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Memory Reconsolidation, Emotional Arousal and the Neuroscience of Enduring Change: Implications for Psychoanalysis

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Lecture #4
Sleep, Napping, Dreaming and Memory Reconsolidation

- Role of sleep in memory-emotion interactions
  - Sleep enhances memory
  - Sleep preferentially enhances emotional memory
  - REM sleep (re)consolidates emotional memories
  - Most dreams occur during REM
- Dreams: Freud and Post-Freudian Dream Theory
- Dreams: A possible outcome variable in psychoanalysis
- Other ways of making clinical use of sleep-related memory reconsolidation

Functions of Sleep

- Development and learning (especially REM)
- Energy conservation
- Brain waste clearance
- Modulation of immune responses
- Cognition
- Performance
- Vigilance
- Psychological state

Zielinski, M. R., McKenna, J. T., & McCarley, R. W. (2016). Functions and mechanisms of sleep. *AIMS neuroscience*, *3*(1), 67.

Synaptic Homeostasis Hypothesis of Sleep

- Sleep selectively attenuates synaptic strength between neurons, ridding the brain of unimportant information
- Re-establishing energy reserves
- Attenuation of cellular stress
- Conclusion: Main functions of sleep are
  - energy reserve restoration
  - re-sculpting the synaptic landscape

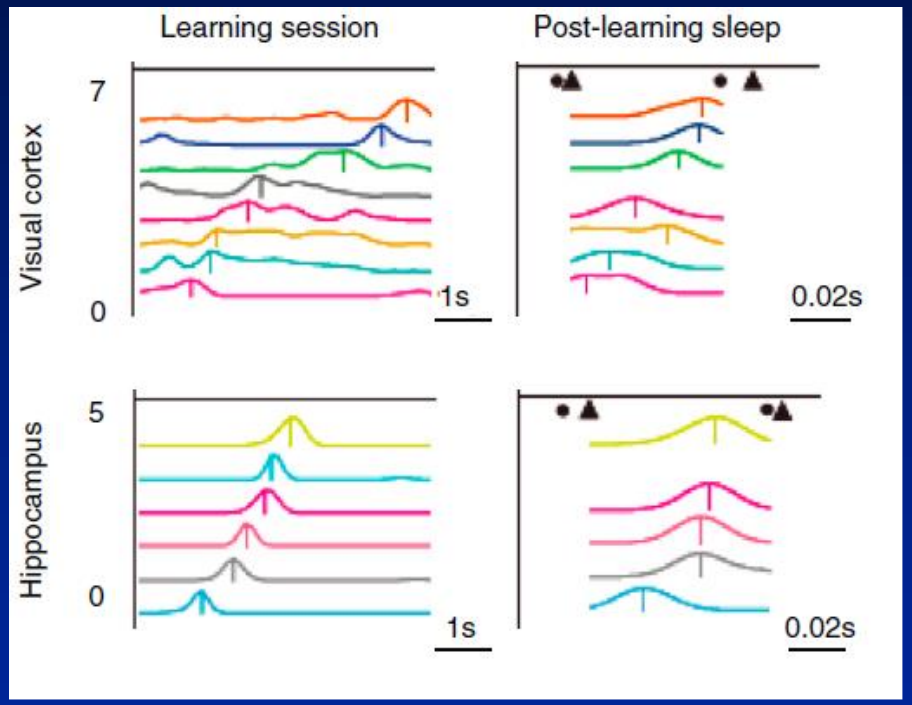
  (figuring out what information to keep and what to discard when intake of new information is suspended – due to sleep)

Tononi, G., & Cirelli, C. (2006). Sleep function and synaptic homeostasis. *Sleep medicine reviews*, *10*(1), 49-62.

Sources of Evidence That Sleep Enhances Memory

- Napping
- Sleep deprivation
- Memory improvement
  - sleep physiology and neuroimaging
- Direct current brain stimulation
- Cellular firing patterns in rodents
- Synaptic and intracellular measures of plasticity

Replay of Memory During Sleep: Hippocampal Place Cells in Rats



Multiunit firing sequences during NREM sleep (right panels) demonstrating recapitulation of firing patterns observed during prior learning (left panels) in both the cortex (upper row) and hippocampus (lower row) cells.

Memory Replay During Sleep Is Complex

- Replay during sleep is a mechanism by which the memory trace is rehearsed and transferred to neocortical areas
- Since the 1990s replay during sleep has been considered important in memory consolidation & integration
- Replay is now understood to be more complex
  - happens while awake
  - can play out in reverse order
  - may represent trajectories never taken
  - may participate in decision-making and planning
- Replay remains a very active area of current research

Findlay G, Tononi G, Cirelli C. The evolving view of replay and its functions in wake and sleep. Sleep Advances. 2020;1(1):zpab002.

Sleep-dependent memory triage: evolving generalization through selective processing

Robert Stickgold[1] & Matthew P Walker[2]

- Highlights discriminatory incorporation of initially pluripotent memories based on salience, e.g. emotion, reward
- Triages memories to several different pathways
  - item learning and unlearning
  - item integration
  - multi-item generalization
- The end goal is building and updating generalized knowledge and beliefs about the particular world in which a given person lives

Stickgold, R., & Walker, M. P. (2013). Sleep-dependent memory triage: evolving generalization through selective processing. *Nature neuroscience*, *16*(2), 139-145.

Information Maintenance and Triage During Sleep

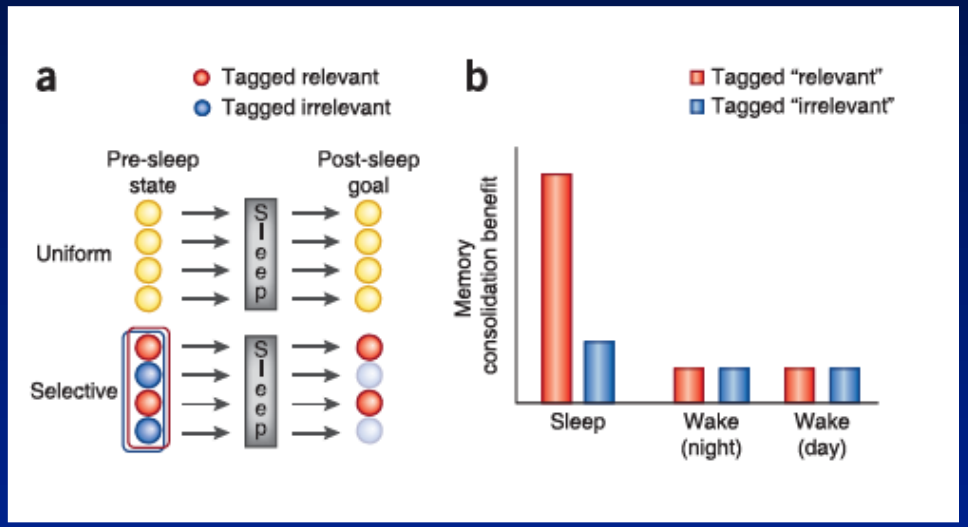


Figure 1 Selective memory consolidation. (**a**) Conceptual difference between uniform consolidation (top) and selective consolidation (bottom). In the latter, sleep returns discriminative offline memory retention, the selection of which is governed by instructional cues of relevance (red) and non-relevance (blue) created in the peri-encoding wake period. (**b**) Conceptual outcome of selective consolidation after sleep and an equivalent time awake (across night or day) following differential tagged relevance at initial encoding.

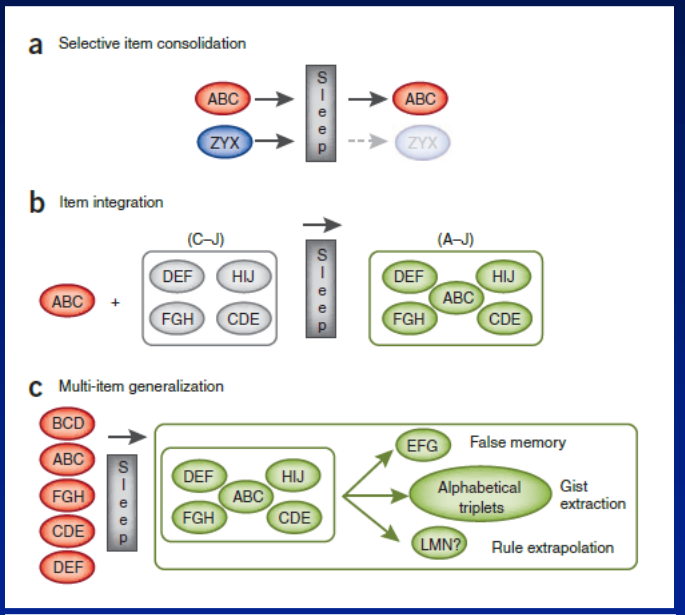


Figure 2 Forms of memory evolution. Categories of offline memory processing. All of these forms of offline memory processing have been shown to occur preferentially during sleep. (**a**) Item consolidation. Individual item-memories can be stabilized and/or enhanced, or they can be forgotten. (**b**) Item integration. Individual new item memories can be integrated into existing associative memory networks, extending the range of the network and enriching the information associated with the new item memory. (**c**) Multi-item generalization. Related item-memories encoded over a brief time interval can generate a new memory network and conceptual schema.

Stickgold, R., & Walker, M. P. (2013). Sleep-dependent memory triage: evolving generalization through selective processing. *Nature neuroscience*, *16*(2), 139-145.

Conclusions Regarding Mechanisms of Sleep-Enhanced Memory

- Memory systems are reorganized during sleep into consistent patterns (schemas)
- This reorganization involves integrating the new with the old, reminiscent of reconsolidation
- This suggests but doesn't prove that old memories are updated
- Sleep preferentially selects what is relevant to a person
- That's what emotion is – a system for determining personal relevance and responding as needed
- Conclusion: the way the brain sorts and saves information during sleep roughly approximates the proposed mechanism for enduring change in psychotherapy

Sleep and Memory: Neutral, Emotion and Their Trade-Off

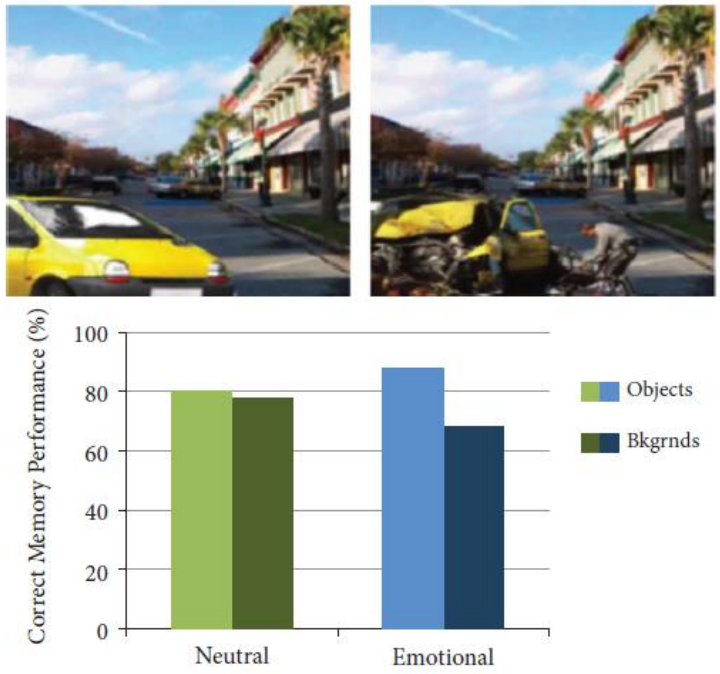


Figure 7.1 Example experimental stimuli (top) and graphical depiction of the trade-off effect as percentage of neutral versus emotionally arousing objects and backgrounds recognized (bottom). Stimuli depicting neutral backgrounds with either a neutral (top left) or negatively arousing (top right) object in the foreground were presented. Participants show increased recognition of emotionally arousing foreground objects with impaired recognition of neutral backgrounds (bkg).

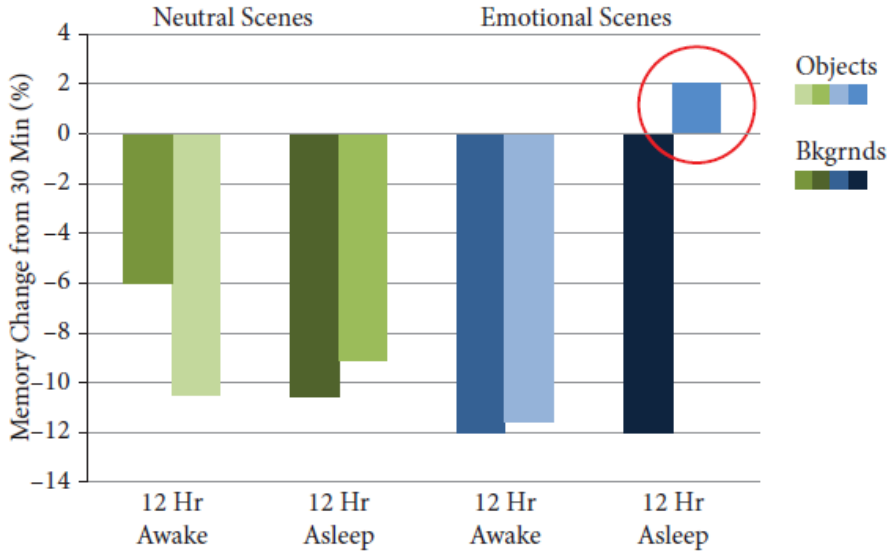
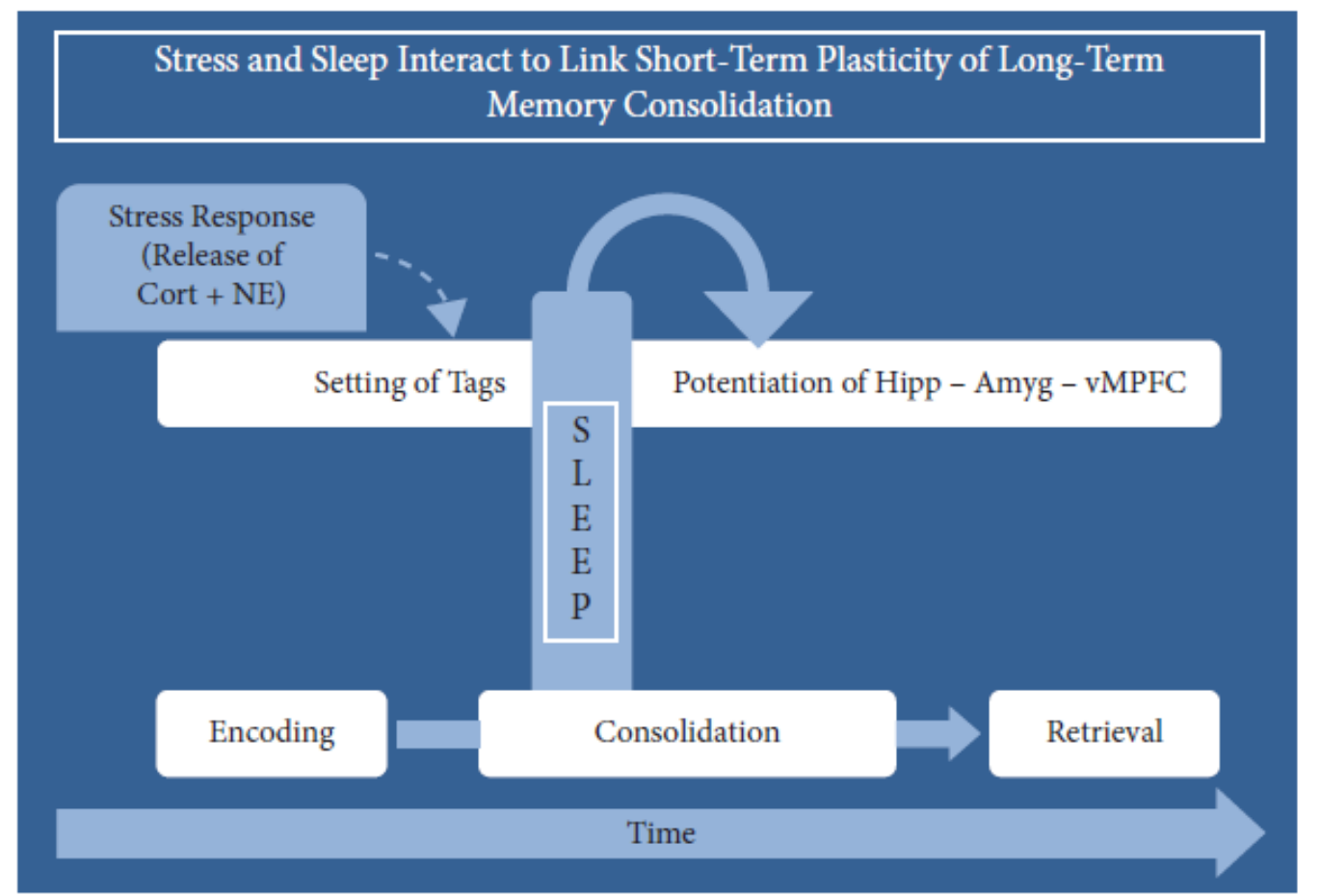


Figure 7.2 Change in recognition memory for neutral and emotionally arousing objects and their associated (neutral) backgrounds after periods of wake versus sleep. Recognition memory for neutral objects and backgrounds (bkg) decreased from 30 minutes posttraining by 6% to 12% across either 12 daytime hours of wakefulness (9 AM to 9 PM) or 12 nighttime hours (9 PM to 9 AM) that included a full night of sleep (minimum of 6 hours of documented sleep time within this time window). Thus, all forms of memory decrease, except for memory for negative emotional objects, which *improved* by 2% over a night of sleep (circled green bar, right).

Two-Step Process: Tagging (cortisol, NE) Followed By Consolidation During Sleep

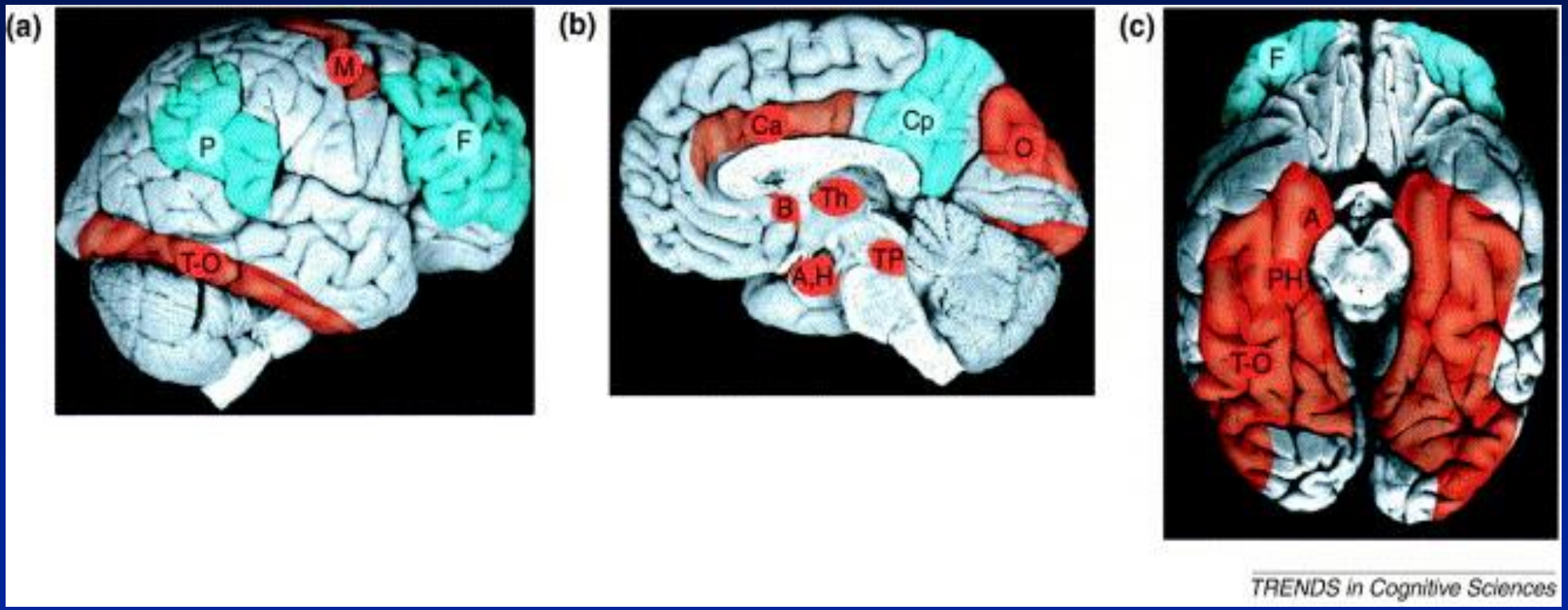


Role of NE in the Consolidation of Emotional Memories

- Neuronal metabolism, transcription and translation processes are activated by NE, thus providing tagged synapses with the proteins required to reinforce and prolong a change in synaptic efficiency
- These arousal-related neuromodulators enhance connectivity within critical emotional memory circuits (amygdala, hippocampus and prefrontal cortex)
- As such, they provide a cellular mechanism for network-level changes

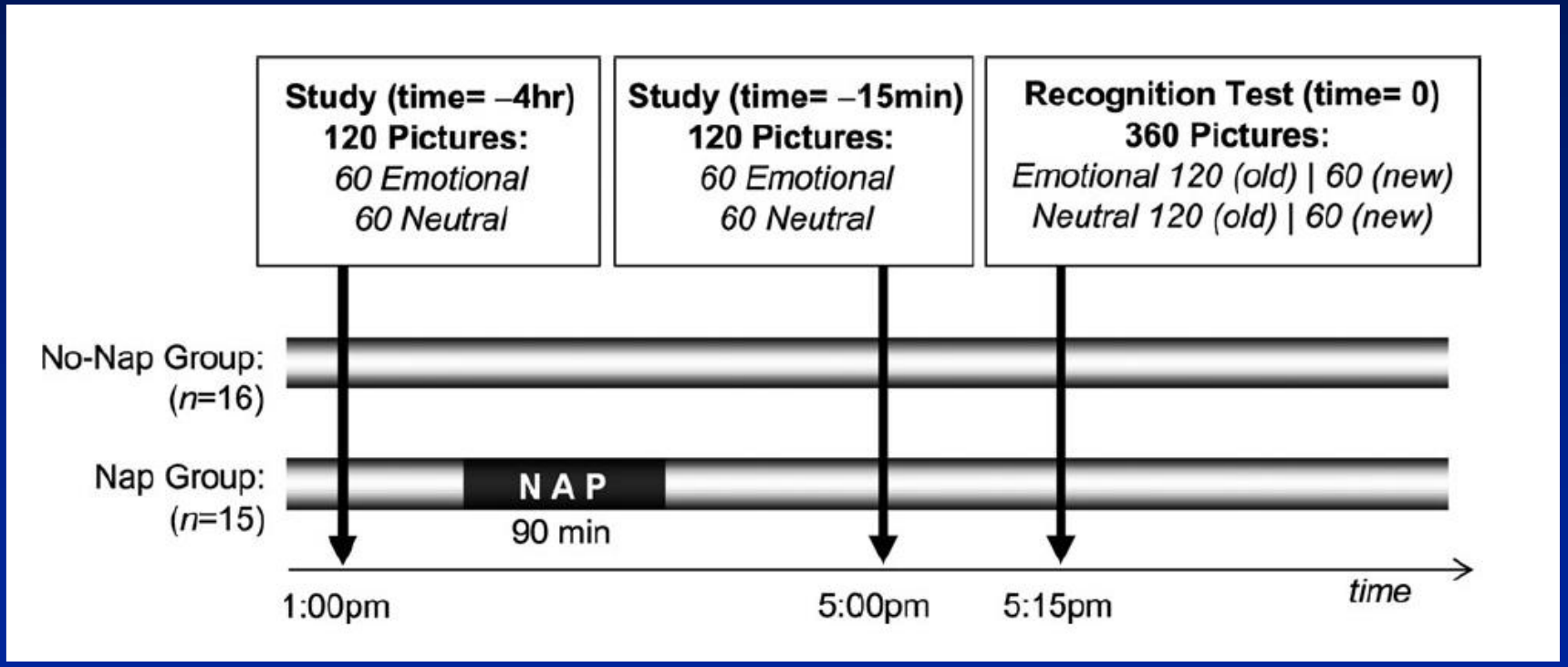
Payne, J. D. (2020). Stress and sleep interact to selectively consolidate and transform negative emotional memories. *Neuroscience of Enduring Change: Implications for Psychotherapy.* P. 163

Functional Neuroimaging of REM Sleep

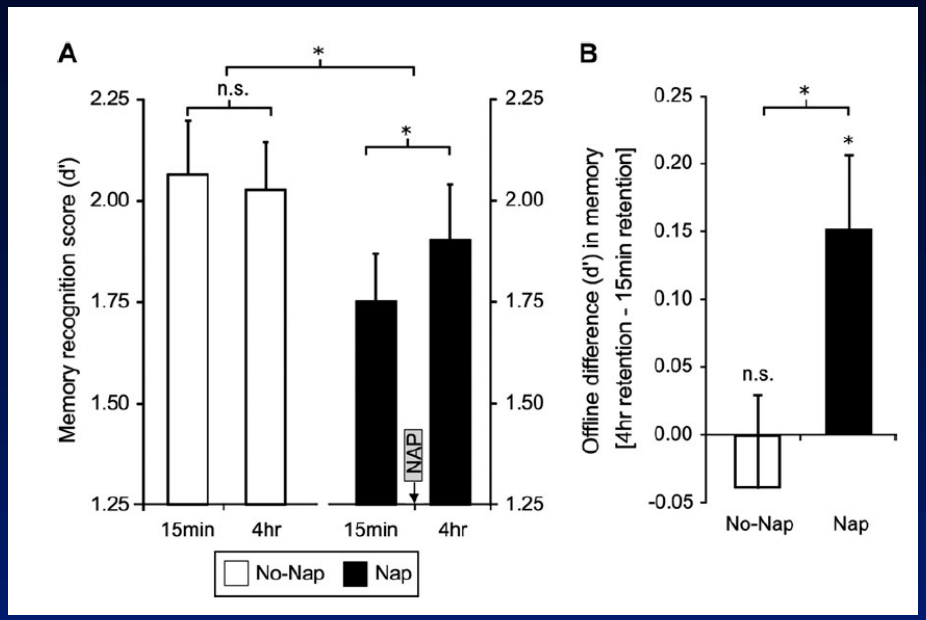


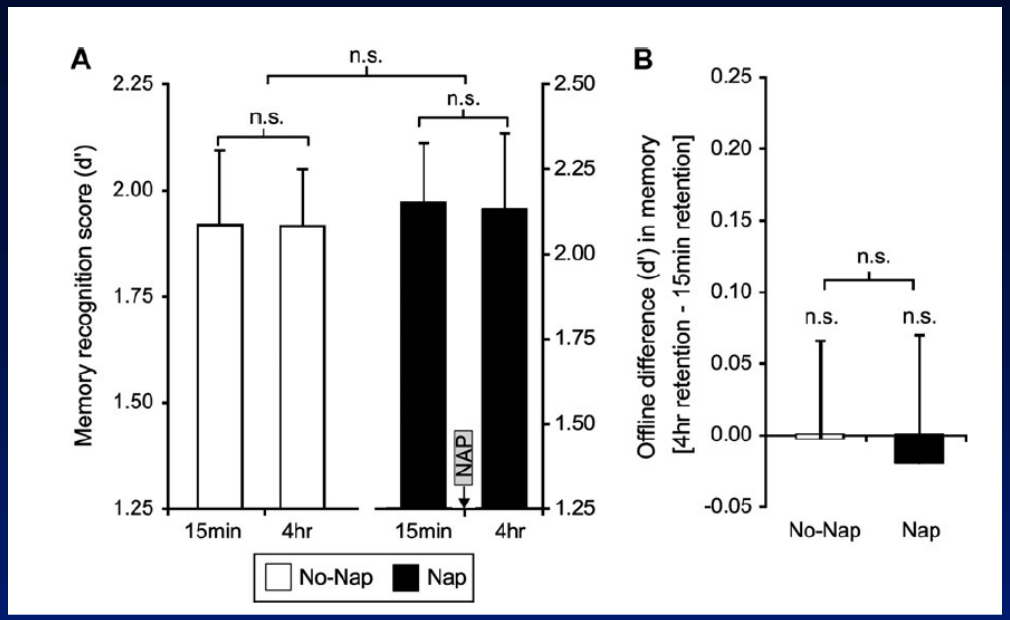
Schwartz, S., & Maquet, P. (2002). Sleep imaging and the neuro-psychological assessment of dreams. *Trends in cognitive sciences*, *6*(1), 23-30.

Preferential Consolidation of Emotional Memories During REM



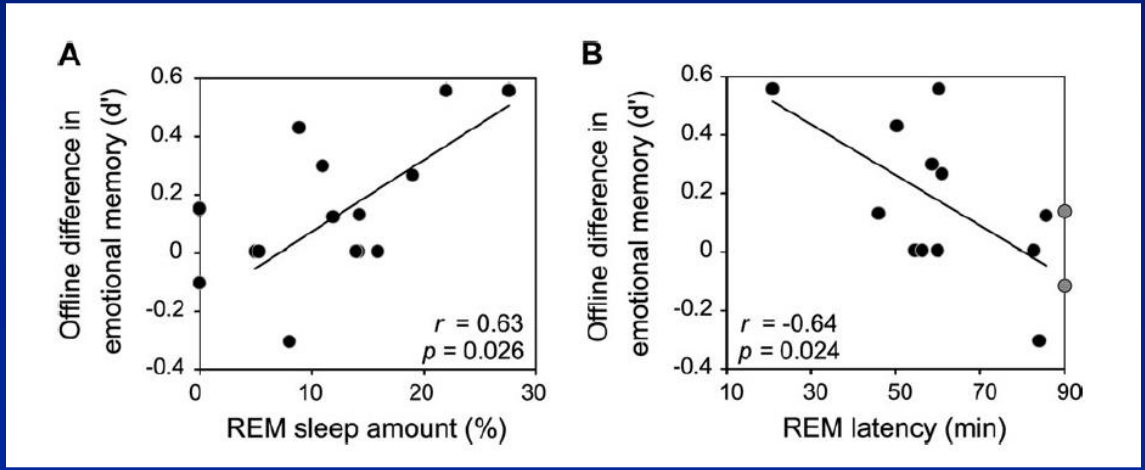
Nishida, M., Pearsall, J., Buckner, R. L., & Walker, M. P. (2009). REM sleep, prefrontal theta, and the consolidation of human emotional memory. *Cerebral cortex*, *19*(5), 1158-1166.





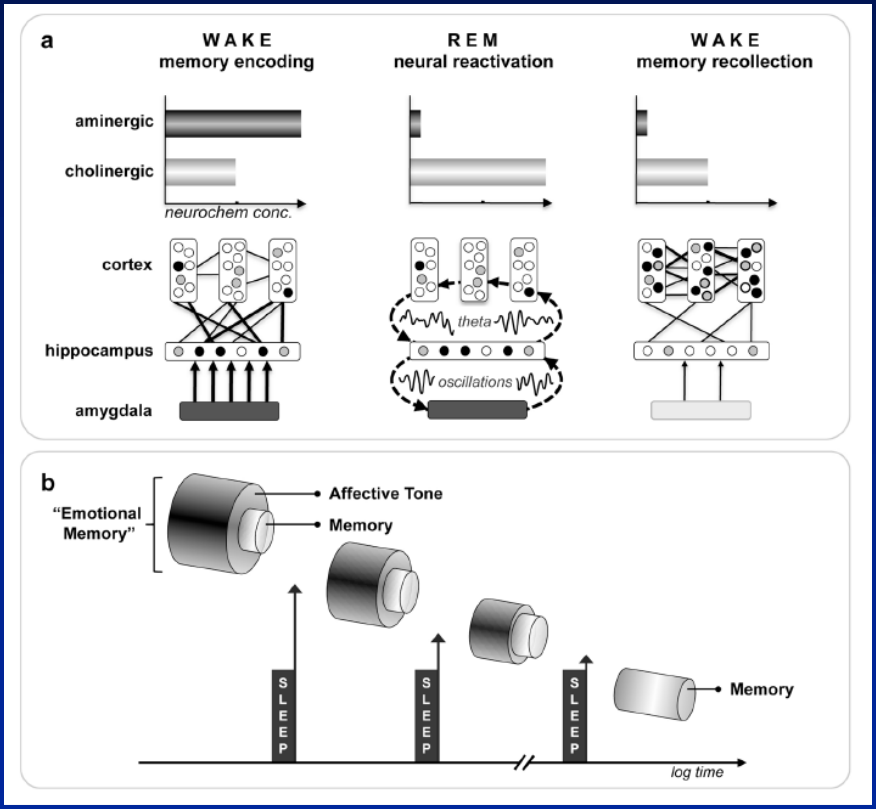
Emotional Material

Neutral Material



Nishida, M., Pearsall, J., Buckner, R. L., & Walker, M. P. (2009). REM sleep, prefrontal theta, and the consolidation of human emotional memory. *Cerebral cortex*, *19*(5), 1158-1166.

"Overnight Therapy"
Sleep to Forget and Sleep to Remember
Why You *Usually* Feel Better in the Morning

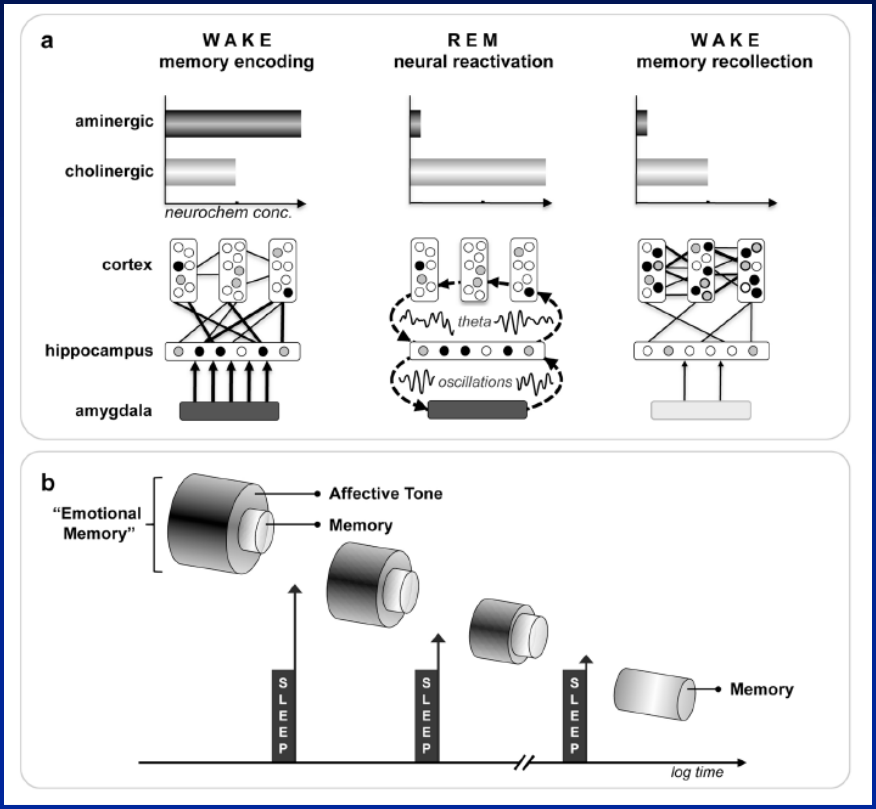


- Coordinated encoding of hippocampal-bound information within cortical modules, facilitated by the amygdala, modulated by high aminergic concentrations

- During REM, same structures are reactivated by synchronous theta oscillations throughout these networks, supporting ability to reprocess previously learned emotional responses

Walker, M. P., & van Der Helm, E. (2009). Overnight therapy? The role of sleep in emotional brain processing. *Psychological bulletin*, *135*(5), 731.

"Overnight Therapy"
Sleep to Forget and Sleep to Remember
Why You *Usually* Feel Better in the Morning



- However, neurochemical milieu of REM has changed, resulting in depotentiation of affective tone and progressive neocortical consolidation of the information
- Stronger cortico-cortical connections support integration into previously acquired autobiographical experience, aiding assimilation of the affective event with past knowledge, which may contribute to the experience of dreams

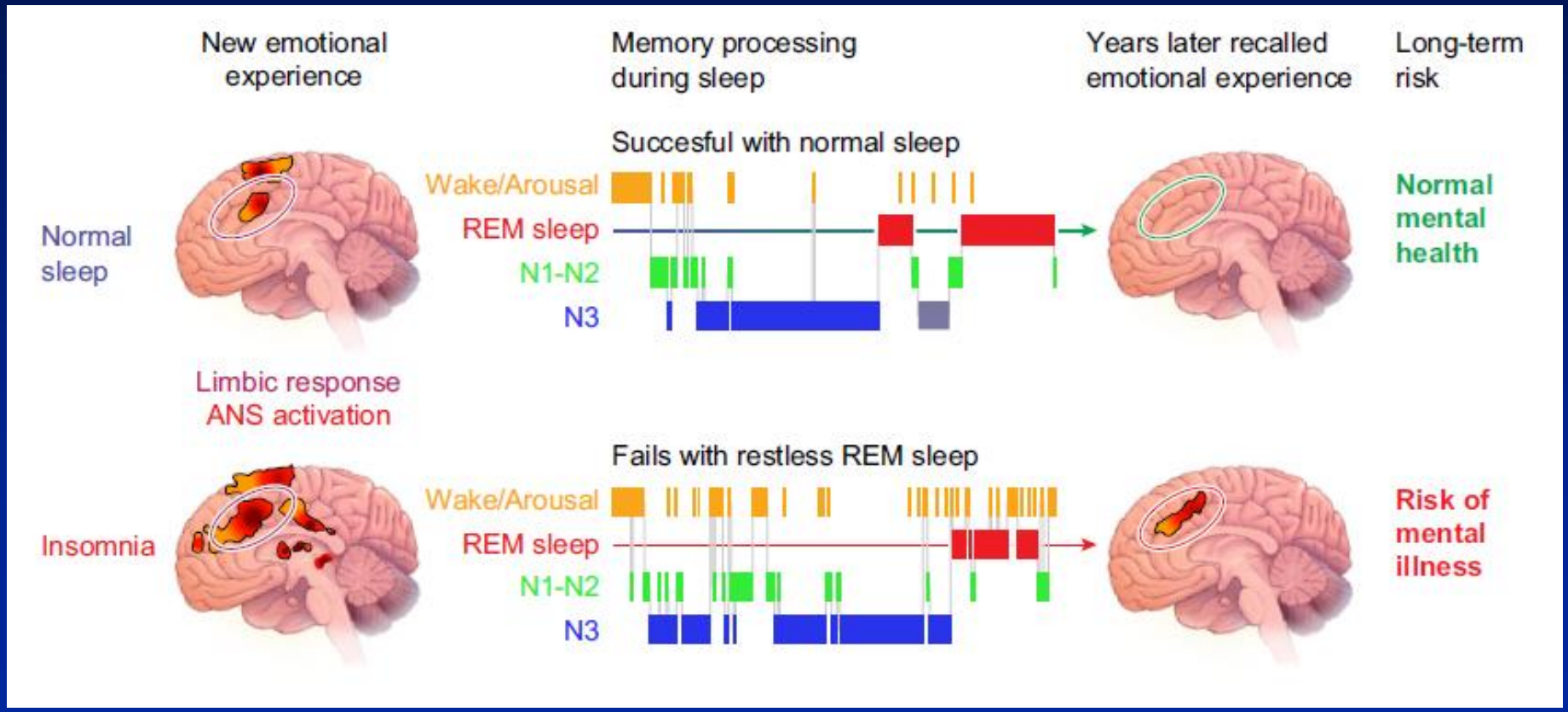
Walker, M. P., & van Der Helm, E. (2009). Overnight therapy? The role of sleep in emotional brain processing. *Psychological bulletin*, *135*(5), 731.

A General Theory of Insomnia: Persistent Limbic Hyperactivation At Night

- Reviewed genetic, developmental (early adversity, life events), neuroimaging, physiological and subjective findings
- Conclusion: insomnia due to persistent limbic activation at night associated with elevated NE
- Sound sleep: consolidated locus ceruleus (source of NE) silencing during REM sleep provides a unique neuromodulatory context for synaptic plasticity in limbic circuits
- Insomnia: elevated NE prevents down-regulation of hyper-arousal and constitutes risk for common mental disorders
- "Sleeping with one eye open" followed by daytime hyper-arousal

Van Someren, E. J. (2021). Brain mechanisms of insomnia: new perspectives on causes and consequences. *Physiological reviews*, *101*(3), 995-1046.

A General Theory of Insomnia: Persistent Limbic Hyperactivation At Night



Van Someren, E. J. (2021). Brain mechanisms of insomnia: new perspectives on causes and consequences. *Physiological reviews*, *101*(3), 995-1046.

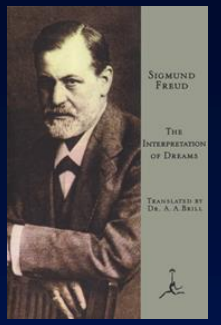
REM Neurotransmitters and Psychopharmacology

- REM is characterized by low serotonin and norepinephrine and high acetylcholine
- This can explain why SSRIs, SNRIs, TCAs and Trazodone inhibit REM (i.e. increasing serotonin and NE)
- Depression often associated with excessive REM, which may reinforce negative memories; thus anti-REM effects may be part of their treatment effectiveness
- Continuing these anti-depressants beyond 6 months of remission could interfere with psychotherapy effectiveness to the extent that it depends on reconsolidation during REM

Consolidation and Reconsolidation of Emotional Memories During REM

- We can't remember everything but need to remember what's most important
- Stress and emotion mark what is most important through enhanced encoding
- NE and cortisol tag daytime memory for preferential sleep processing
- NE facilitates LTP during NREM, which is critical for memory consolidation
- Emotional memories are preferentially consolidated during REM sleep when most dreams occur
- Low NE during REM may down-regulate and integrate emotional content
- Consolidation involves integrating new information with old
- Reconsolidation of specific memories (updating old memories) during sleep is a new area of research currently being investigated
- Conclusion: Dreams could reflect the process of consolidation or reconsolidation of emotional memories; provides a new perspective on the clinical importance of dreams

Freud's Dream Theory



1900

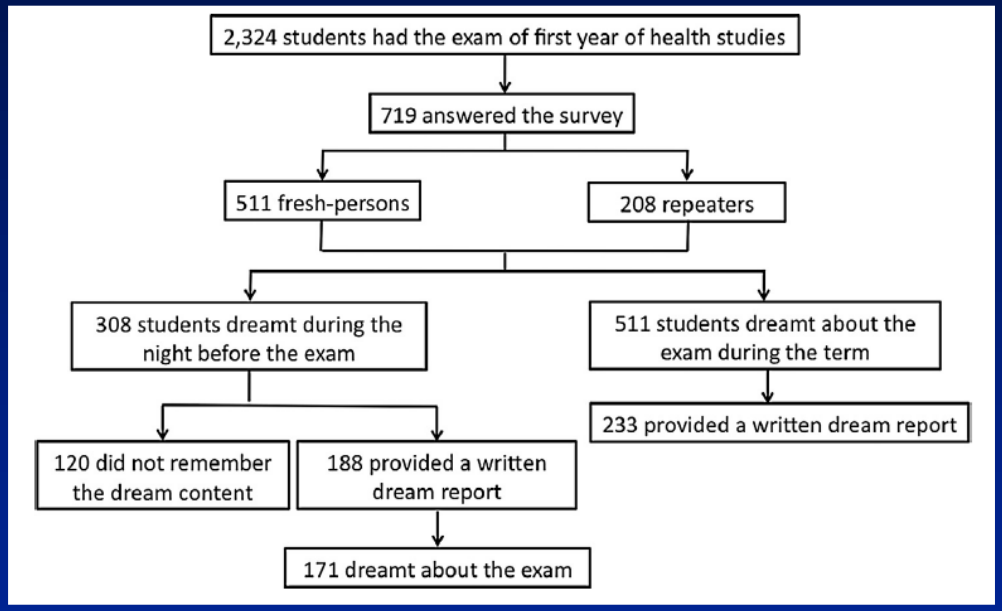
- Dreams were considered the "royal road to the unconscious"
- Freud believed that dreams represented the disguised fulfillment of repressed wishes
- Because awareness of forbidden wishes would be too arousing, and disrupt sleep, the true meaning of the dream (the latent dream) is disguised by the unconscious "primary process"
- What patients experience and report is the manifest dream
- To understand the latent dream requires free association to the elements of the dream (what they mean to this particular person)
- A critical element of dream interpretation is the emotional component
- Dreams have a purpose: to maintain sleep (by keeping arousal in check)
- Freud saw clinical symptoms as similar to dreams: the result of unconscious conflict

Hartmann: Nightmare After Trauma As Paradigm for All Dreams

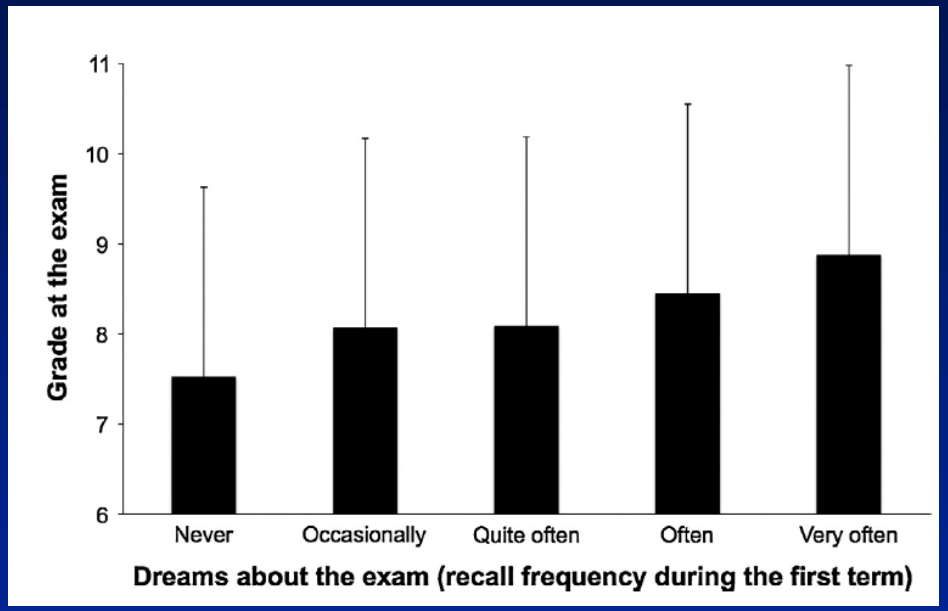
- Examined dream sequences during the weeks and months after trauma in 40 separate people
- A paradigm for how emotional concerns are handled by the processing systems in our brains (often difficult to detect), as 75-95% of dreams contain emotional contexts
- First observe concrete dream about the actual event (but not always)
- Then dreams contextualize the dominant emotion (e.g. tidal wave)
- Dreaming makes connections in mental networks more broadly than is possible during waking
- Connections not random but guided by emotional concerns
- The connections are functional by "weaving in" or integrating new material

Hartmann, E. (1998). Nightmare after trauma as paradigm for all dreams: A new approach to the nature and functions of dreaming. *Psychiatry*, *61*(3), 223-238.

Examination Dreams in Medical School -- And Their Benefits!



78% of dreams involved problems with the exam: being unprepared, late, forgetting answers. Having an exam dream the night before associated with better grade (p=.01).



The association between the frequency of dreams about the exam during the first term and performance (grade, from 0 to 20) at the exam Spearman correlation r = 0.1, p=.01

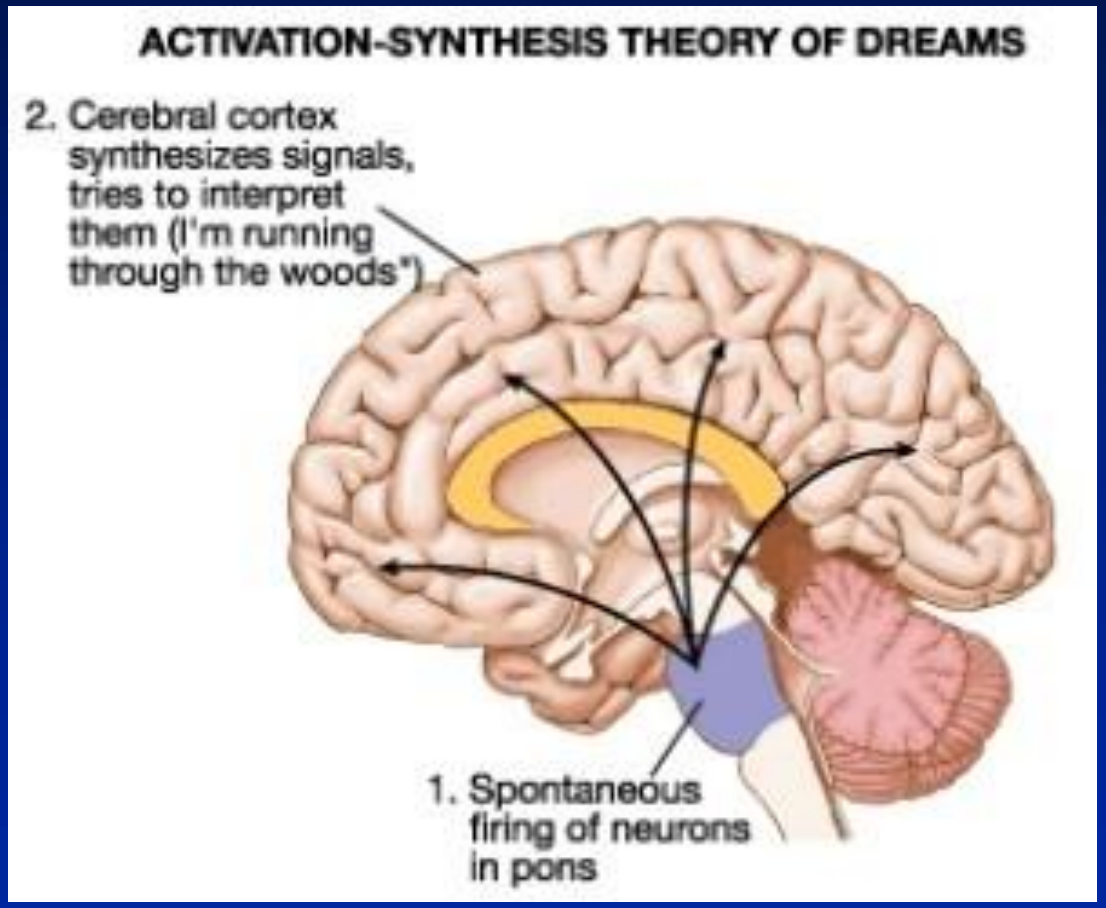
Arnulf, L. et al. (2014). Will students pass a competitive exam that they failed in their dreams? *Consciousness and Cognition*, *29*, 36-47.

Dream Content After Divorce Predicted Adjustment 1 Year Later

- 49 subjects going through divorce completed sleep studies at the time of the breakup and 1 year later
- 31 were depressed
- Depressed Ss who incorporated ex-spouse in their dreams were less depressed and better adjusted at follow-up than Ss who did not
- These dreams were rated as having stronger affect
- Suggests that dreams with strong affect that include the stressor may facilitate recovery from depression
- Dreams appear to prepare people for and improve their ability to deal with dangerous or threatening situations

Cartwright, R. D. (1991). Dreams that work: The relation of dream incorporation to adaptation to stressful events. *Dreaming, 1*(1), 3–9.

Hobson: Activation-Synthesis Hypothesis of Dreams



Hobson, J. A., & McCarley, R. W. (1977). The brain as a dream state generator: an activation-synthesis hypothesis of the dream process. *The American journal of psychiatry*.

- Overfitting occurs when a statistical model fits a training data set exactly but can't generalize to a different data set
- All Deep Neural Networks (DNNs) face the issue of overfitting
- This ubiquitous problem in DNNs is often solved by experimenters via "noise injections" in the form of noisy or corrupted inputs
- This paper argues that the brain faces a similar challenge of overfitting, and that nightly dreams evolved to combat the brain's overfitting during its daily learning
- Dreams are a biological mechanism for increasing generalizability
- Sleep loss, specifically dream loss, leads to an overfitted brain that can still memorize and learn but fails to generalize appropriately

Hoel, E. (2021). The overfitted brain: Dreams evolved to assist generalization. *Patterns*, *2*(5), 100244.

Can Manifest Dream Content Be Used As A Psychoanalytic Treatment Outcome Variable?

- Reconsolidation of emotional memories likely happens during REM sleep/dreaming
- If so, manifest dream content may be a real time "read out" of reconsolidation as it is happening
- Psychoanalysts have a primary interest in altering unconscious processes that are clinically problematic and less interested in symptoms as an outcome
- Dreams are a potentially interesting outcome variable
- Hypothesis: changes over time in manifest dream content may be an index of MR processes related to Rx

In the Context of Chronic Depression and Early Life Trauma, How Might Dreams Change During Psychoanalytic Treatment?

- Trauma, by definition, involves being emotionally overwhelmed
- Trauma also involves being alone, unprotected and helpless
- Characteristics of dreams that might change
  - Quality of object relations – engagement with others
  - Bystander vs. actively engaged – agency
  - Helpless victim – problem solving
  - Overwhelming affect – expansion of emotional range
  - High arousal – decrease in nightmares
- Reports of early life trauma might also change with treatment
- Outcome variables will include symptoms and functioning
- Hypothesis: both dreams and trauma reports will change in parallel with each other and with clinical improvement

Dreams and Early Trauma Memories May Be Indicators of Memory Reconsolidation That Covary With Treatment Outcome

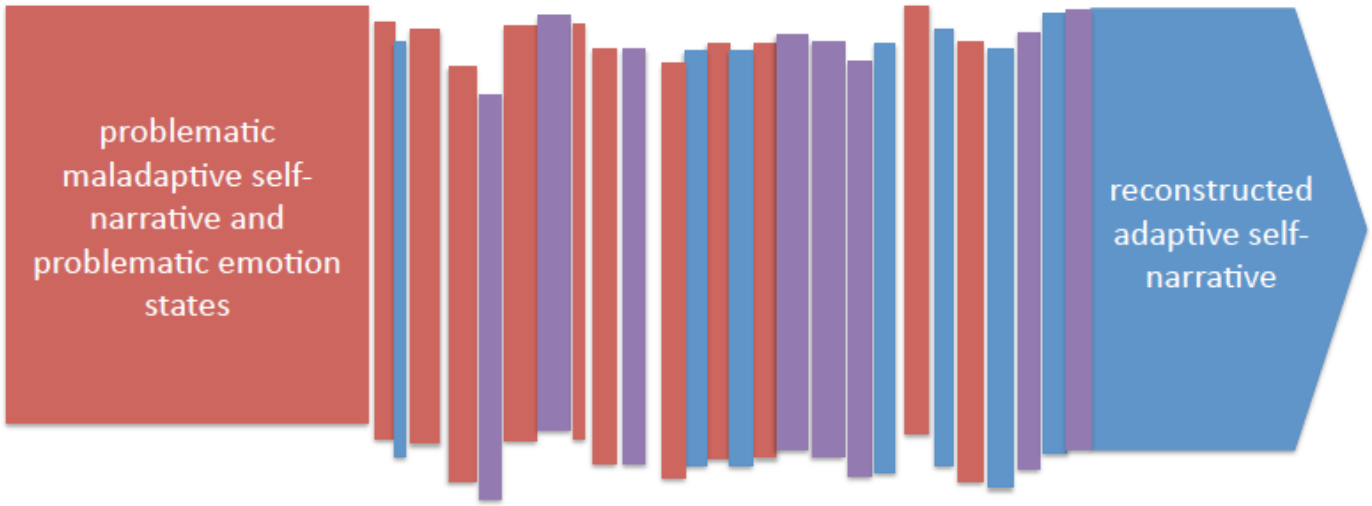
- 30 patients with depression and early childhood adversity from a multi-center trial in the EU of high (4-5x/wk) vs. low (1x/wk) frequency psychoanalysis are being studied
- They will be compared to 15-30 patients currently treated with emotion-focused therapy and 15-30 controls
- Childhood trauma memories and dream reports will be obtained pre-treatment and 1 year later and correlated with clinical improvement
- Prediction: memories, dreams and clinical status "improve" together
- Coding systems (applicable to both) will be developed during this fellowship in preparation for data analysis later this year

Future Research on Dreaming, MR and the Process of Change in Psychotherapy

- Record and track what is happening in each therapy session
- Code parts of each session for Narrative Emotion Process Coding System: Problem, Transition and Change markers
- Step 1: activate old memories and old painful feelings
- Step 2: in session create new emotional experiences counter to expectation (prediction error)
- Assess for changes in emotional state and RMP after the session
- Awakening by phone that night during REM (based on remote monitoring of actigraphy and other physiology) to obtain dream report(s)
- Monitor for changes in emotional state and RMP the next day and beyond
- Observe for changes in recurrent pattern over time
- Step 3: practice new ways of construing and responding
- Observe long-term outcome

Narrative-Emotion Process Coding System (NEPCS; Angus Lab, 2015)

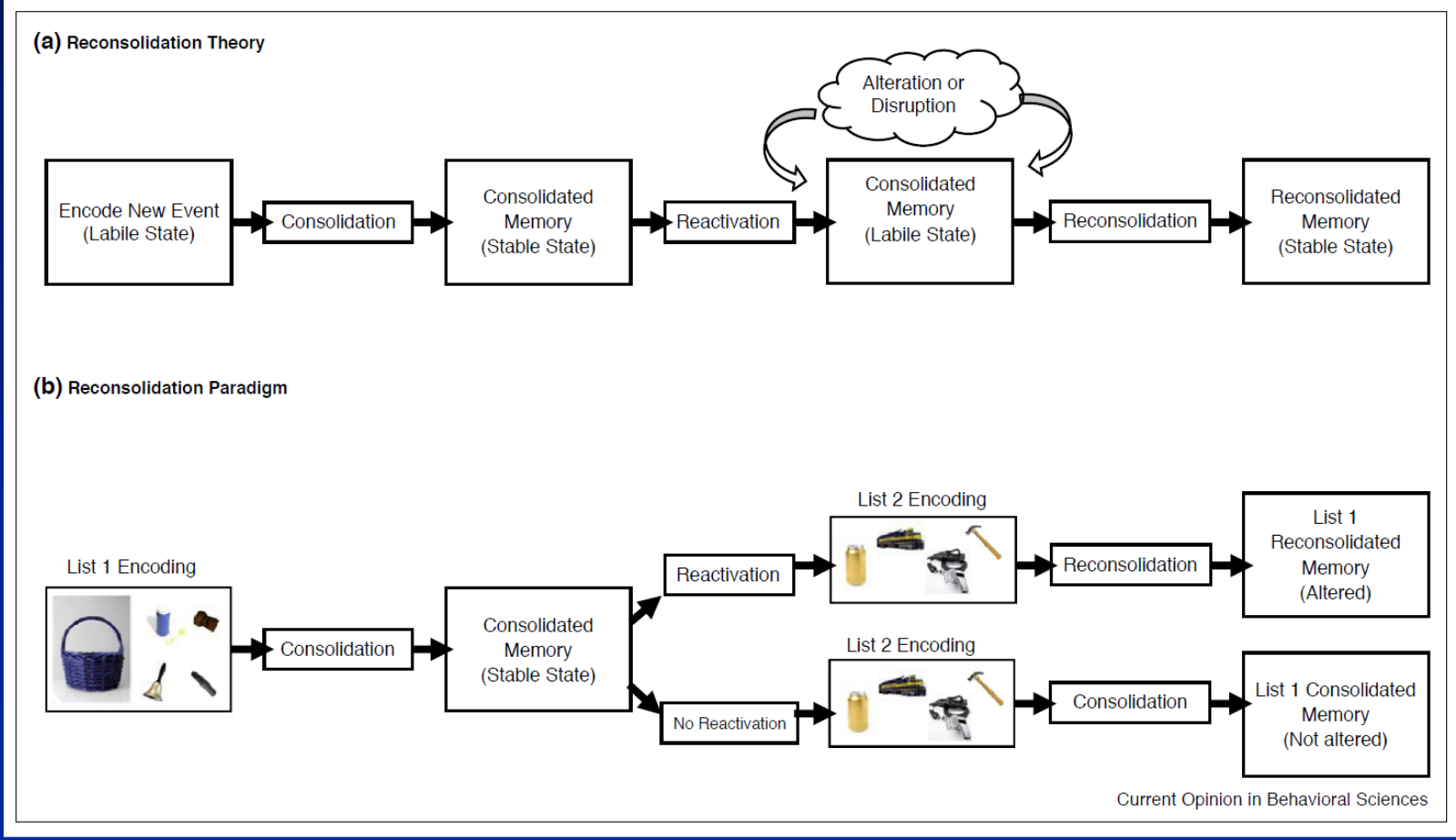
Problem Markers				Transition Markers				Change Markers	
Same Old Story	Empty Story	Unstoried Emotion	Superficial Story	Reflective Story	Inchoate Story	Experiential Story	Competing Plotlines	Unexpected Outcome	Discovery Story



Other Ways of Working With Memory Reconsolidation During Sleep

- Napping
- Rehearsal
- Rescripting
- Targeted Memory Reactivation

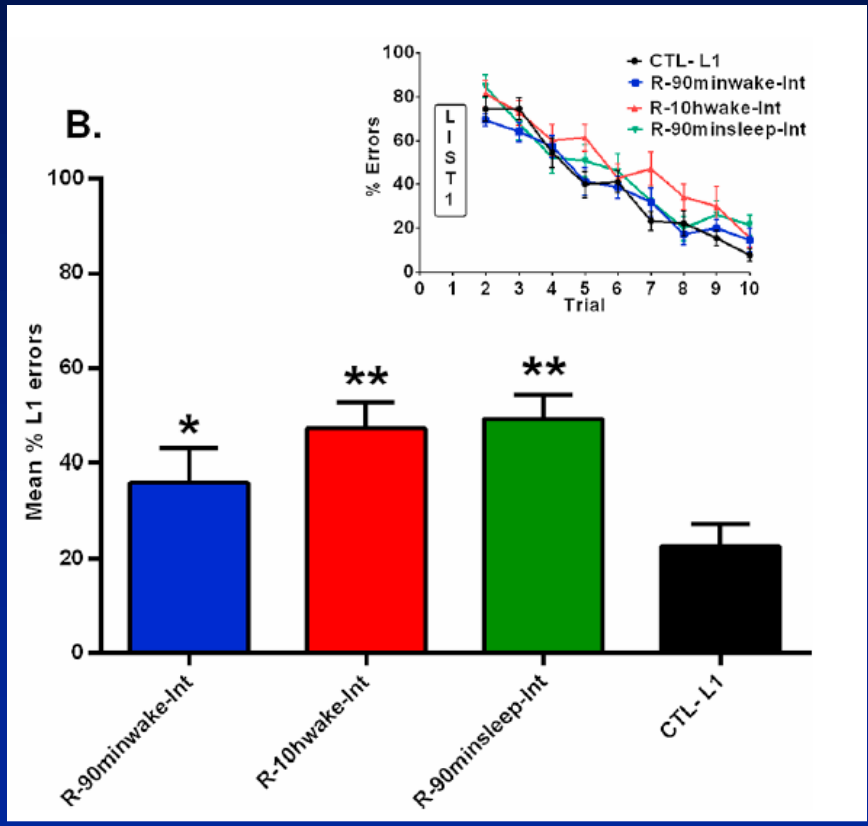
Napping after List 1 Reduced Errors Induced By Learning List 2



Napping after List 1 Reduced Errors Induced By Learning List 2

List 1		List 2	
ITE	OBN	OEN	SRO
ASP	UOD	PRI	CRE
FLI	AIO	AIC	POA
NEB	FOT	KEC	CLO
COS	GLE	TIU	PLA

Day 1 – List 1
Day 2 – Reminder …List 2
Day 3 – Test List 1



Moyano, M. D., Diekelmann, S., Pedreira, M. E., & Forcato, C. (2019). Sleep accelerates re-stabilization of human declarative memories. *Neurobiology of learning and memory*, *162*, 1-8.

Conclusions: Sleep, Napping, Dreaming and Memory Reconsolidation

- The story of how emotion and memory interact to create change is incomplete without understanding how sleep and dreaming participate
- Sleep plays a major role in integrating new information with past knowledge
- Evidence supports the role of naps in promoting consolidation
- Emotional events during the day are preferentially tagged for encoding and later processing, and are preferentially processed during sleep relative to neutral content
- Emotional events are preferentially processed during REM and integrated with previous knowledge

Conclusions: Sleep, Napping, Dreaming and Memory Reconsolidation

- The low NE milieu of REM helps ensure that the emotional content of the memories is modulated while dreaming
- Freud correctly associated dreaming and modulated emotional arousal, but didn't know about REM (discovered in 1953), REM neurochemistry, or the need for randomness in deep neural networks to promote the generalizability of newly acquired information
- Dreams do have meaning and are clinically useful, just as Freud said
- Dreams could be a marker of memory reconsolidation as it is happening

Conclusions: Sleep, Napping, Dreaming and Memory Reconsolidation

- Changes over time in dreams and childhood memories of trauma could be useful markers of outcome in psychoanalysis and psychodynamic psychotherapy