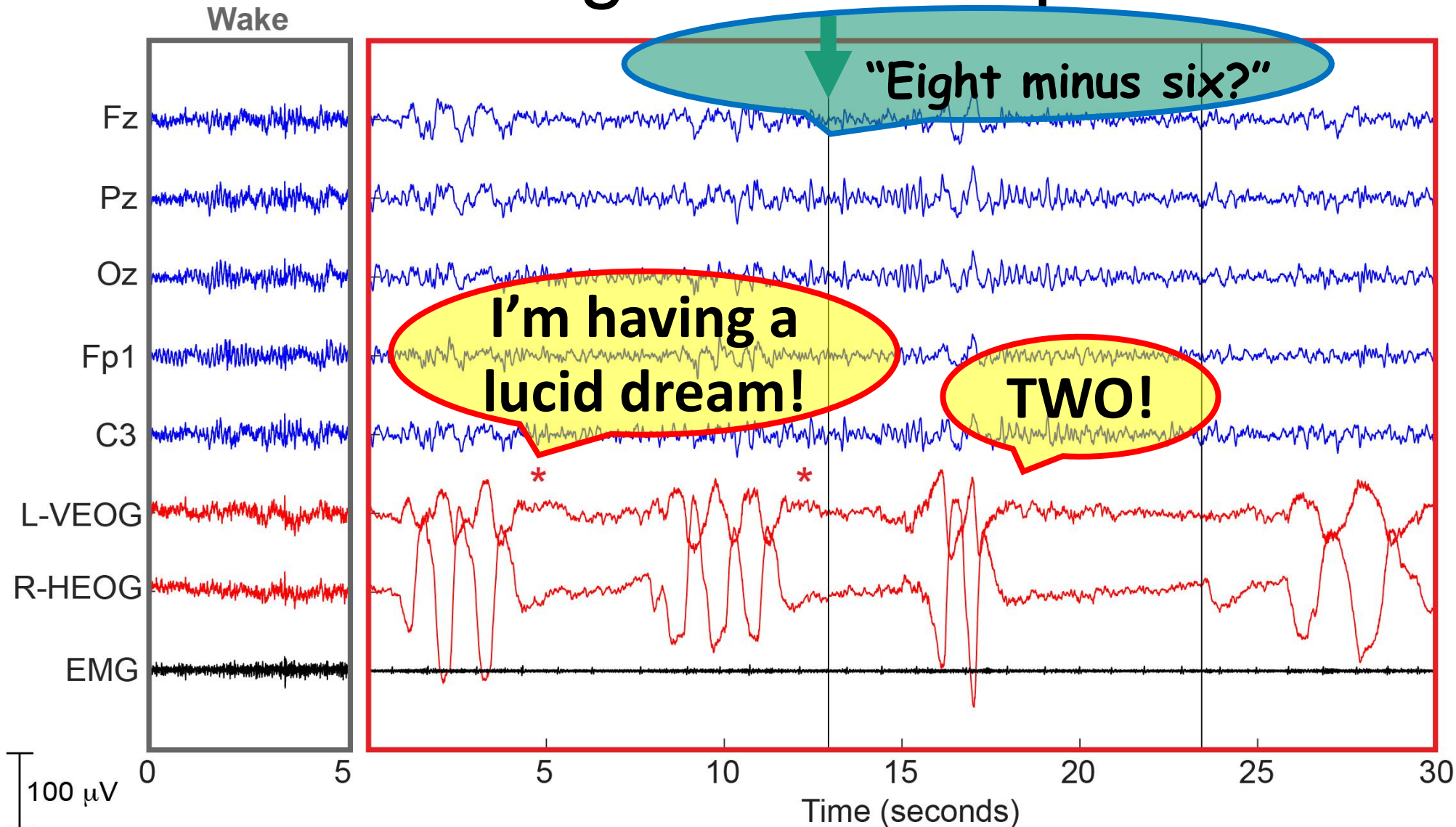
1st lucid dream
on night #1,
answered math
questions on
night #3



Karen Konkoly
et al. 2021

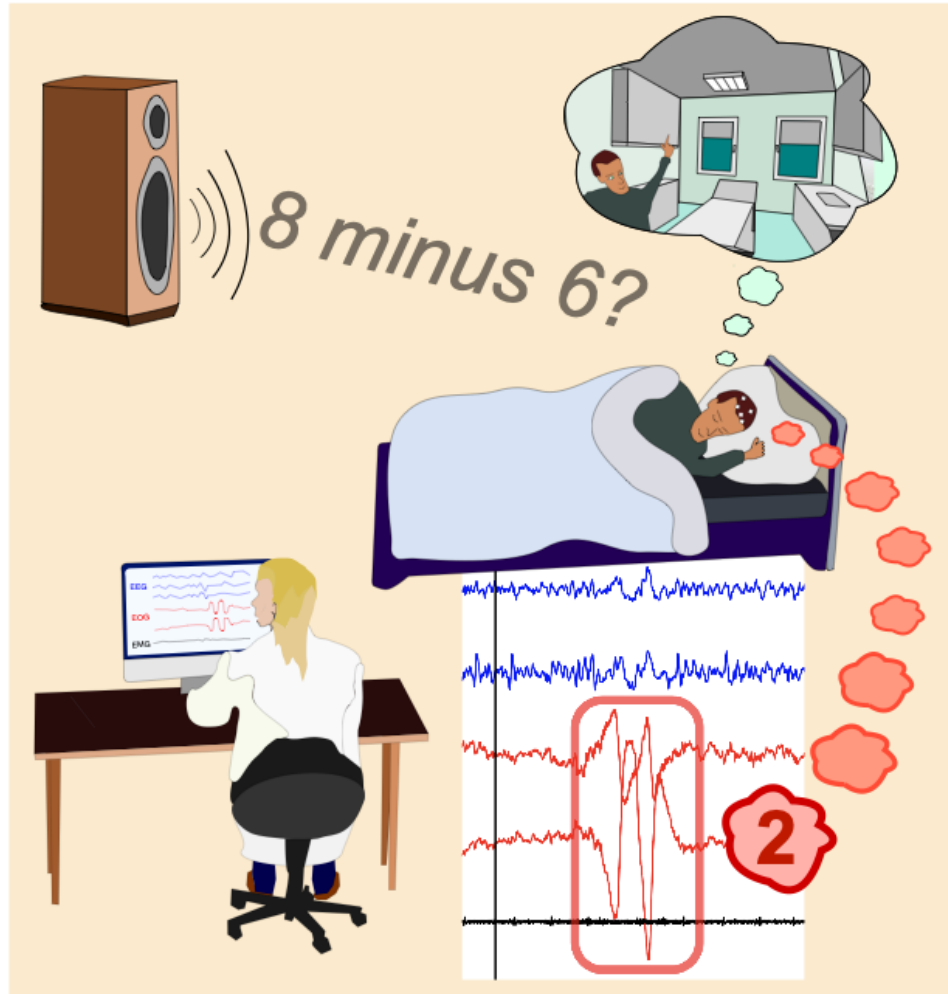
USA
Germany
France

The Netherlands



Real-Time Two-Way Communication during REM Sleep

Targeted
Lucidity
Reactivation



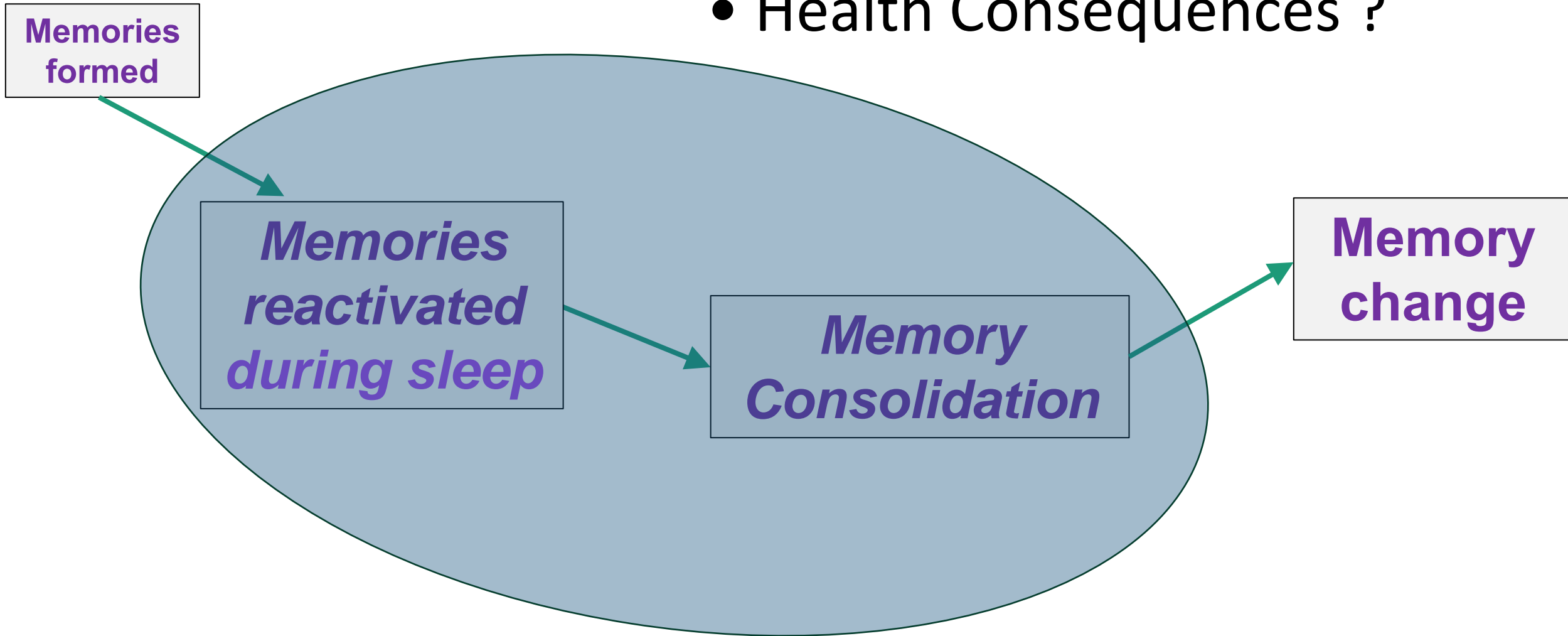
Communication signals allow dreamers to answer questions, perform tasks, and tell us about their dream experiences: **eye movements, muscle twitches, sniffs**

Konkoly, Appel, Chabani, Mangiaruga, Gott, Mallett, Caughran, Witkowski, Whitmore, Mazurek, Berent, Weber, Türker, Leu-Semenescu, Maranci, Pipa, Arnulf, Oudiette, Dresler, & Paller
2021 *Current Biology*



USA
Germany
France
The Netherlands

- Modifiable via TMR
- Health Consequences ?



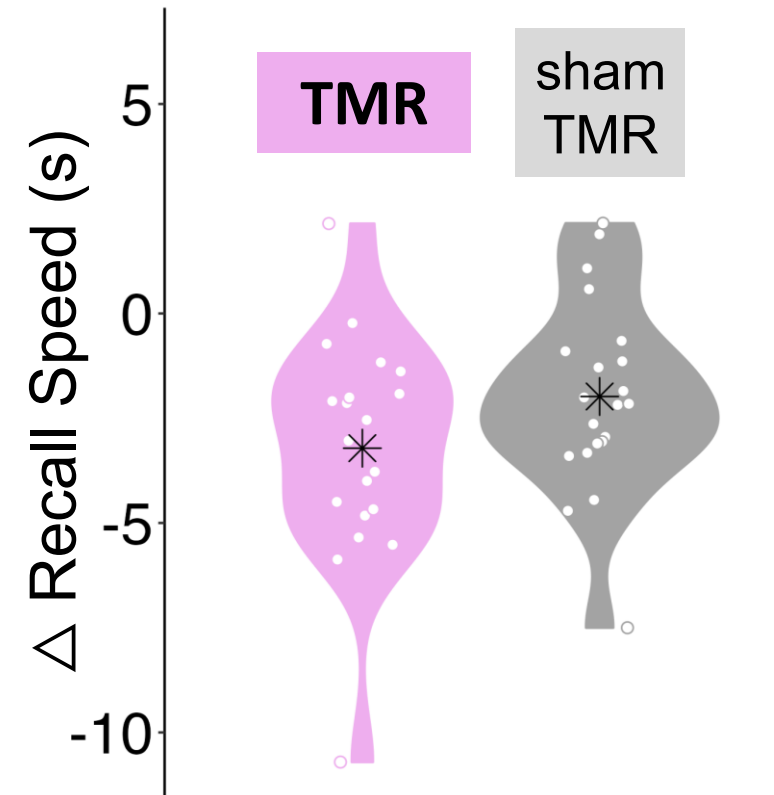
Potential Uses of TMR / Sleep Engineering

1) Improving memory, at home, with wearable sleep tech
– early stages of memory decline

- Healthy young participants learned 20 simulated family names, then over 1-3 nights: TMR at home ($n=20$) or sham TMR ($n=21$)

TMR produced faster cued recall
(Day 5 compared to Day-2 baseline)

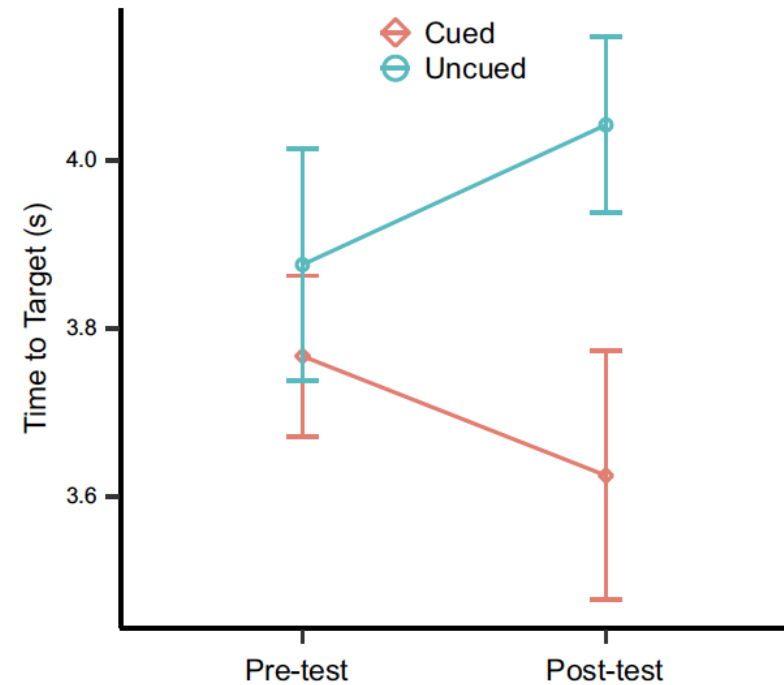
Erika Yamazaki, Whitmore, & Paller
manuscript in preparation (poster at CNS 2024)



Potential Uses of TMR / Sleep Engineering

- 1) Improving memory, at home, with wearable sleep tech
 - early stages of memory decline
 - improve therapies that entail some sort of learning

- TMR to enhance rehabilitation
 - motor-control rehab post-stroke **at home**
Marc Slutzky et al – work in progress
 - simulated in healthy participants in lab
Larry Cheng et al 2021 *J Neurosci*
- TMR to enhance
 - Imagery Rehearsal Therapy for nightmare
Sophie Schwartz et al 2022 *Current Biology*
 - Therapy for PTSD van der Heijden et al 2024 *Current Biology*



Potential Uses of TMR / Sleep Engineering

- 2) Improving sleep quality by helping people develop better
 - physical and mental sleep habits
- Biofeedback from polysomnography to help people develop better habits at sleep onset
- TMR to inject calm into sleep — based on a relaxation session or other procedures prior to sleep, then cues during SWS
 - collaborations with Remington Mallett, Jessica Payne
- TMR for sleep apnea — Erika Yamazaki **

Potential Uses of TMR / Sleep Engineering

3) Using lucid dreaming for various goals

- Creative problem-solving

Karen Konkoly et al 2024 PhD dissertation

- Contemplative practices during sleep (Tibetan Dream Yoga)

Gabriela Torres-Platas et al 2024 Society for Neuroscience

- To promote dream-lucidity and enhance CBT for nightmares

Jen Mundt ***

Ananth Acharya
James Antony
Adrianna Bassard
Laura Batterink
Mark Beeman
Galen Bodenhausen
Stephan Boehm
Donna Bridge
Bruce Caughran
Larry Cheng
Jessica Creery
Guillen Fernández
Susan Florczak
Brian Gonsalves
Jay Gottfried
Marcia Grabowecky
Daniela Grimaldi
Steve Hillyard
Motoyasu Honma
Rob Hurley
Xiaoqing Hu
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Karen Konkoly
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Sandy Weintraub
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Nathan Whitmore
Sadie Witkowski
Erika Yamazaki
Phyllis Zee
Rick Zinbarg

<http://kenpaller.com>

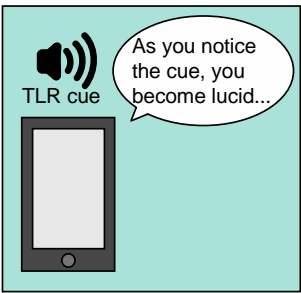
NIH / NINDS, NHLBI
National Science Foundation
Mind Science Foundation
Mind and Life Institute
Bial Foundation
Tiny Blue Dot Foundation
BrightFocus Foundation
Alzheimer's Association



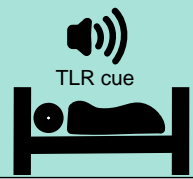
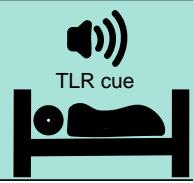
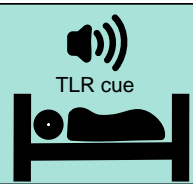
Using TLR to induce lucid dreams at home

Konkoly, Whitmore, Mallett,
Mazurek, & Paller,
under review

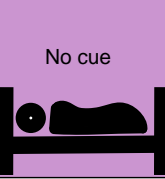
TLR training every evening



Nights 1, 3, 5 & 7



Nights 2, 4 & 6



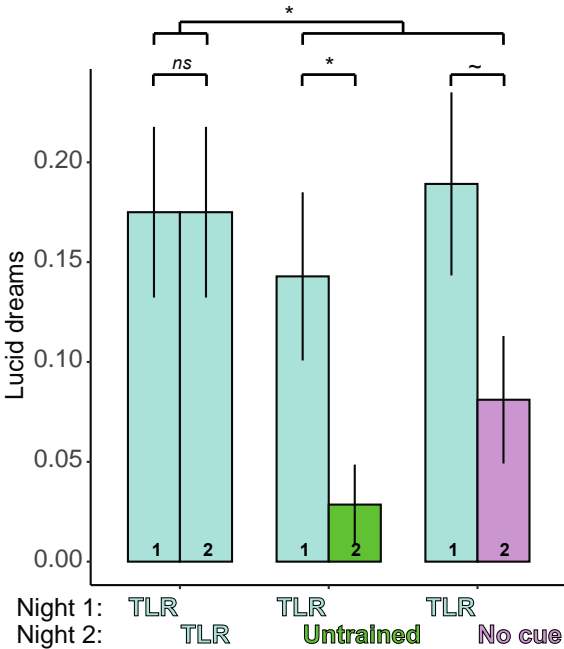
TLR-cue

Untrained-cue group

No-cue group

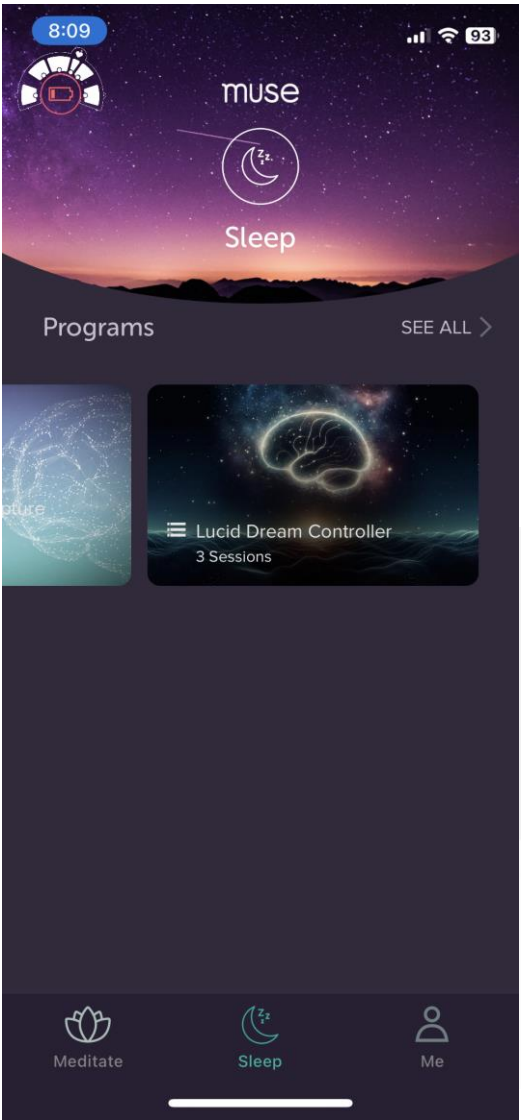
Overnight cue: 6-hour delay

N = 112



TMR at home:

- Honma et al., 2016 *Neurosci of Consciousness*;
- Sanders et al., 2019 *Psychological Science*;
- Whitmore et al., 2022 *J Sleep Research*

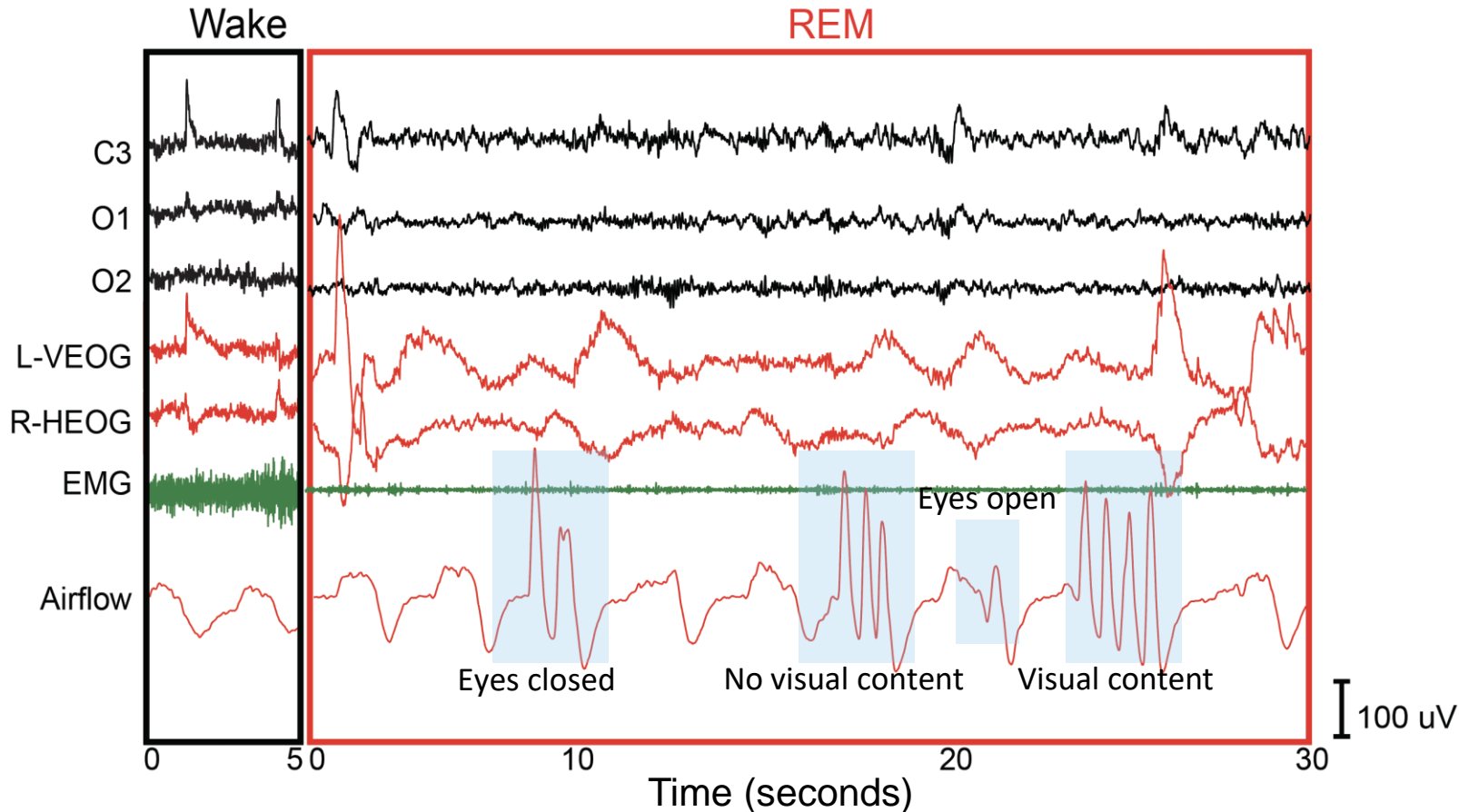


Muse-S



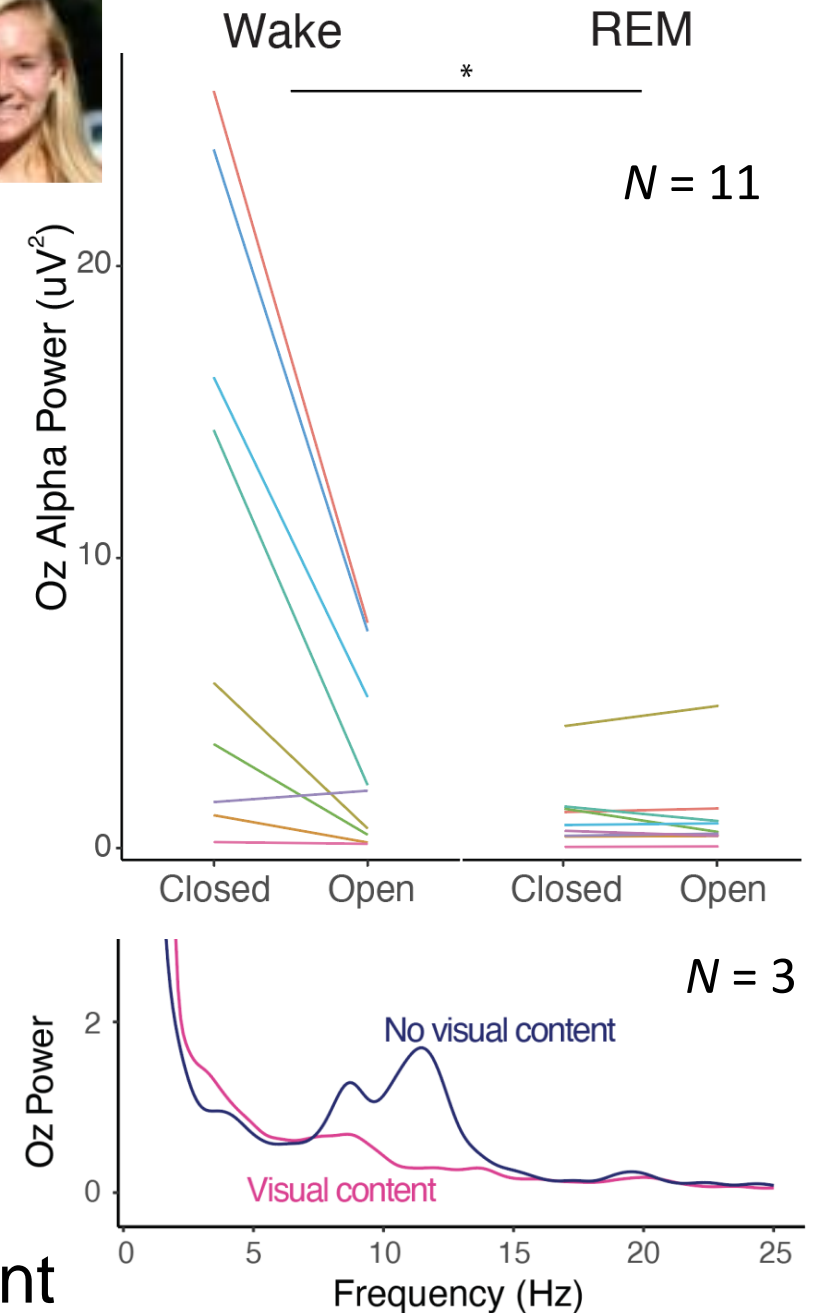
When you close your eyes in a dream...

Konkoly, Al-Youssef, Mazurek, Mallet, Morris, Gales, Arnulf, Oudiette, & Paller, unpublished



Close → visual content eliminated about half of the time

Alpha power increased only if visual content was absent





Cues during REM to promote creative problem-solving

Before sleep: puzzles until 4 unsolved

4am: Training for lucid-dream induction

REM sleep: TLR, cues for 2 puzzles

Morning: Attempt puzzles again

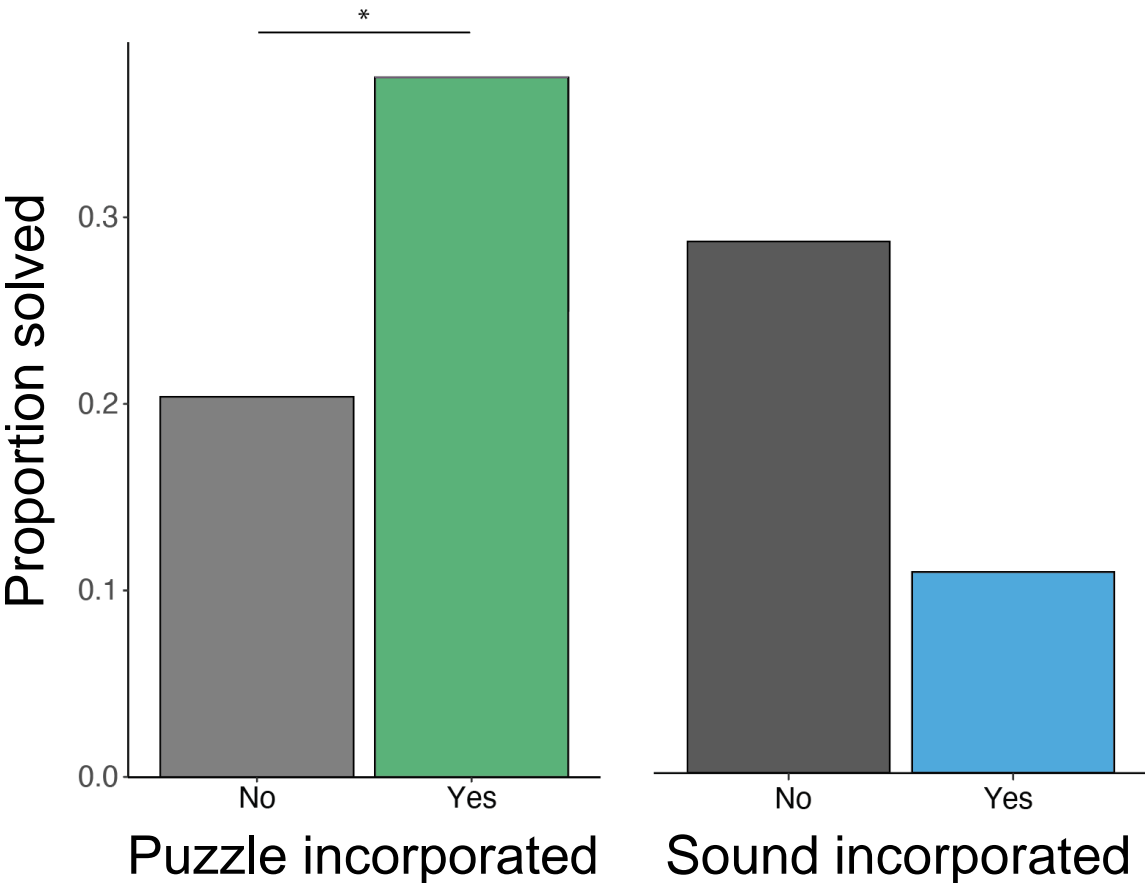
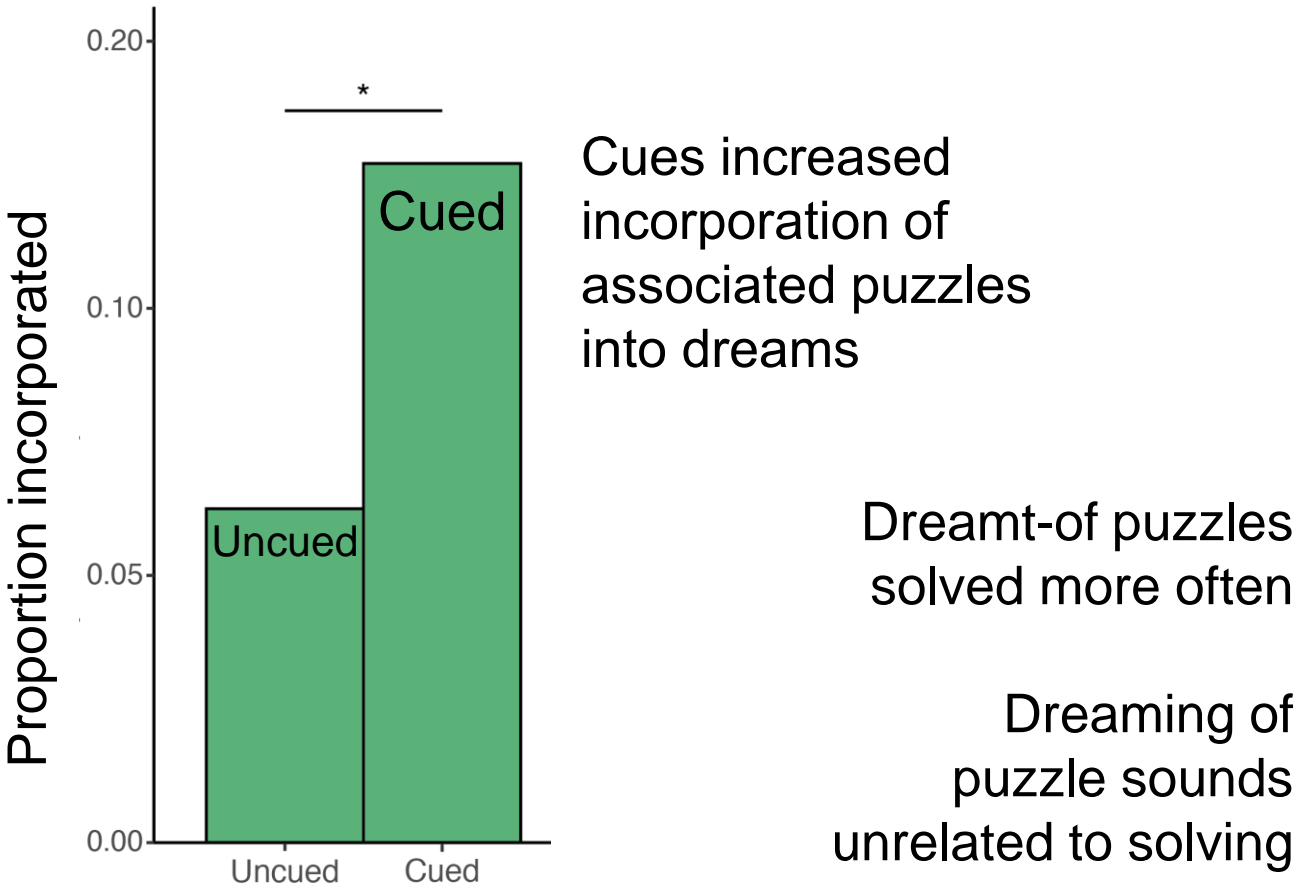
 

Trees

A landscaper is given instructions to plant 4 trees so each is exactly the same distance from each of the others. How is that done?

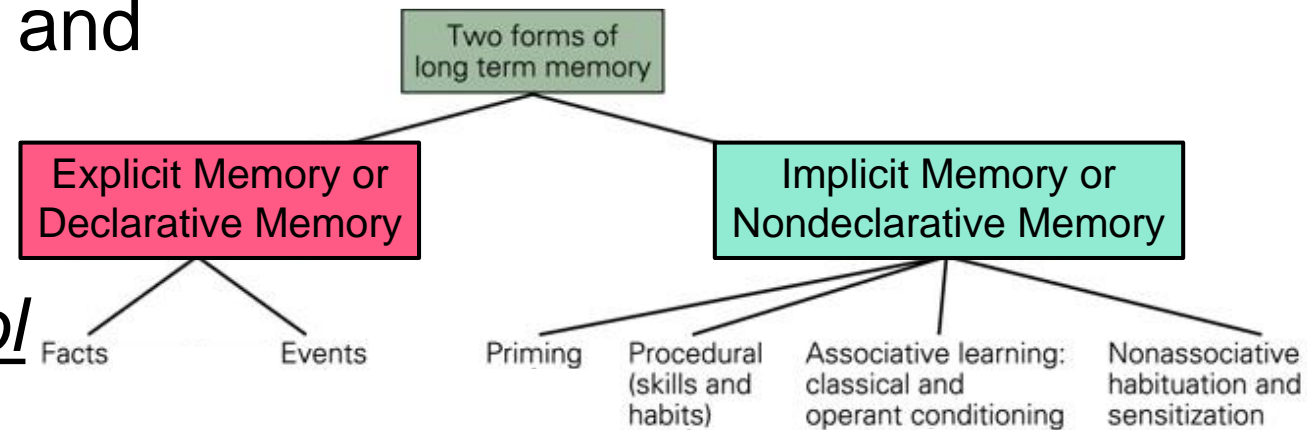
Konkoly, Morris,
Hurka, Sanders,
Beeman, & Paller

N = 20
two nights each



Sleep Quality: The Cognitive Dimension

- Memories are reactivated during sleep and during dreams and that reactivation influences what we remember later;
 - many types of memory *and* other aspects of cognition/emotion;
 - neurocognitive habits and well-being / *wake up on right side of bed*
- The nature of this reactivation, especially which memories we reactivate, is an important determiner of high-quality sleep
- Memory processing during sleep is not as easy to measure as standard metrics such as minutes of slow-wave sleep, but it can potentially be observed (>stress) and should be acknowledged as part of understanding sleep quality and sleep's pervasive repercussions
- Untrained minds wander all night habitually... but we can have control



*Scientific
American*

2018



*Frontiers
For Young
Minds*

2018



SLEEP LEARNING GETS REAL

Experimental techniques demonstrate how to
strengthen memories when our brains are offline

By Ken A. Paller and Delphine Oudiette

*Do House-Elves Clean Your Brain
While You Sleep?*

Sleep and Memory

- Research de-bunked by Simon & Emmons 1956
- 50-year dark ages for this research Oudiette & Paller 2013 *TICS*
- Theories... e.g., *Brain & Psyche* by Jonathan Winson 1984
- Hippocampal Replay: Matthew Wilson & Bruce McNaughton 1994
- REM sleep versus slow-wave sleep (SWS)
- Learning, then odor cue during sleep Rasch, Büch

