

# Sleep, Emotion, and Memory

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# Conflict of Interest Disclosures for Speakers

Mohan Dutt, MD has no relevant financial relationships with ineligible companies to disclose.

# Learning Objectives

After completing this lecture participants should be able to

- Discuss the role that sleep plays in emotional control
- Define the different types of emotional regulatory processes
- Define the different types of memories
- Understand the role that sleep plays in memory formation

# Agenda

## Emotions

1. Overview
2. Sleep's role in emotional regulation

1. Non-declarative

2. Emotional

## Dementia

## Memory

1. Overview
2. Declarative

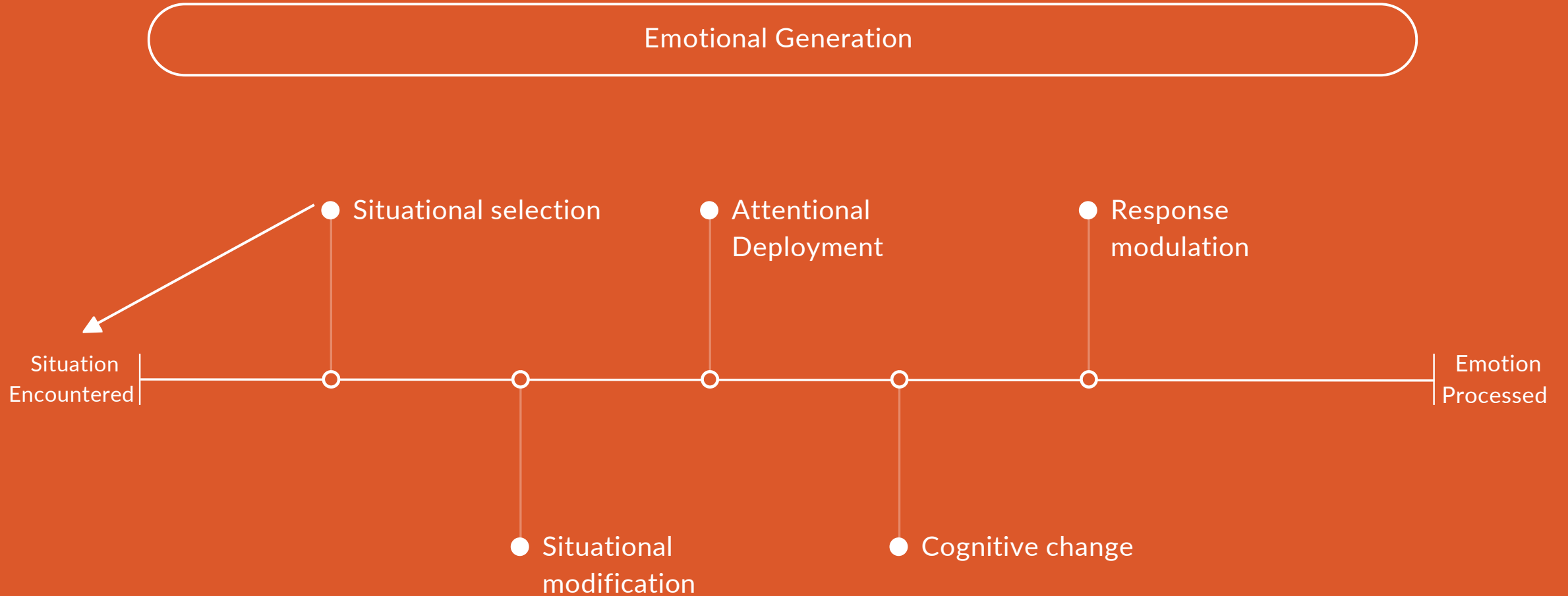
# Emotional Regulation



# Neurobiological process of emotional generation



# Process Model



# Role of sleep



## Studies

- Sleep deprived residents more likely to experience negative emotions
- Sleep deprived adults report worsening mood
- fMRI imaging demonstrates



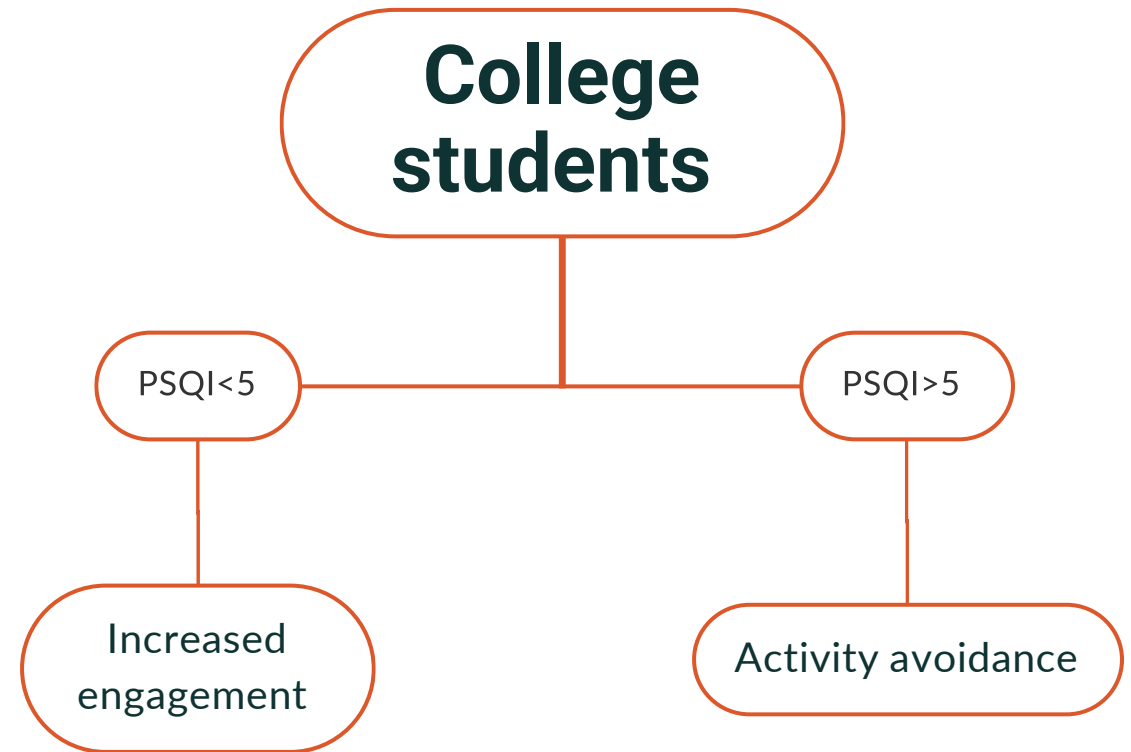
Amygdala Activity



Medial prefrontal  
cortex connectivity



# Situational avoidance



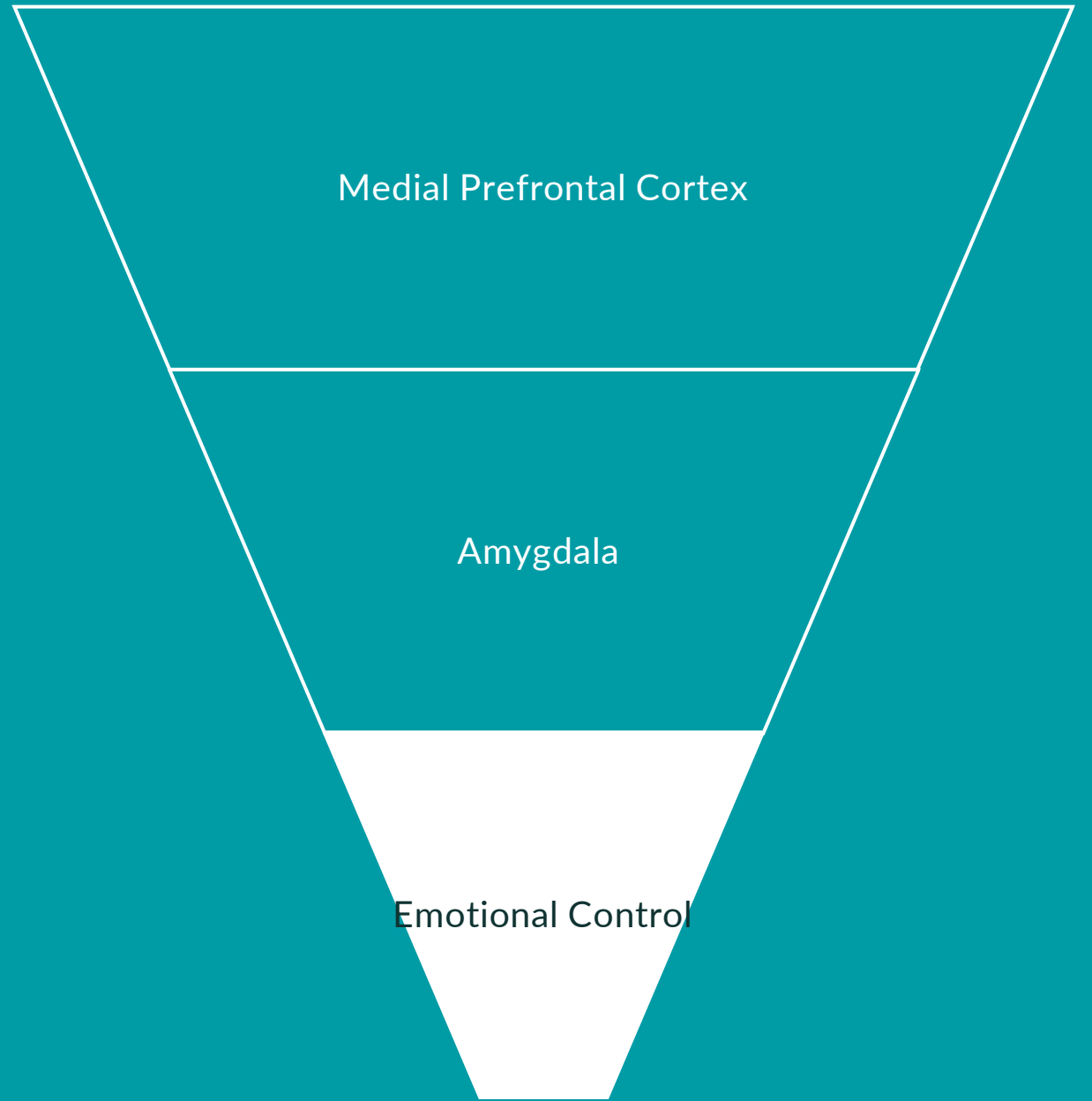
**Poor sleep leads to a likely misunderstanding of situation, and thus any response elicited in the situation is likely to be maladaptive**

## **Situational modification**

- **Studies**

- Married couples were more likely to experience increased conflict following a night of poor sleep (as measured by PSQI)
  - Poor sleepers demonstrated
    - Lack of empathetic accuracy
    - Inaccuracy in gauging partners emotions
- Poor sleep associated with difficulty in understanding non-verbal cues





# Cognitive Change

**Cognitive change, is the process by which an individual can change the meaning or appraisal of an emotionally generating stimulus**

## Meta-analysis

- In "normal" sleepers cognitive reappraisal activates prefrontal cortex, and modulates amygdala bilaterally.

## fMRI

- In shortened sleep individuals were less able to regulate emotions, however there was no findings of loss of prefrontal cortex to amygdala connectivity.

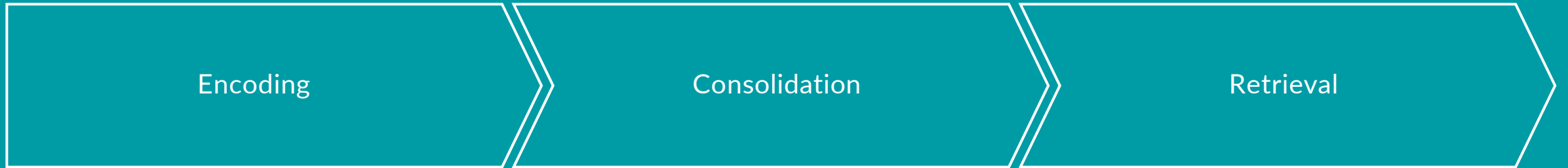
## Adolescents

- In a study of 13-17 year olds; 1 night of sleep loss did not demonstrate a loss of ability in using reappraisal in the face of negative stimuli.

# Summary

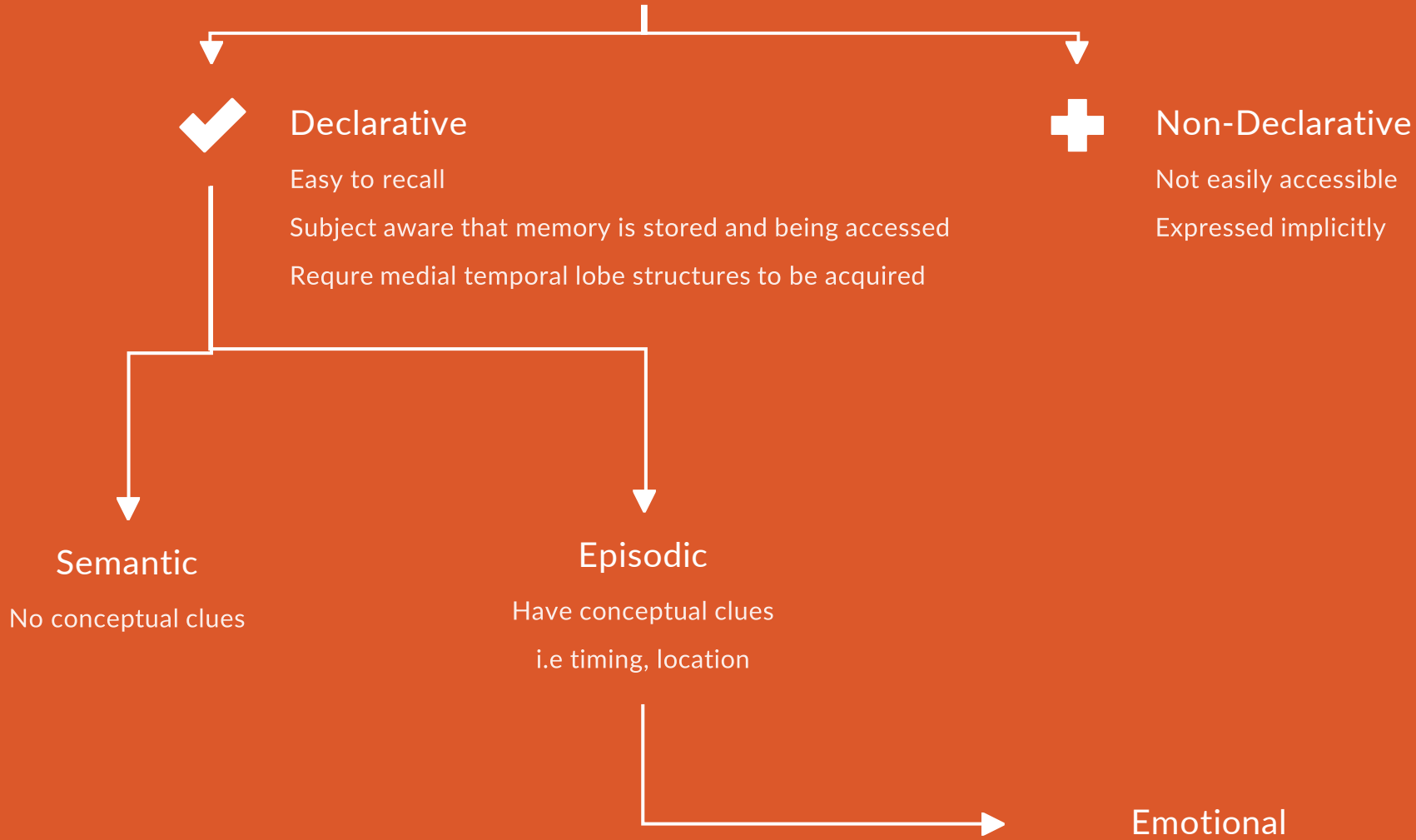
- Poor sleep is associated with inability to regulate emotions at all stages of the process
- Mechanism still not defined
- Loss of top down control of amygdala by prefrontal cortex
  - Not seen in fMRI studies

# Memory formation



*Consolidation is a sleep dependent process in which in which memory traces are strengthened, stabilized and integrated into pre-existing knowledge networks.*

☾ Memory



## Two stage memory formation

Proposed by David Marr in 1971

For declarative memories encoding occurs in the hippocampus, and then memories transferred to neo-cortex, which is a sleep dependent process.

For non-declarative memories storage locations vary based on the type of information being stored.







# Memory models

Defining the role of sleep in memory formation

## Dual process model

NREM sleep is for consolidation of declarative memories

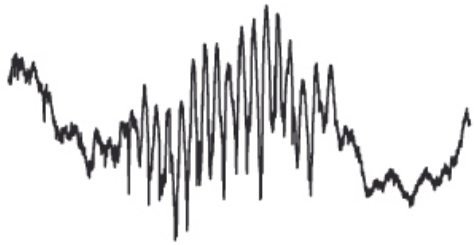
REM sleep is for consolidation of non-declarative memories

## Active system consolidation hypothesis

Theta waves encode memories during wakefulness

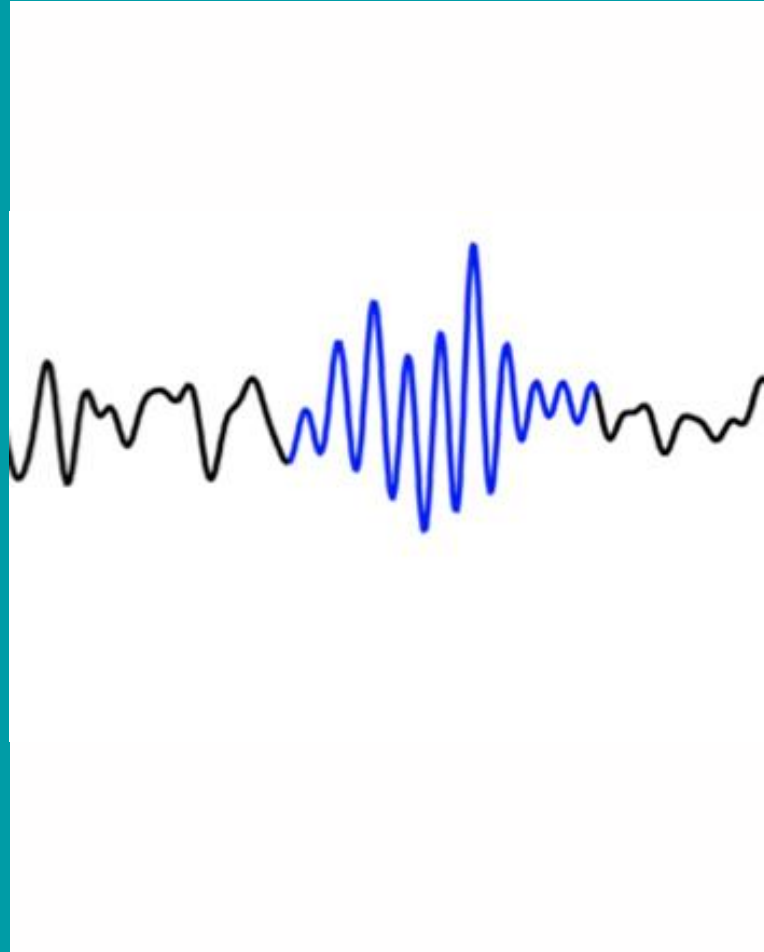
Hippocampal sharp wave ripples consolidate memories during sleep

# Wave forms

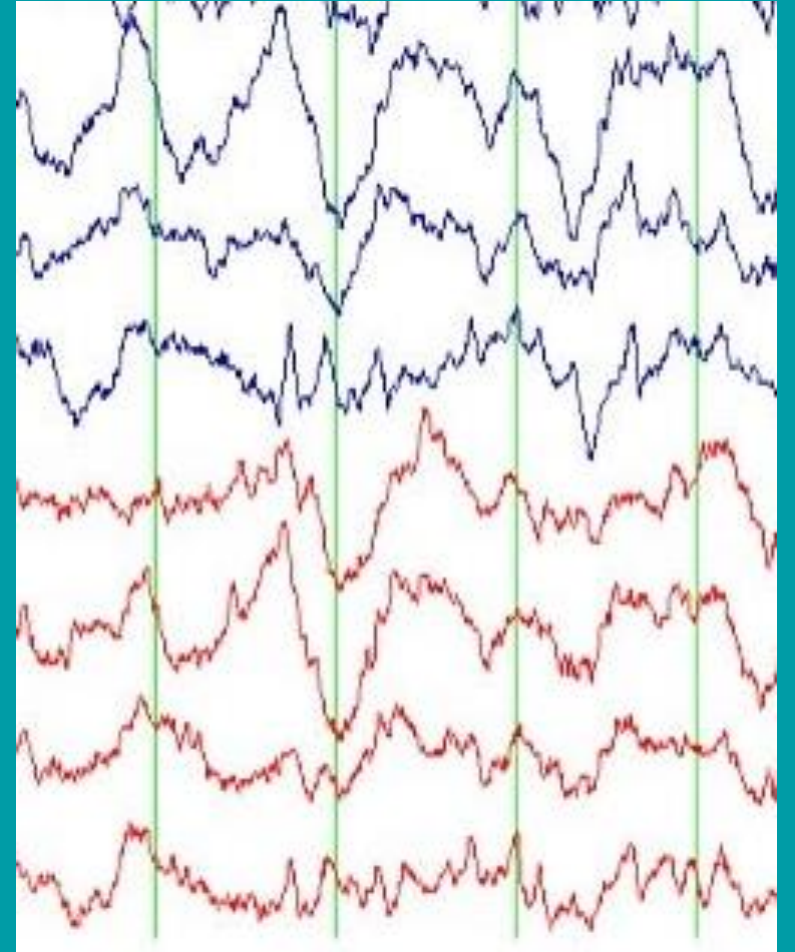


Short Sharp Wave Ripple  
in the Hippocampus

Hippocampal sharp wave ripple



Sleep Spindle



Delta wave

# Sleep and declarative memory

## Summary of studies

### Hippocampal memory activation

- Researchers compared participants with temporal lobe epilepsy and either bilateral or unilateral hippocampal sclerosis
- Episodic memories encoded using the aid of cueing
- Strengthening of memories seen only in control and unilateral sclerosis groups
- Hippocampal volume, and slow wave density during slow wave sleep was positively correlated to memory benefit.

### Interference

- Researchers used odor cues to entrain object location task
- Participants received the cue during wakefulness or SWS
- Task was repeated the following morning following an interference task
- Slow wave sleep was found to entrain memories independent of REM sleep

### Nap Study

Compared ability to recall object location following either a 40 minute vs 90 minute nap  
Participants who napped for 90 minutes had greater memory recall than those with 40 minutes of sleep  
Amount of slow wave sleep was positively correlated with memory performance  
Recall performance was independent of REM sleep

# Sleep and non-declarative memory

## Summary of studies

### REM suppressing agents

- Fluvoxamine and reboxetine administered prior to post training sleep of procedural memory tasks
- Investigators found that there was an increase in task performance
- Correlates with similar studies of MAO-I, studies with TCAs demonstrate deleterious effect on memory, suggesting a cholinergic process

### Slow wave sleep suppression

- Investigators slow wave sleep suppressing tone during post training sleep
- Task performance decreased compared to control
- Sleep spindles were seen to be increased in post test sleep

### Night - half paradigm

- Initial studies led to belief that REM sleep was necessary for storage of procedural memories
- Given data demonstrating importance of sleep spindles in formation of memories it is possible that late N2 and not REM is needed for strengthening of procedural memories

# Emotional Memories

***Episodic memories with an associated emotional valance attached to them***

- Emotional memories thought to be strengthened by activation of the amygdala.
- Increase in plasticity causes emotional memories to be stored for longer periods of time
- As they are episodic, they are thought to be under regulation of NREM sleep, however REM is also thought to play a role
  - Amygdala and limbic system active during REM sleep

# The role of sleep in emotional memories

## Summary of studies

### Sleep deprivation

- Participants subjected to total vs REM specific sleep deprivation
- Neutral and emotional memories deteriorated with total but not REM sleep deprivation

### Cueing

- Emotional memories cued during both NREM and REM sleep
- Cueing during NREM not REM was associated with strengthening of emotional memory
- Valence of emotion was associated with stronger memory response

**Sleep to remember,  
sleep to forget**

## The role of REM

- REM continues to be thought of as a key modulator of emotional experience
- Fear conditioning
- Studies demonstrate that sleep had a positive effect in discrimination between fearful and non-fearful stimuli
  - Magnitude of discrimination correlated with amount of REM sleep
  - Theta rhythm thought to be the carrier frequency for emotional memory encoding

REM sleep not only serves to consolidate and strengthen emotional memories, but that recurrent reactivations strip away the emotional context of the memory, so that only memory of the event remains.

# Altering sleep architecture

Can we improve memory?

## Auditory stimulation

Pink noise targeted to upstate phase of slow oscillation (closed loop) was shown to increase amplitude of SO's, power of spindles, and improvement in declarative memory tasks.

## Transcranial direct current stimulation (tDCS)

Studies demonstrate an increase in power of SO and delta frequency bands, conflicting effect on spindles.

Varied evidence for improvement in declarative memory, no evidence for improvement in procedural

Some evidence for improved memory in children with ADHD, and individuals with schizophrenia

## Pharmacological stimulation

Many studies demonstrated an increase in SWS with addition of medication

Oxybate, tiagabine, and IL-6 demonstrated possible positive effects on memory



**The worldwide prevalence is approximately 50 million people, with an estimates 10 million new cases per year.**

## **Dementia**

- 2018 Meta-review reviewing 18 longitudinal studies and 240000 subjects demonstrates
  - Sleep disturbances (all types) led to 1.19 higher chance to develop all-cause dementia.
  - Sleep disordered breathing was predictive risk factor for all cause dementia
  - Insomnia increased risk of Alzheimer's dementia
- 2021 study following short sleepers
  - Short sleepers in 50s, 60s, and 70s demonstrated 30% greater incidence of all cause dementia

# Sleep Disordered breathing

- Alzheimer's Dementia

In rat studies hypoxemia increased rates of amyloid beta plaques, and tau protein.

## Vascular dementia



# Summary

- There is still no governing therapy regarding sleep's role in memory formation
- Sleep is likely encoded in a two-step fashion
- The process of memory formation is primarily governed by NREM sleep
  - Spindles, SOs, SWS, SWR
- REM may function to lessen the emotional impact of emotional memories over time
- Sleep disturbances increase risk for all-cause dementia

# References

- Gross JJ. Emotion Regulation: Conceptual and Empirical Foundation. In: Gross JJ. Handbook of Emotion Regulation, Second Edition. New York, NY: The Guilford Press; 2013.
- Ochsner KN, Silvers JA, Buhle JT. Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences*. 2012;1251(1):E1-E24.
- Tempesta D, Soggi V, De Gennaro L, Ferrara M. Sleep and emotional processing. *Sleep Medicine Reviews*. 2018;40:183-195.
- Zohar D, Tzischinsky O, Epstein R, Lavie P. The Effects of Sleep Loss on Medical Residents' Emotional Reactions to Work Events: a Cognitive-Energy Model. *Sleep*. 2005;28(1):47-54.
- Dinges DF, Pack F, Williams K, et al. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4-5 hours per night. *Sleep*. 1997;20(4):267-277.
- Yoo S-S, Gujar N, Hu P, Jolesz FA, Walker MP. The human emotional brain without sleep — a prefrontal amygdala disconnect. *Current Biology*. 2007;17(20):R877-R878.
- Sotres-Bayon F, Bush DE, LeDoux JE. Emotional perseveration: an update on prefrontal-amygdala interactions in fear extinction. *Learn Mem*. 2004;11(5):525-535.
- Franzen PL, Buysse DJ, Dahl RE, Thompson W, Siegle GJ. Sleep deprivation alters pupillary reactivity to emotional stimuli in healthy young adults. *Biological Psychology*. 2009;80(3):300-305.
- Fairholme CP, Manber R. Sleep, Emotions, and Emotion Regulation. *Sleep and Affect*: Elsevier; 2015.
- Palmer CA, Alfano CA. Sleep and emotion regulation: An organizing, integrative review. *Sleep Medicine Reviews*. 2017;31:6-16.
- Carney CE, Edinger JD, Meyer B, Lindman L, Istre T. Daily activities and sleep quality in college students. *Chronobiol Int*. 2006;23(3):623-637.
- Gordon AM, Chen S. The Role of Sleep in Interpersonal Conflict. *Social Psychological and Personality Science*. 2014;5(2):168-175.
- Ferri J, Schmidt J, Hajcak G, Canli T. Neural correlates of attentional deployment within unpleasant pictures. *NeuroImage*. 2013;70:268-277.
- Buhle JT, Silvers JA, Wager TD, et al. Cognitive Reappraisal of Emotion: A Meta-Analysis of Human Neuroimaging Studies. *Cerebral Cortex*. 2014;24(11):2981-2990.
- Tamm S, Nilsson G, Schwarz J, et al. Sleep restriction caused impaired emotional regulation without detectable brain activation changes—a functional magnetic resonance imaging study. *Royal Society Open Science*. 2019;6(3):181704.
- Reddy R, Palmer CA, Jackson C, Farris SG, Alfano CA. Impact of sleep restriction versus idealized sleep on emotional experience, reactivity and regulation in healthy adolescents. *Journal of Sleep Research*. 2017;26(4):516-525.
- Zhang J, Lau EYY, Hsiao JH-W. Using emotion regulation strategies after sleep deprivation: ERP and behavioral findings. *Cognitive, Affective, & Behavioral Neuroscience*. 2019;19(2):283-295.
- Squire LR, Zola SM. Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Sciences*. 1996;93(24):13515-13522.
- Rasch B, Born J. About sleep's role in memory. *Physiological reviews*. 2013;93(2):681-766.
- Ackermann S, Rasch B. Differential effects of non-REM and REM sleep on memory consolidation? *Curr Neurol Neurosci Rep*. 2014;14(2):430.
- Damien L, Eden D, Arnaud R, Virginie B, Karim B, Mounir C. Slow-wave sleep: From the cell to the clinic. *Sleep Medicine Reviews*. 2018;41:113-132.
- Roneil GM, Phyllis CZ. Brain Stimulation for Improving Sleep and Memory. *Sleep Medicine Clinics*. 2020;15(1):101-115.

# References Continued

- Peigneux P, Fogel S, Smith C. Chapter 22 - Memory Processing in Relation to Sleep. In: Kryger M, Roth T, Dement WC. Principles and Practice of Sleep Medicine (Sixth Edition): Elsevier; 2017.
- Susanne D, Simon B, Björn R, Jan B. Offline consolidation of memory varies with time in slow wave sleep and can be accelerated by cuing memory reactivations. *Neurobiology of Learning and Memory*. 2012;98(2):100-111.
- Fuentemilla L, Miró J, Ripollés P, et al. Hippocampus-Dependent Strengthening of Targeted Memories via Reactivation during Sleep in Humans. *Current Biology*. 2013;23(18):1769-1775.
- Diekelmann S, Büchel C, Born J, Rasch B. Labile or stable: opposing consequences for memory when reactivated during waking and sleep. *Nature Neuroscience*. 2011;14(3):381-386.
- Rasch B, Pommer J, Diekelmann S, Born J. Pharmacological REM sleep suppression paradoxically improves rather than impairs skill memory. *Nat Neurosci*. 2009;12(4):396-397.
- Vertes RP, Eastman KE. The case against memory consolidation in REM sleep. *Behav Brain Sci*. 2000;23(6):867-876; discussion 904-1121.
- Landsness EC, Crupi D, Hulse BK, et al. Sleep-dependent improvement in visuomotor learning: a causal role for slow waves. *Sleep*. 2009;32(10):1273-1284.
- McGaugh JL. The amygdala modulates the consolidation of memories of emotionally arousing experiences. *Annu Rev Neurosci*. 2004;27:1-28.
- Lehmann M, Schreiner T, Seifritz E, Rasch B. Emotional arousal modulates oscillatory correlates of targeted memory reactivation during NREM, but not REM sleep. *Scientific Reports*. 2016;6(1):39229.
- Kaida K, Niki K, Born J. Role of sleep for encoding of emotional memory. *Neurobiology of Learning and Memory*. 2015;121:72-79.
- Goldstein AN, Walker MP. The Role of Sleep in Emotional Brain Function. *Annual Review of Clinical Psychology*. 2014;10(1):679-708
- Menz MM, Rihm JS, Salari N, et al. The role of sleep and sleep deprivation in consolidating fear memories. *NeuroImage*. 2013;75:87-96
- Zhang Y, Gruber R. Can Slow-Wave Sleep Enhancement Improve Memory? A Review of Current Approaches and Cognitive Outcomes. *Yale J Biol Med*. 2019;92(1):63-80
- Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: A systematic review and metaanalysis. *Alzheimer's & Dementia*. 2013;9(1):63-75.e62
- Shi L, Chen S-J, Ma M-Y, et al. Sleep disturbances increase the risk of dementia: A systematic review and meta-analysis. *Sleep Medicine Reviews*. 2018;40:4-16.
- Li L, Zhang X, Yang D, Luo G, Chen S, Le W. Hypoxia increases A $\beta$  generation by altering  $\beta$ - and  $\gamma$ -cleavage of APP. *Neurobiology of Aging*. 2009;30(7):1091-1098.