To Sleep, To Dream, Perchance to Remember

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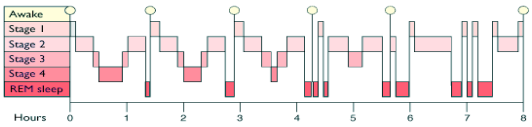
Thanks

- W.J. Jacobs
- M. Moscovitch
- Richard Bootzin
- Bob Stickgold
- Bruce McNaughton

can the analysis of dreams tell us how sleep relates to memory consolidation?

Stages of Sleep



in the study of dreams, a major distinction has been drawn between REM and NREM

REM is more prevalent in the latter part of the night

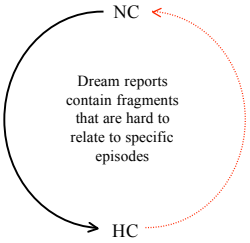
NREM (SWS) is more prevalent in the early part of the night

Structure of Dreams

- REM Dreams
  - highly fragmented with often bizarre content
  - episodic elements, if any, are disconnected and hard to relate to waking life events
- NREM Dreams
  - veridical episodic memories possible
  - recent episodes are predominant; remote episodes appear but are less frequent
  - NREM dreams late at night are often more REM-like

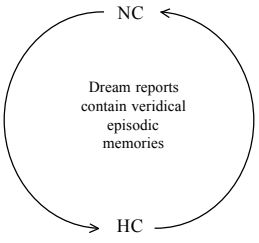
(e.g. Cavallero et al., 1992; Cicogna, Cavallero & Bosinelli, 1986, 1991; Foulkes, 1962; Hobson et al., 2000; Stickgold et al., 2000, 2003)

REM SLEEP



(e.g. Buzsaki, 1996, 1998)

NREM SLEEP



(e.g. Sirota, Csicsvari, Buhl, & Buzsaki, 2003)

Memory Consolidation

- post-registration events that stabilize memory
  - short-term vs. long-term
  - hippocampal - neocortical interaction as basis of long-term consolidation effects

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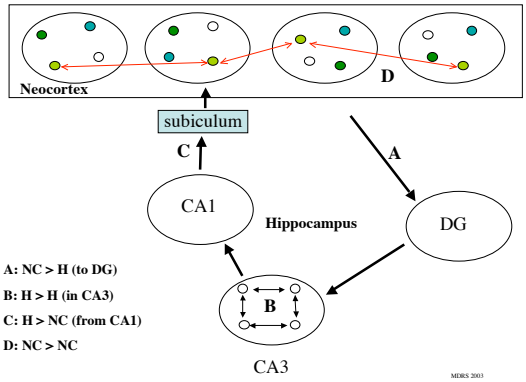
Hippocampal-Cortical Interactions: A Consensus View



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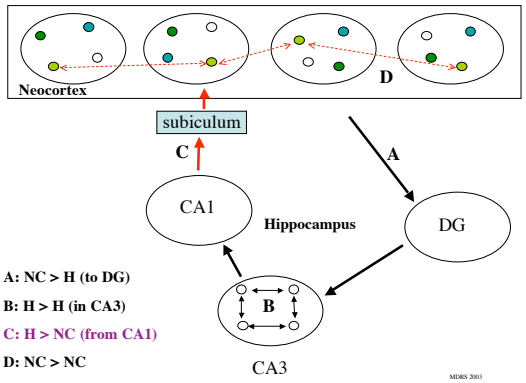

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ENHANCEMENT OF MEMORY CONSOLIDATION AS A FUNCTION OF SLEEP STAGE

	REM	NREM
Episodic	**NO** (e.g. Plihal & Born, 1997, 1999)	YES (e.g. Plihal & Born, 1997, 1999)
Procedural/ Implicit	YES (e.g. Plihal & Born, 1997, 1999; Wagner et al. 2002)	MAYBE (e.g Plihal & Born, 1997; Walker et al. 2002)

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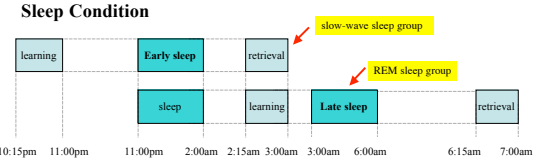
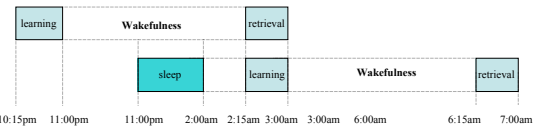
Plihal & Born, 1997

Sleep Condition



Wake Control Condition



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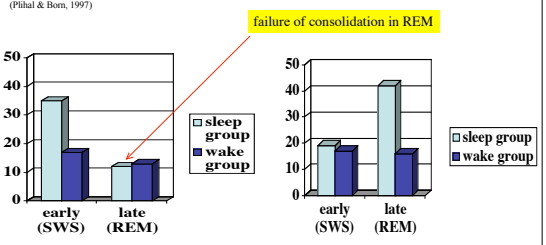
Percent improvement in recall after early or late retention interval.

(Plihal & Born, 1997)



Retention interval

Paired-associate list (episodic)

Retention interval

Mirror tracing (procedural)

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What accounts for:

differences in episodic content of dreams
differential effects on memory consolidation

differences in hippocampal-neocortical interactions as a function of:

REM/NREM
Early vs Late Sleep
Variations in Neurotransmitters

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	REM	NREM
A **NC-->HC**	↑ Hasselmo (1999), Buzsaki (1996)	↑ Sirota, Csicsvari, Buhl & Buzsaki (2003)
B **HC-->HC**	↑ Louie & Wilson (2001), Hirase et al (2001)	↑ Wilson & McNaughton (1994); Pavlides & Winston (1989); Lee & Wilson (2002); Hirase et al (2001)
C **HC-->NC**	↓ Hasselmo (1999) (Hippocampal output diminished during REM sleep).	↑ Sirota, Csicsvari, Buhl & Buzsaki (2003), Buzsaki (1996)
D **NC-->NC**	↑ Hasselmo (1999)	↓ Hasselmo (1999)

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Neuromodulation across the Sleep-Wake Cycle

	Active Wake	Quiet Wake	SWS	REM
ACh	++	+	−	+++
NE 5-HT	++	+	+	−

ACh: ***acetylcholine***
NE: ***norepinephrine (noradrenalin)***
5HT: ***serotonin***

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BUT

- none of these dichotomies seem to capture all the results
- for example, REM-like dreams can be seen in NREM late in the night
- something else must be involved

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A New Possibility

- GLUCOCORTICOIDS

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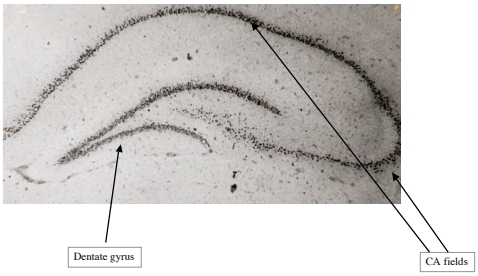
glucocorticoid receptors in hippocampus

Courtesy of Bruce McEwen



CORTICOSTERONE BINDING in RAT

Hippocampal subregions:	
Subiculum (S)	405 ± 49
CA1 pyramidal cells	365 ± 20
CA2 pyramidal cells	572 ± 30
CA3 pyramidal cells	250 ± 61
CA4 pyramidal cells	192 ± 6
Dentate gyrus (DG)	258 ± 58
Entorhinal cortex	100 ± 0.4
Lateral septal nucleus	117 ± 8
Medial septal nucleus	40 ± 1
Cortical amygdala	77 ± 15
Medial amygdala	34 ± 1
Parietal cortex	27 ± 2

from Sapolsky, McEwen & Rainbow, *Brain Research*, 1983.

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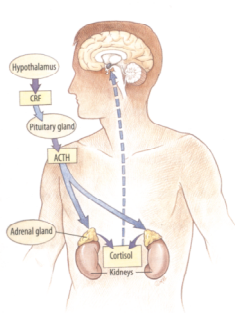
Stress response system

The HPA axis



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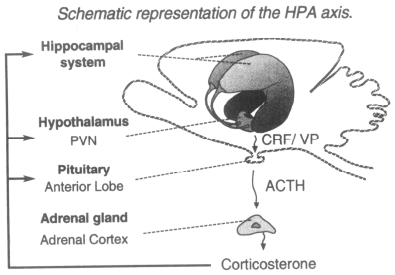

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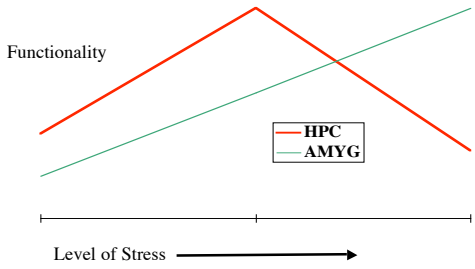
Dose - Response



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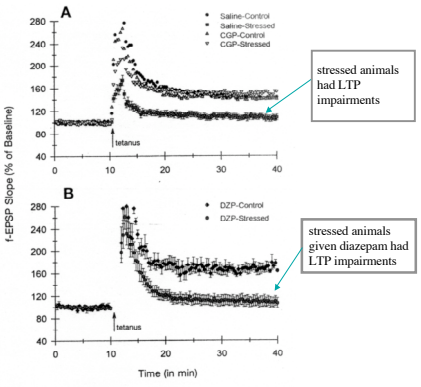
stress impairs LTP in CA1 region of hippocampal slices

stress involved 60 tail shocks while under restraint, then rats were sacrificed and slices taken



(Kim, Foy & Thompson,

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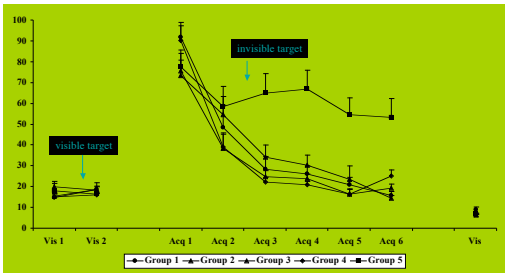
Latency to find target platform



Nadel, L., Thomas, K.G.F., Laurance, H.E., Skelton, R., Tal, T. & Jacobs, W.J, 1998.

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Why CORT?

- cort variations with REM/NREM
- cort variations with early/late sleep

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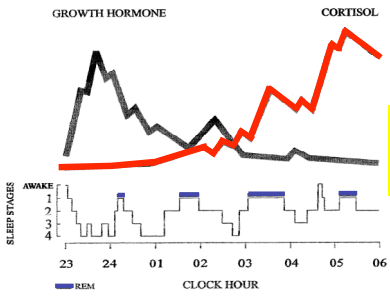

*Cortisol increases steadily across the night, with mini - peaks corresponding to REM episodes.

From, Lavie (1996).

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Why CORT?

- cort variations with REM/NREM
- cort variations with early/late sleep
- **cort modulates critical neurotransmitters**

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Why CORT?

- cort variations with REM/NREM
- cort variations with early/late sleep
- cort modulates critical neurotransmitters
- **similar phenomenology with cort variations in wake**

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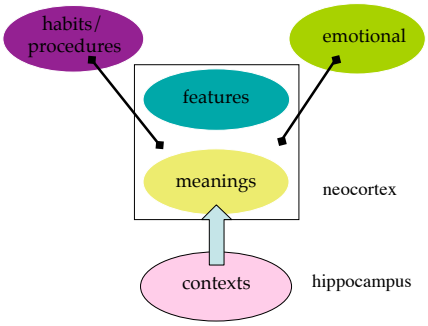
Episodic Memory: Binding by Context



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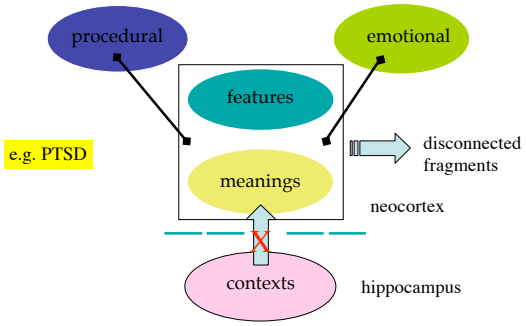
Episodic Memory under Stress



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Why CORT?

similar phenomenology with cort variations in wake
cort variations with REM/NREM
cort variations with early/late sleep
cort modulates critical neurotransmitters

CA1 and CA3 have different CORT receptor profiles

MR (type I) and GR (type II)

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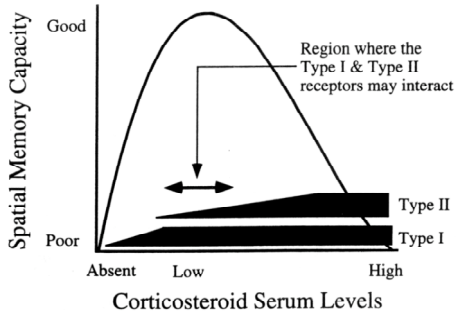

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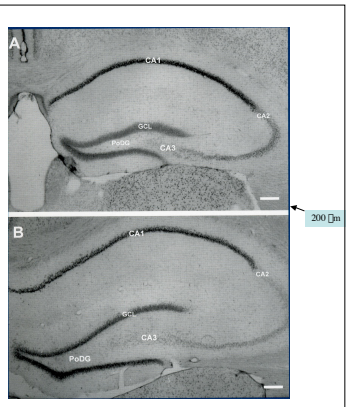
Distribution of GR in the mouse (A) and rat (B).

Patel & Bulloch, 2003

"…only when MR and GR are co-localized within a hippocampal subregion - as in CA1 and dentate gyrus - are the two corticoid receptor subtypes capable of mediating modulatory effects on 5-HT responses according to a U-shaped corticosterone dose-dependency." (Karten, 2000, p. 120)



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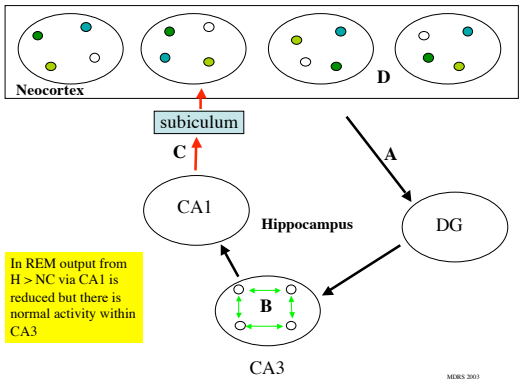
Why GR-MR Distribution Matters



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Why CORT?

similar phenomenology with cort variations in wake
cort variations with REM/NREM
cort variations with early/late sleep
cort modulates critical neurotransmitters

underlying cort distributions in H match, in that CA1 and CA3 have different profiles

Cort injections overturn consolidation facilitation normally seen in NREM (Plihal & Born, 1999)

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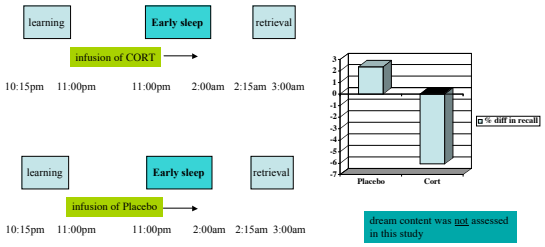
Plihal & Born, 1999

Sleep Condition



CORT injection did not alter sleep stage, but did raise CORT levels and eliminated the facilitation seen in memory consolidation in the placebo group

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Thus

- it might be CORT level, not sleep stage, or time of night, that is the causal agent in determining both the nature of dreams and memory consolidation effects

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Implications

what is going on in REM/Hi CORT

what is going on in NREM/Lo CORT

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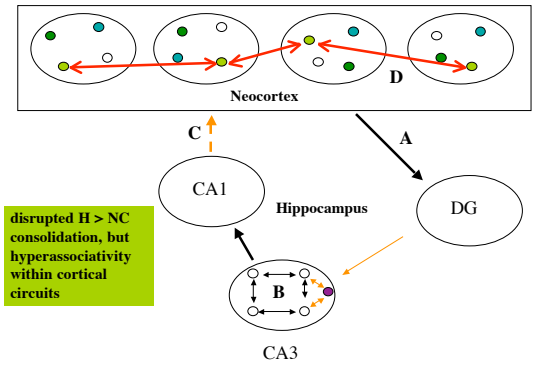
Hippocampal-Cortical Interactions: During REM/HI CORT



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- during REM/Hi CORT:

impaired H > NC feedback
- dreams are fragmented with little contextual content
- consolidation of episodic memory is diminished

hyperassociativity in NC
- dream output seems to come from NC alone
- consolidation of procedural memory is enhanced
- semantic priming by "weak" primes is enhanced (Stickgold etal. 1999)

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implications for location of episode memories

- if, as appears to be the case, dream output during REM comes from NC, with little or no contribution from H
  - the nature of memories reported from REM should tell us something about whether NC can store episodes as a result of consolidation
  - the virtual absence of coherent episodic content in REM dreams suggests that NC by itself cannot store and retrieve meaningful episodic memories

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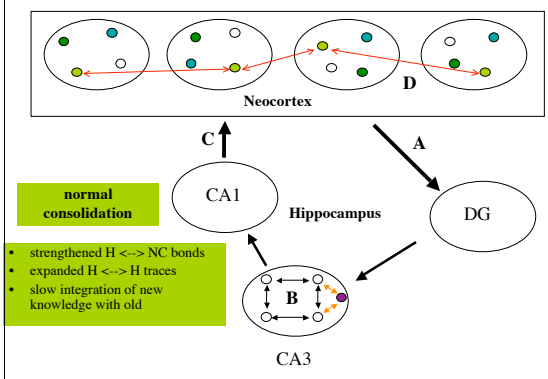
Hippocampal-Cortical Interactions: During NREM/Lo CORT



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broader implications

- if episodic memory is not stored in NC as a consequence of consolidation, as the content of REM dreams suggests, what then is the purpose of consolidation?

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Perchance to Speculate

What dreams can tell us about memory and its consolidation

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what is outcome of NC <---> H interactions over time?

- transfer? replication? integration/transformation?

  possibilities:
  - episodic memory initially represented in H; then **transferred** to NC
  - episodic memory initially represented in H; then **replicated** in NC
  - episodic memory represented in NC; needs H intervention to allow full accessibility (creation/strengthening of links) until consolidated
  - **is H merely an index?**
  - while standard consolidation theory seems to accept this "index" idea, **multiple trace theory** (Nadel & Moscovitch) supposes that H represents critical contextual information, that cannot be fully replicated in NC
  - what transpires in NC, by this view, is a strengthening of linkages among semantic representations, leading to the extraction from episodes of statistical regularities -- **the "gist" of experience**, and the integration of this new knowledge with existing knowledge

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To Dream, Perchance to Fly

- a great deal has been learned about the nature and role of dreams in recent years, and a role for sleep, and dreams, in memory consolidation seems secure
- we know little about why some dreams are so bizarre, how we can, for example, fly -- we suggest that high levels of CORT, typically seen in REM, may be responsible
- study of how these dreams break the boundaries of normal thought could illuminate mechanisms of creativity, consciousness, and the dynamical neural processes that maintain the logic of waking life

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