from sleep to attention – lecture 2 – April 4, 2012

defining sleep?

mentation – report on content upon arousal

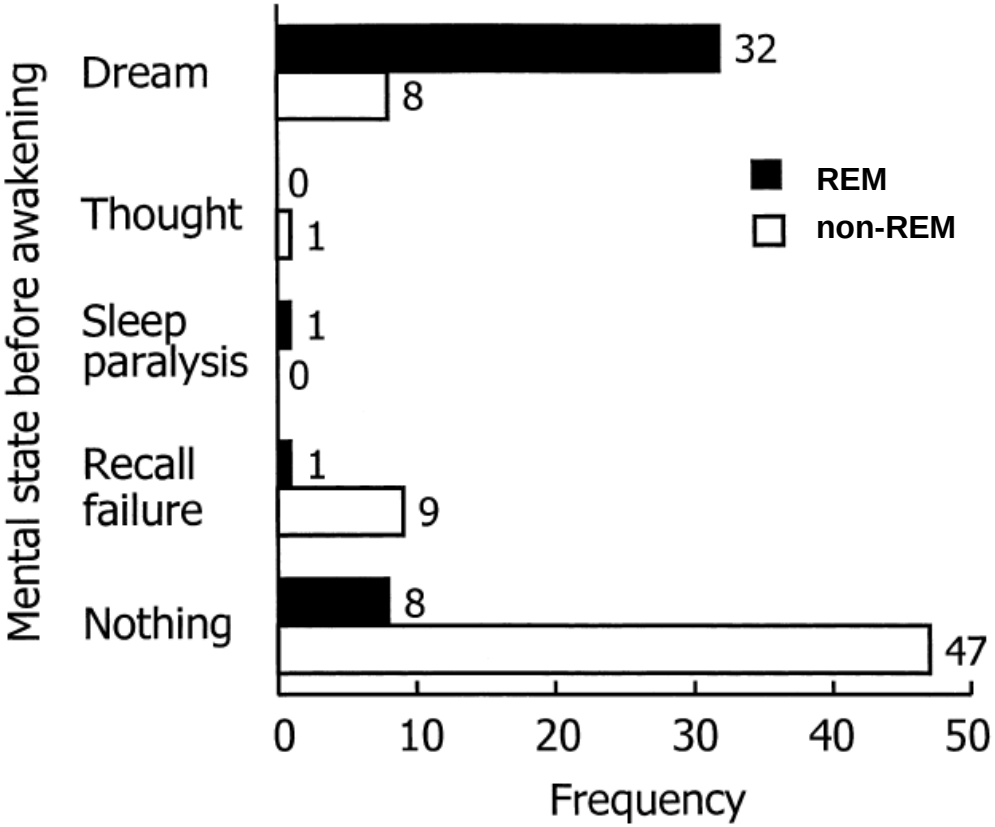
behavior

arousal thresholds/stimulus detection – (i.e., attention)

electrophysiology

- EEG - electroencephalogram (cortical LFPs)
- EMG – electromyogram (recording of muscle potentials)
- EOG – electrooculogram (recording of eye movements)

the frequency and vividness of dream content is much higher in REM sleep than in non-REM sleep



Takeuchi et al., 2001, J. Sleep Res.

defining sleep?

mentation – report on content upon arousal

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arousal thresholds/stimulus detection

electrophysiology

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monitoring behavior works sometimes, but one can certainly be awake and immobile for an extended period of time

defining sleep?

mentation – report on content upon arousal

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arousal thresholds/stimulus detection

electrophysiology

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arousal threshold/stimulus detection may work reasonably well, but the waking state may also be accompanied by serious inattention…and arousal from sleep depends on the meaningfulness of the stimulus

defining sleep?

mentation – report on content upon arousal

behavior

arousal thresholds/stimulus detection

electrophysiology

- EEG - electroencephalogram (cortical LFPs)
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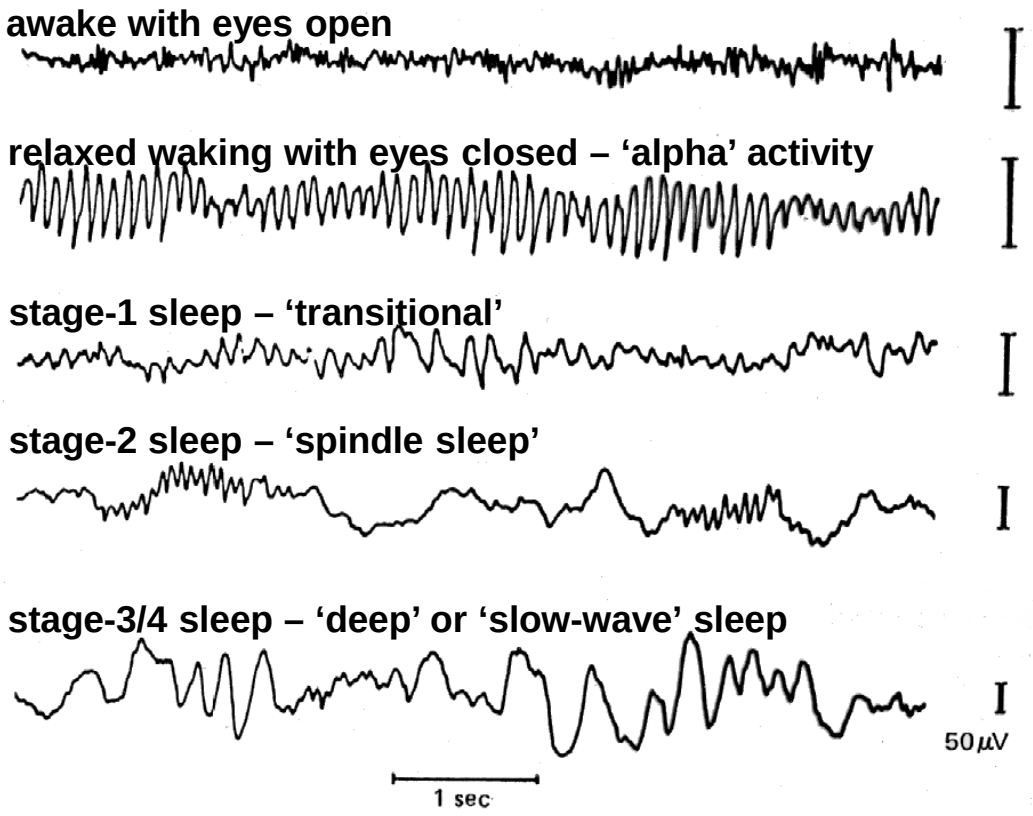
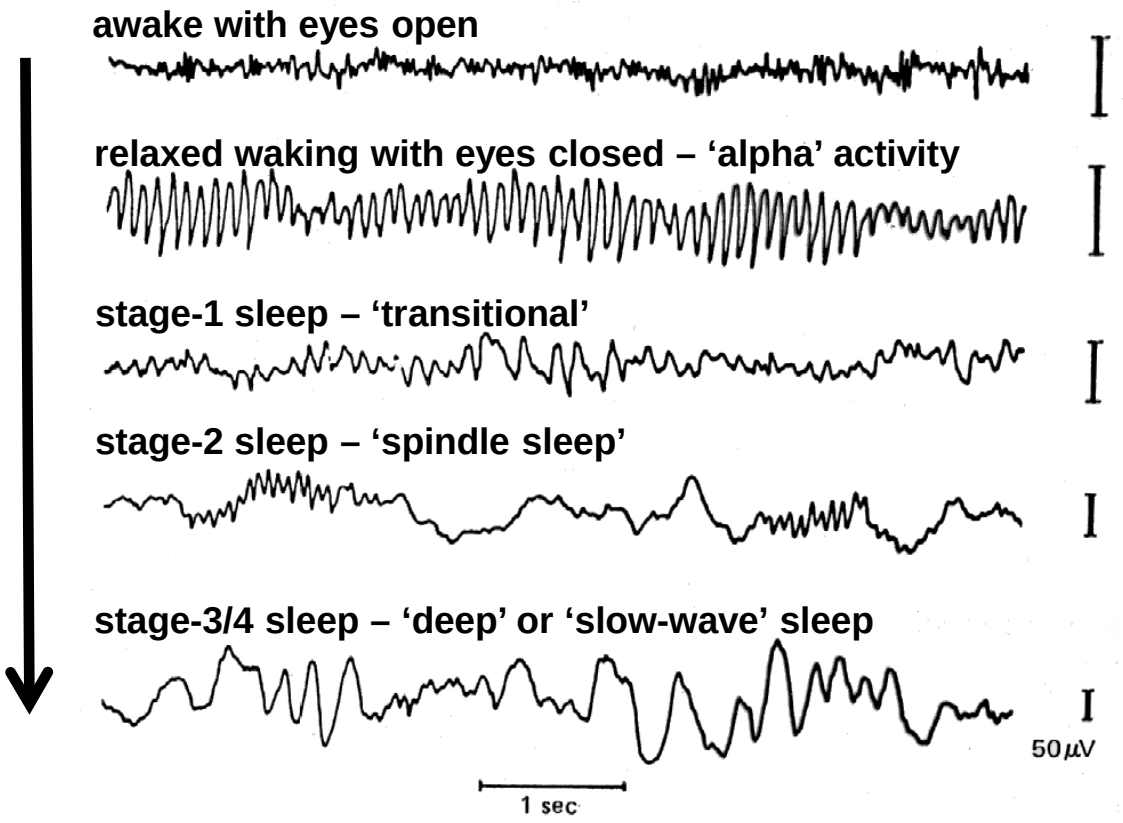
extended immobility is associated with alterations in cortical EEG patterns

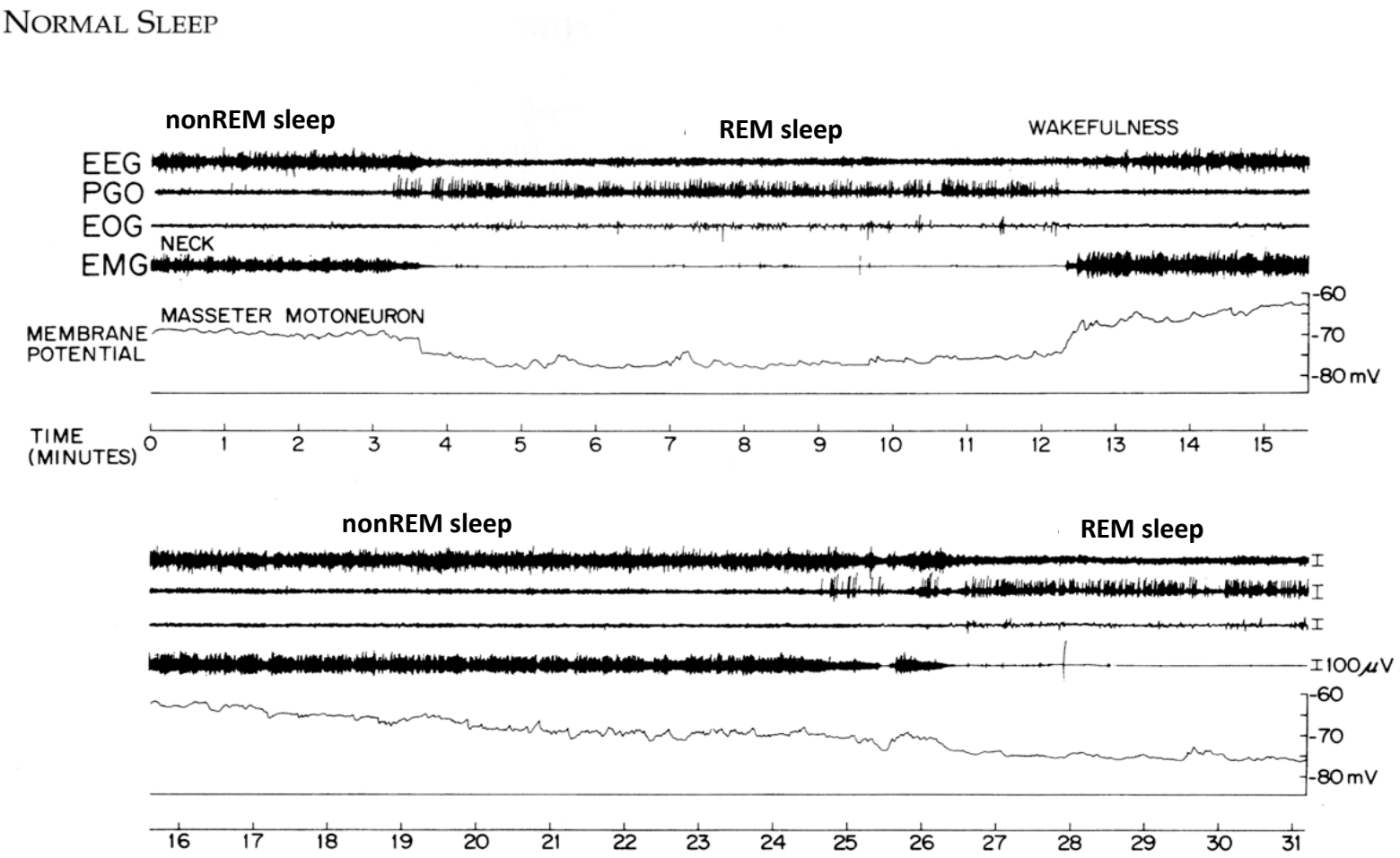


the basic patterns of cortical EEG/LFP activity in the cerebral cortex closely track sleep depth as assessed by arousal thresholds

increasingly greater magnitude stimuli required for perception/arousal



science settles (sort of) on a combinatorial approach to defining sleep



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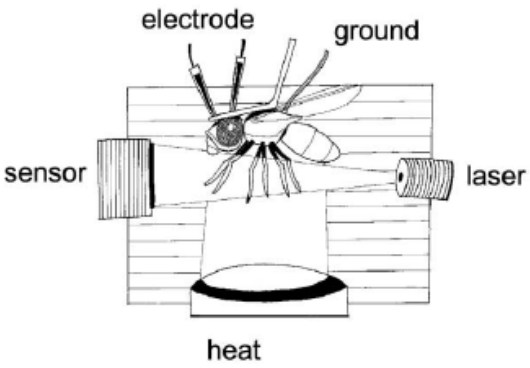
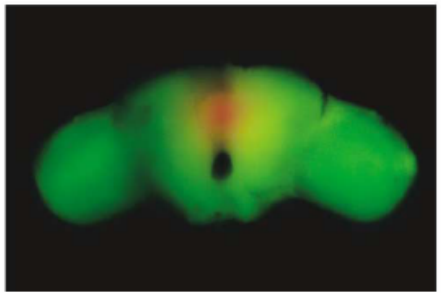
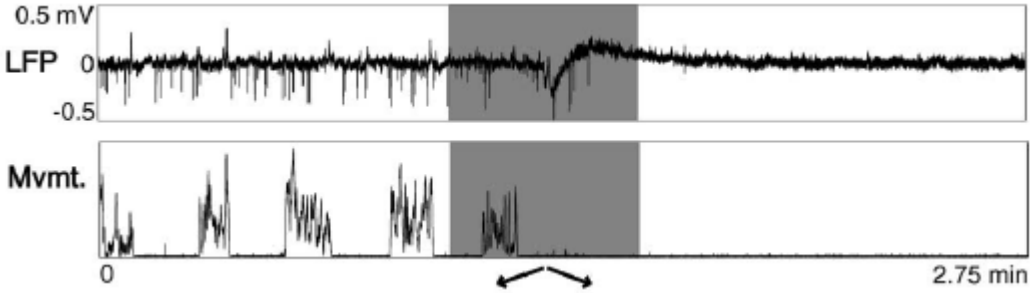






‘sleep’ in insects, defined by monitoring motion and arousal threshold, is not associated with the patterns of LFP s observed in birds and mammals

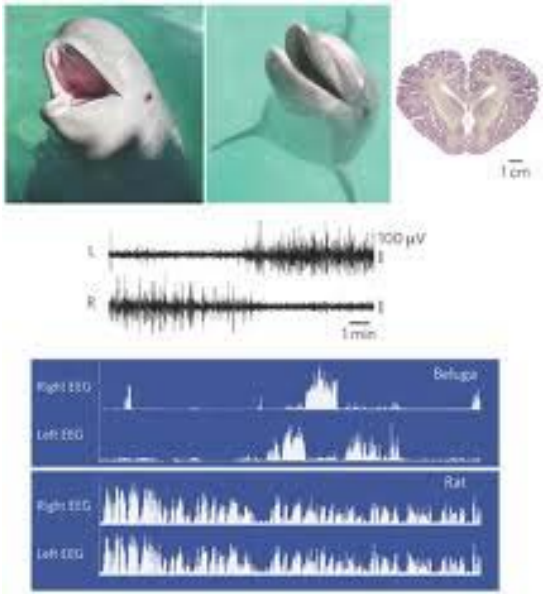
So…sleep may be reasonably well defined by a set of criteria that include measures of behavior, arousal thresholds, and electrophysiology

But…using such a combinatorial scheme to define sleep, we still have the following problems:

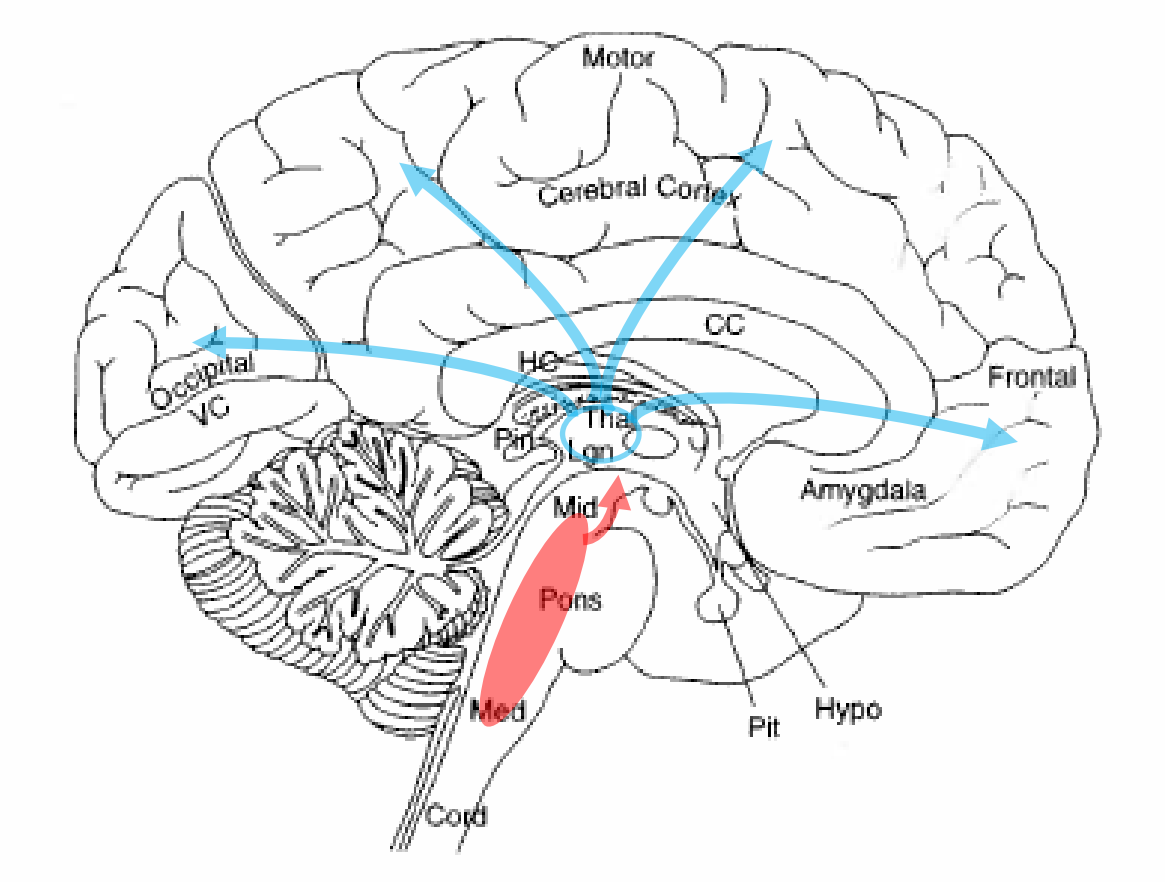
1. **two almost entirely different states of sleep in the mammal (REM and non-REM sleep) are defined**

2. **different definitions of sleep for insects, reptiles, and mammals**

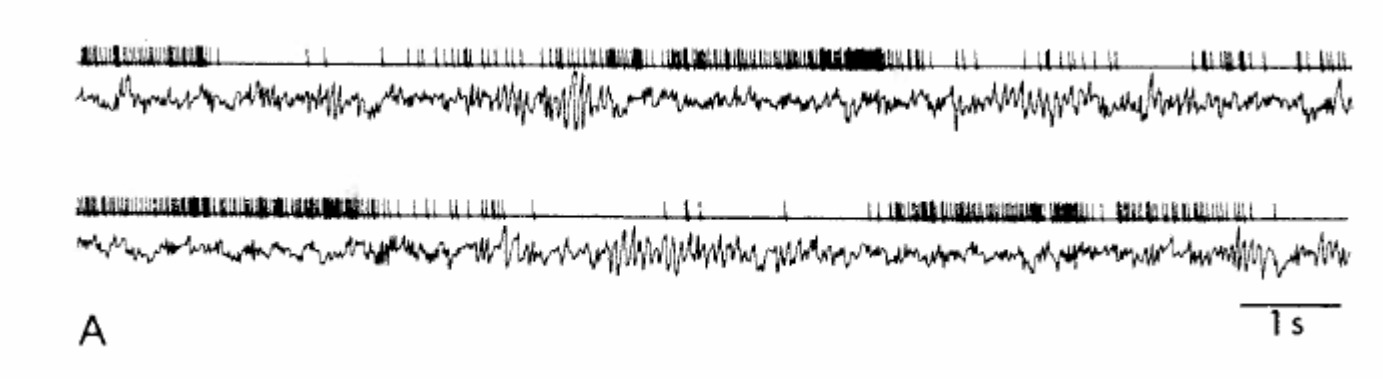
3. **birds and mammals may be half asleep and half awake**



to slow-wave or not to slow-wave? – the patterning of LFP activity within the thalamocortical system is largely determined by brainstem and hypothalamic neuromodulatory neurons and brainstem reticular formation neurons via their projections to the thalamic reticular nucleus



depressed activity of brainstem reticular formation neurons closely follows the production of spindle and slow-wave cortical EEG events



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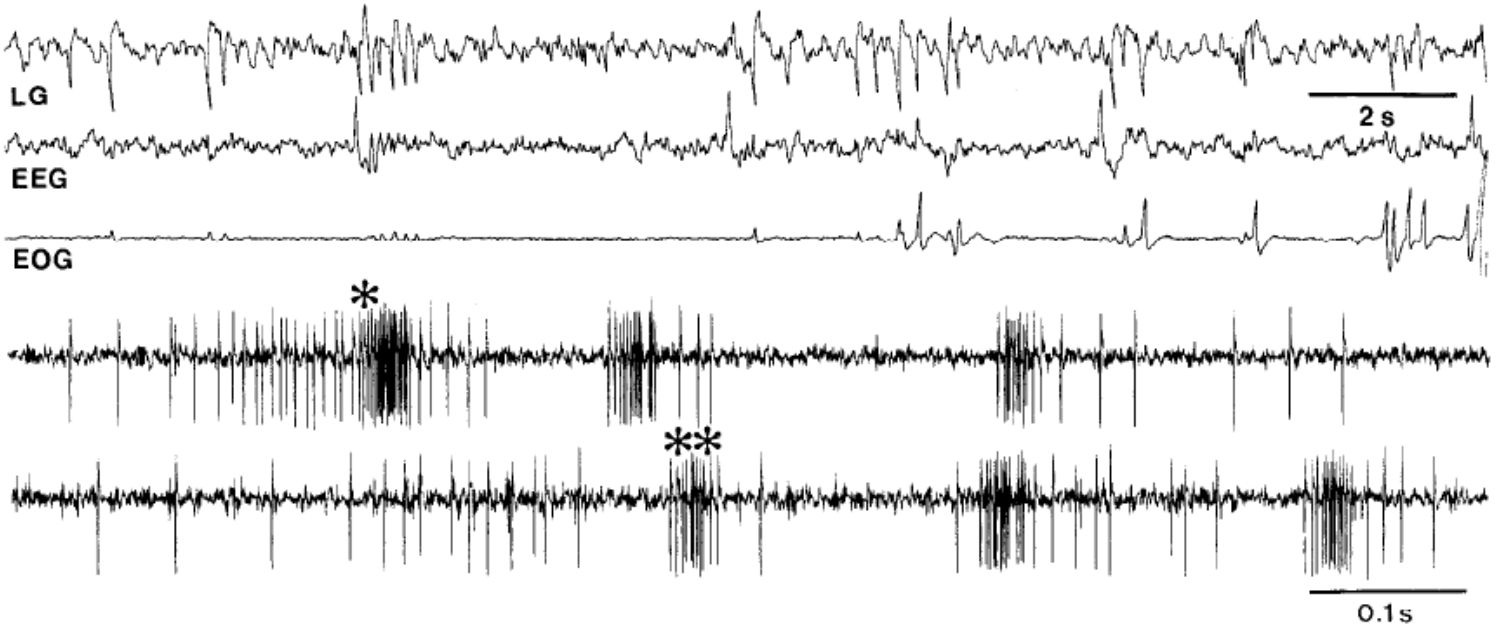
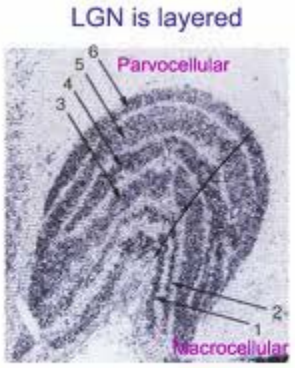
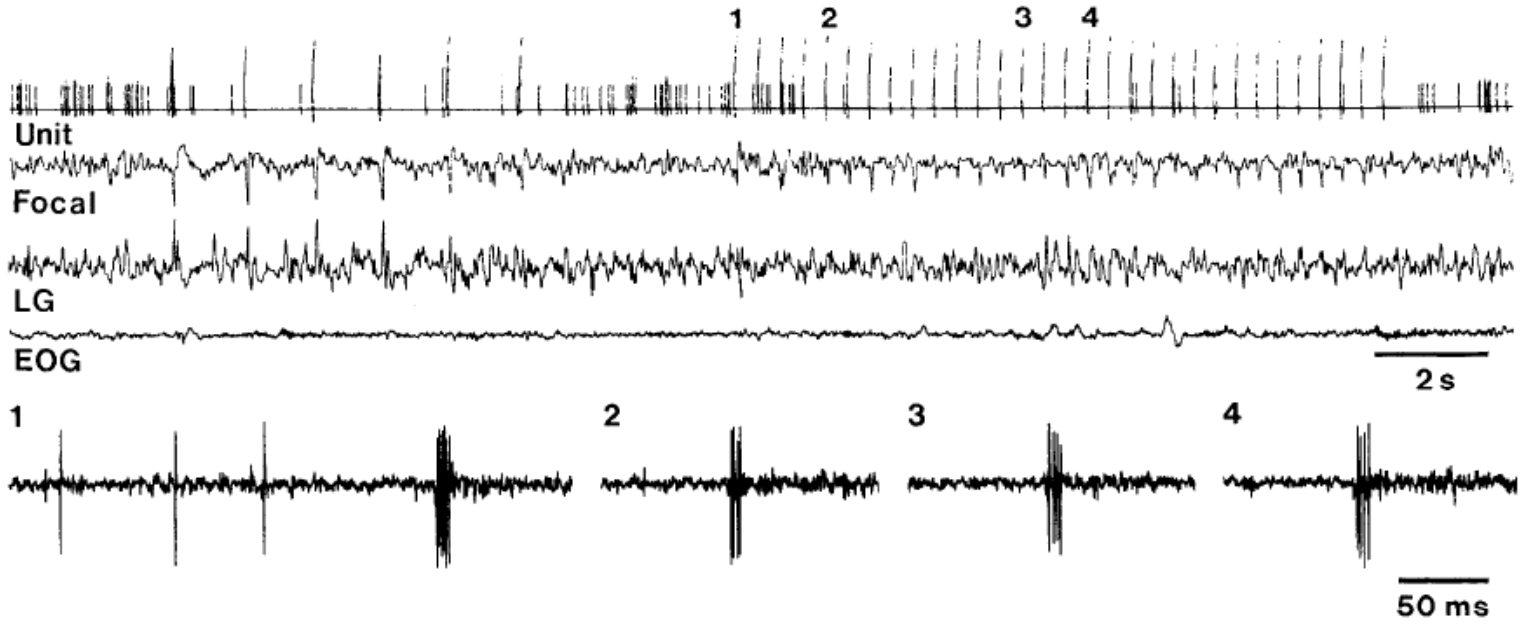
REM sleep is characterized by phasic events generated by bursting of brainstem reticular formation neurons – these 'events' may take the form of eye movements, twitches of non-axial musculature, and/or LFP events in the lateral geniculate nucleus that are called 'PGO waves'



Steriade et al., 1990, J. Neuroscience



PGO spikes can also be elicited in waking states, but primarily in response to surprise stimuli (such as a hand clap) that attracts attention in the form of an orienting response

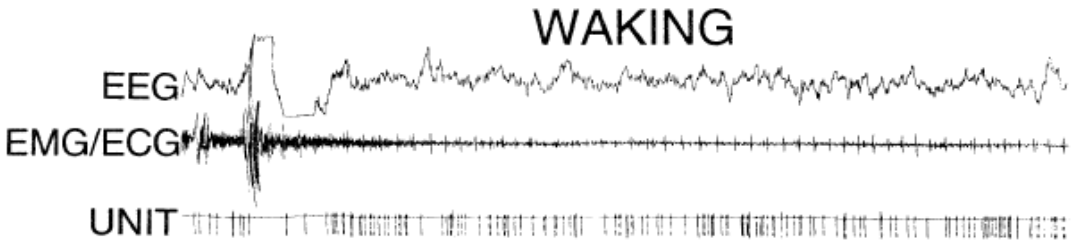


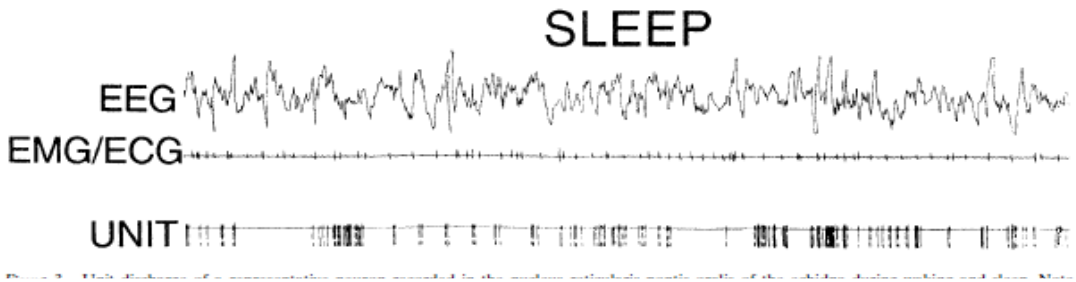
Steriade et al., 1990, J. Neuroscience

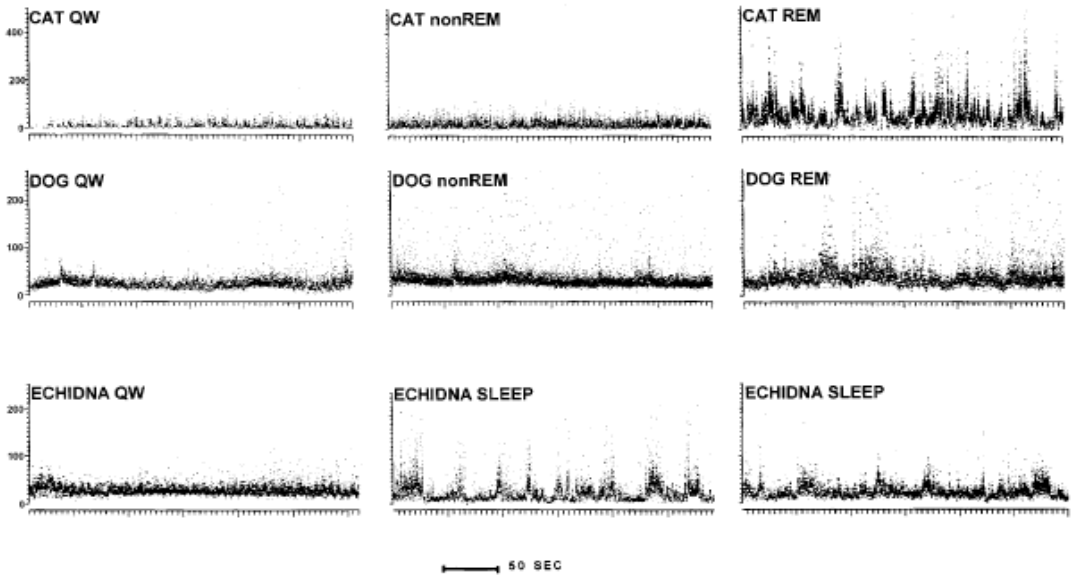
the mysterious echidna, a member of the monotreme order of mammals

at first thought to be the only mammal to lack REM sleep

later, Siegel shows that echidna non-REM (slow-wave) sleep is punctuated by REM-like brainstem burst events



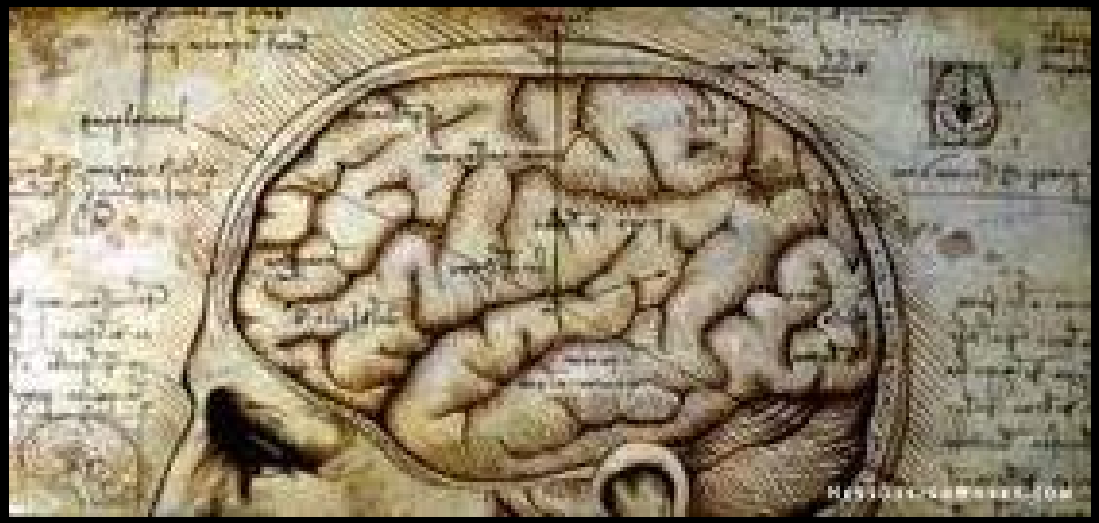




Siegel et al., 1996 J. Neuroscience.

from sleep to attention – lecture 3 – April 6, 2012

control of sleep/wake state production I



The Common Sense [senso comune], is that which judges of things offered up to it by the other senses. The ancient speculators have concluded that that part of man which constitutes his judgment is caused by a central organ to which the other five senses refer everything by means of impressibility [impressiva]; and to this centre they have given the name Common Sense. And they say that this Sense is situated in the centre of the head between Sensation and Memory. And this name of Common Sense is given to it solely because it is the common judge of all the other five senses i.e. Seeing, Hearing, Touch, Taste and Smell. This Common Sense is acted upon by means of Sensation which is placed as a medium between it and the senses. Sensation is acted upon by means of the images of things presented to it by the external instruments, that is to say the senses which are the medium between external things and Sensation. In the same way the senses are acted upon by objects. Surrounding things transmit their images to the senses and the senses transfer them to the Sensation. Sensation sends them to the Common Sense, and by it they are stamped upon the memory and are there more or less retained **according to the importance or force of the impression**. That sense is most rapid in its function which is nearest to the sensitive medium and the eye, being the highest is chief of the others. Of this then only we will speak, and the others we will leave in order not to make our matter too long. Experience tells us that the eye apprehends ten different natures of things, that is: Light and Darkness, one being the cause of the perception of the nine others, and the other its absence:--Colour and substance, form and place, distance and nearness, motion and stillness. – **Leonardo Da Vinci**

themes –

Brain mechanisms for sleep and attention overlap extensively. For example, the cerebral cortex, where conscious perception is realized, undergoes radical changes in the patterning of synaptic potentials (as revealed by EEG/LFP recordings) between the lowest-attention state (stage ¾ non-REM sleep) and high attention states (waking, REM sleep).

Changes in sleep/wake state and attention are sometimes mediated by groups of neurons that are highly interconnected (brainstem reticular and thalamic reticular neurons).

The classroom is very hot.

what do we know so far?

A definition for sleep that can be universally applied is difficult to come by. However, by combining the use of arousal thresholds, behavioral measurements (e.g., amount of movement or posture), and electrophysiological measurements a reasonably complete definition can be attained. Still, we end up with two very different forms of sleep which stand at opposite ends of the spectrum of attention.

At the core of changes in the form of cortical EEG/LFPs that accompany changes in sleep/wake state (wake, non-REM sleep stages 1-4, REM sleep), are changes in the activity of brainstem reticular and thalamic reticular neurons.

the mysterious echidna, a member of the monotreme order of mammals

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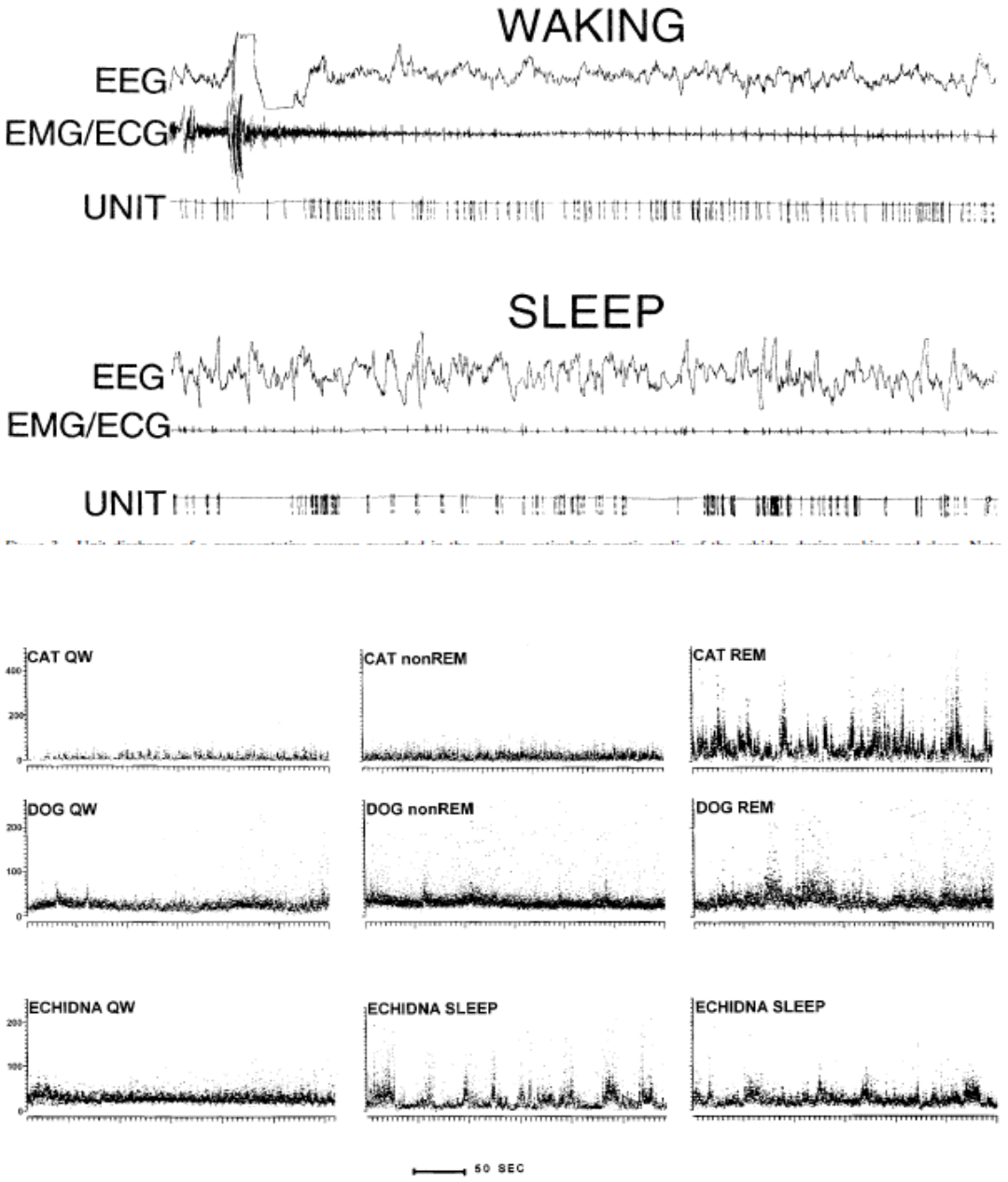

Siegel et al., 1996 J. Neuroscience.

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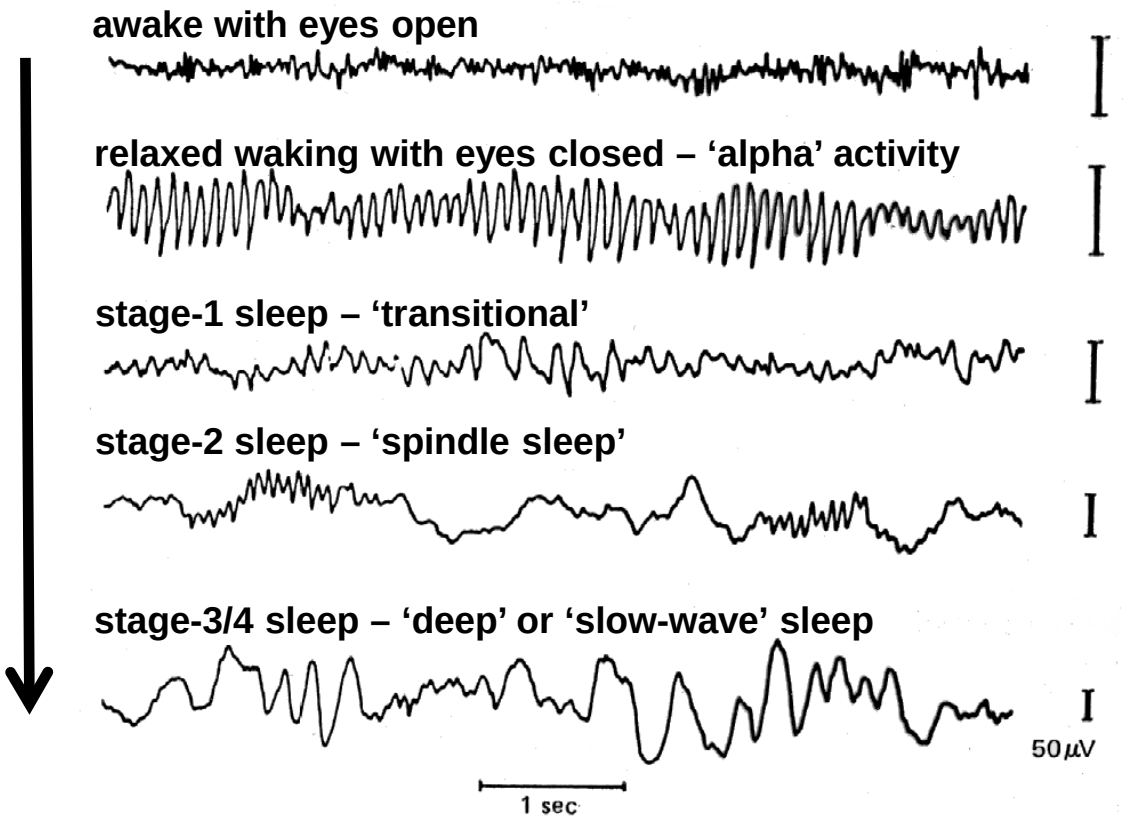

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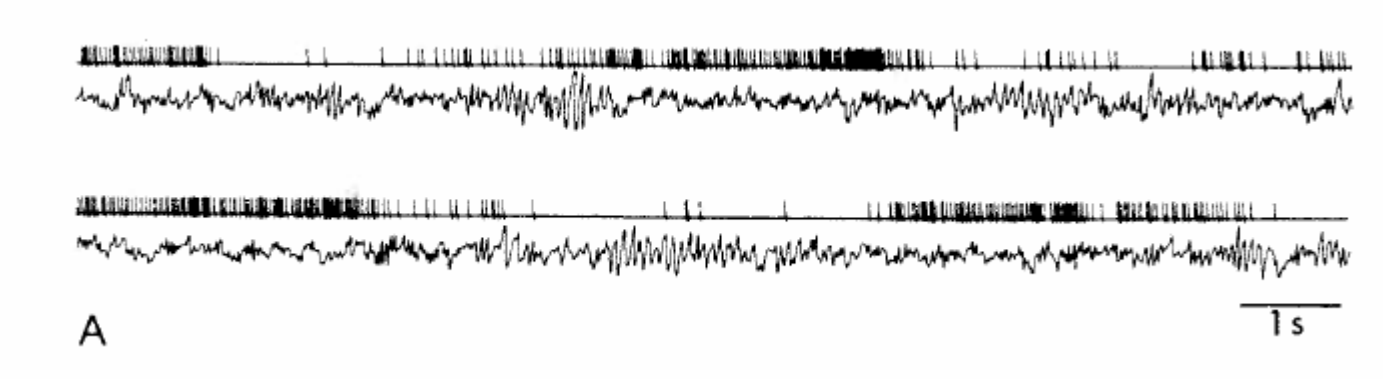

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transitions between sleep and wake cortical EEG/LFPs involve interactions between:

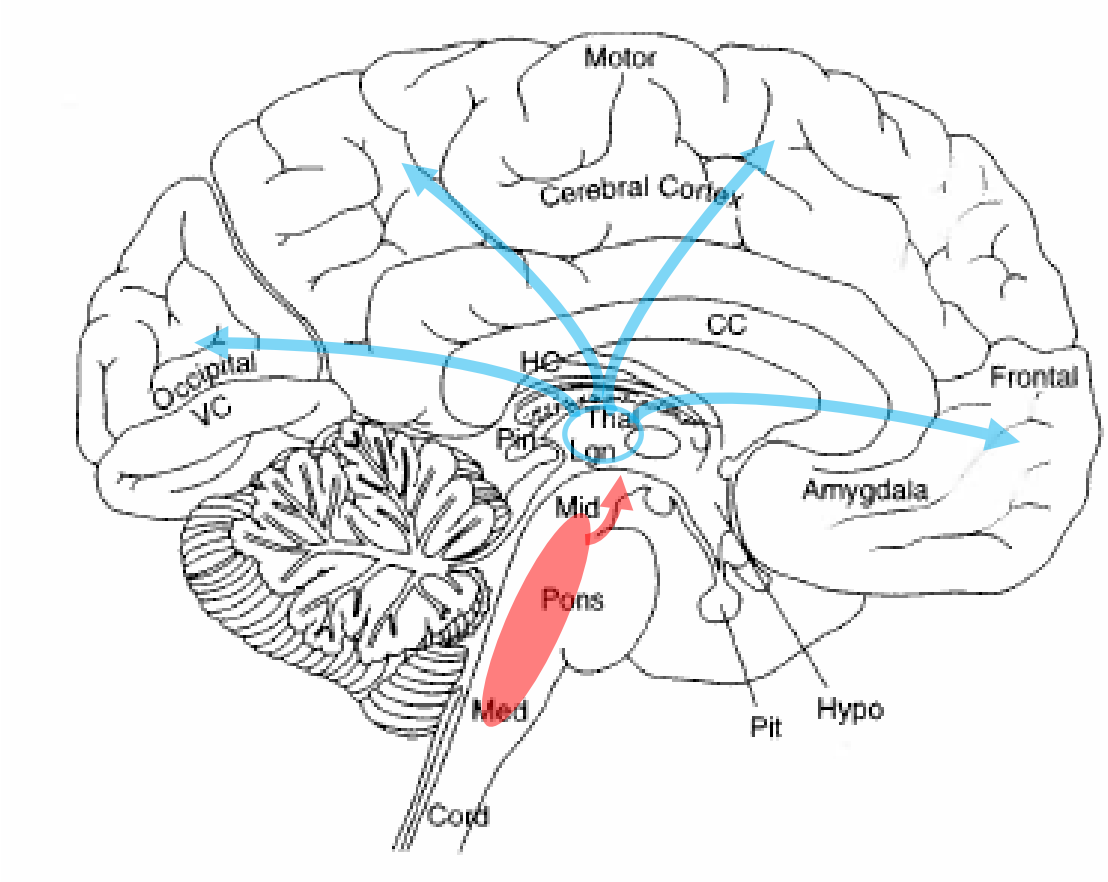
-cerebral cortex

-specific thalamic nuclei

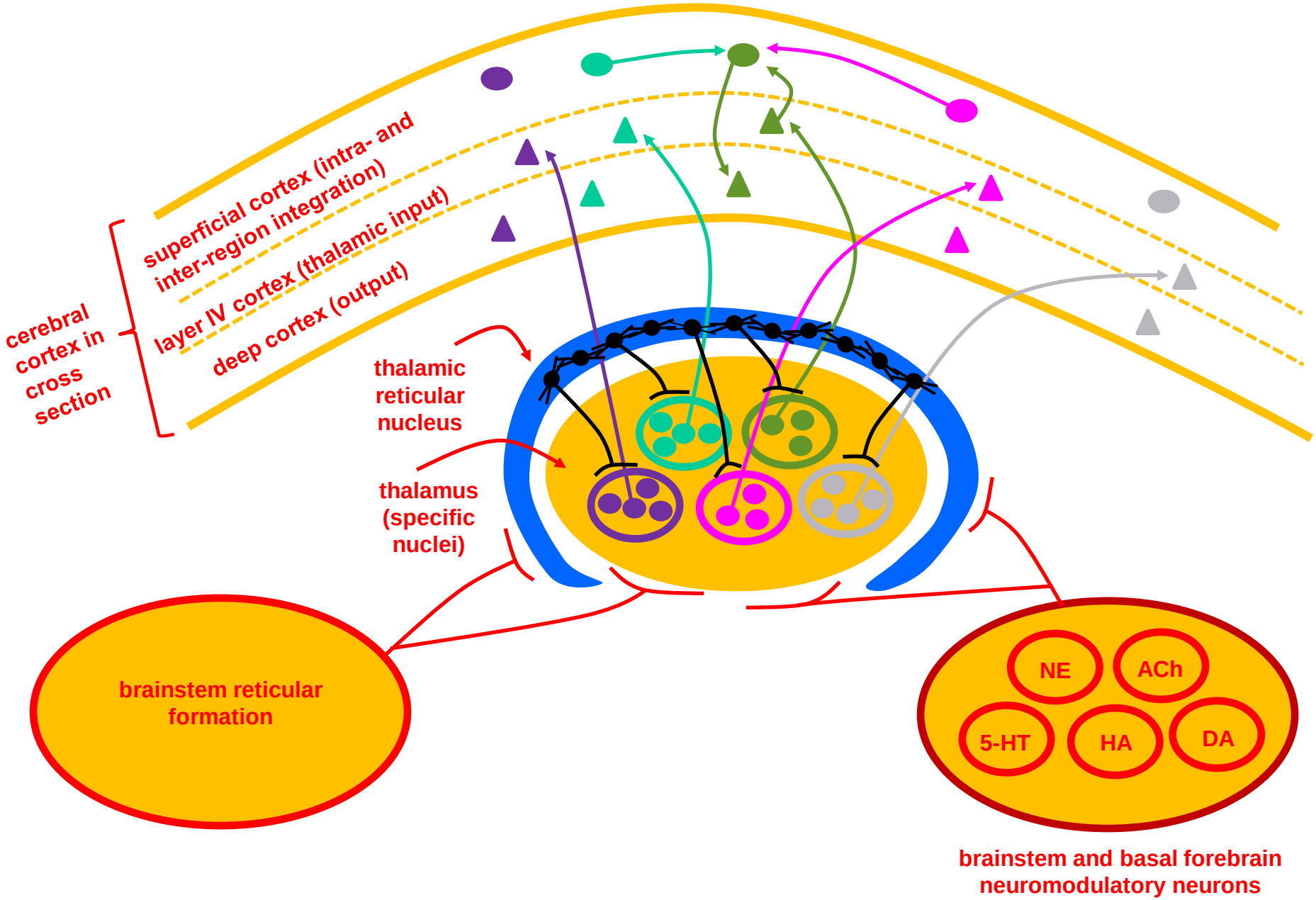
-thalamic reticular neurons

-brainstem reticular neurons

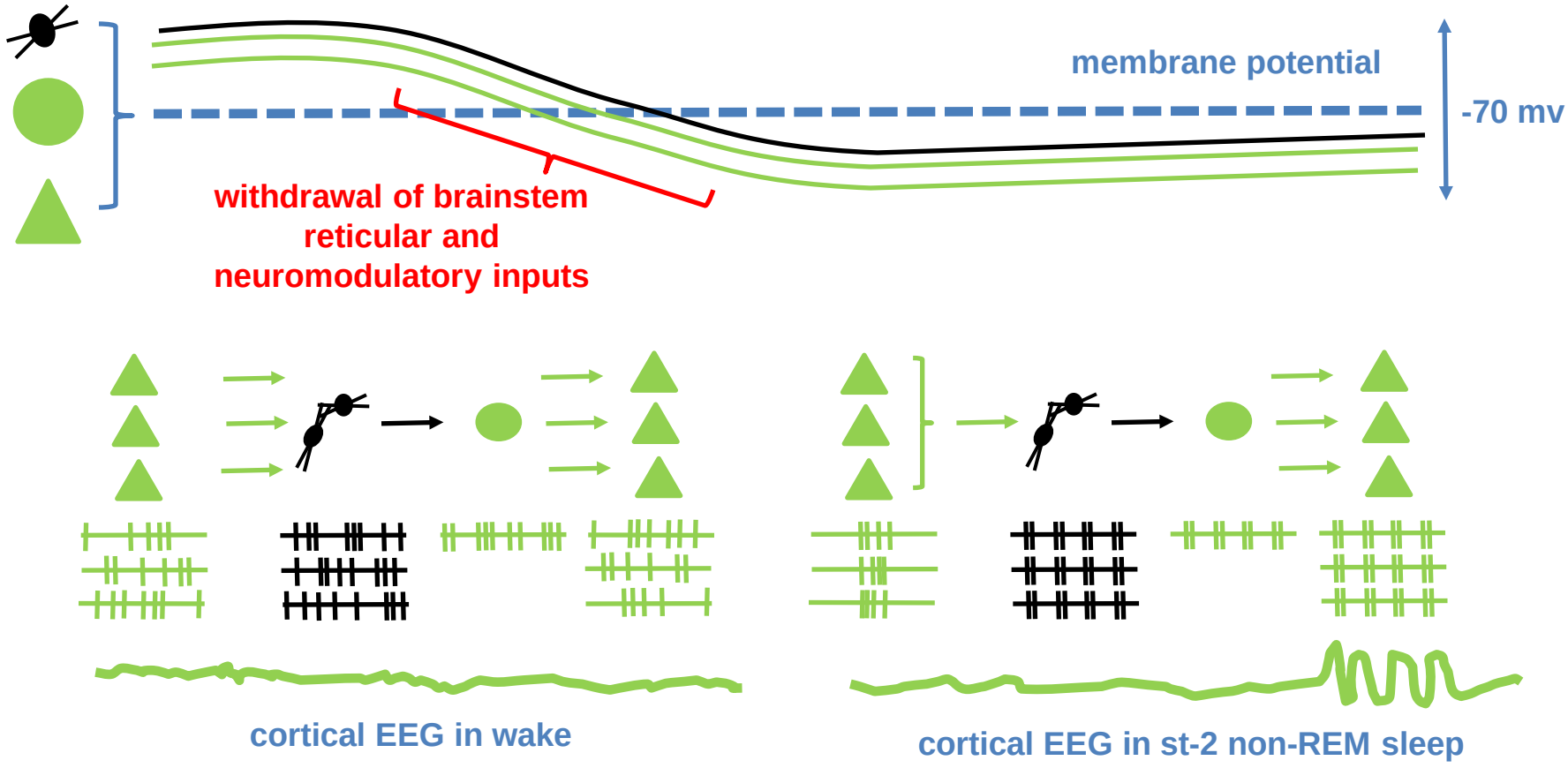
-brainstem/basal forebrain neuromodulatory neurons



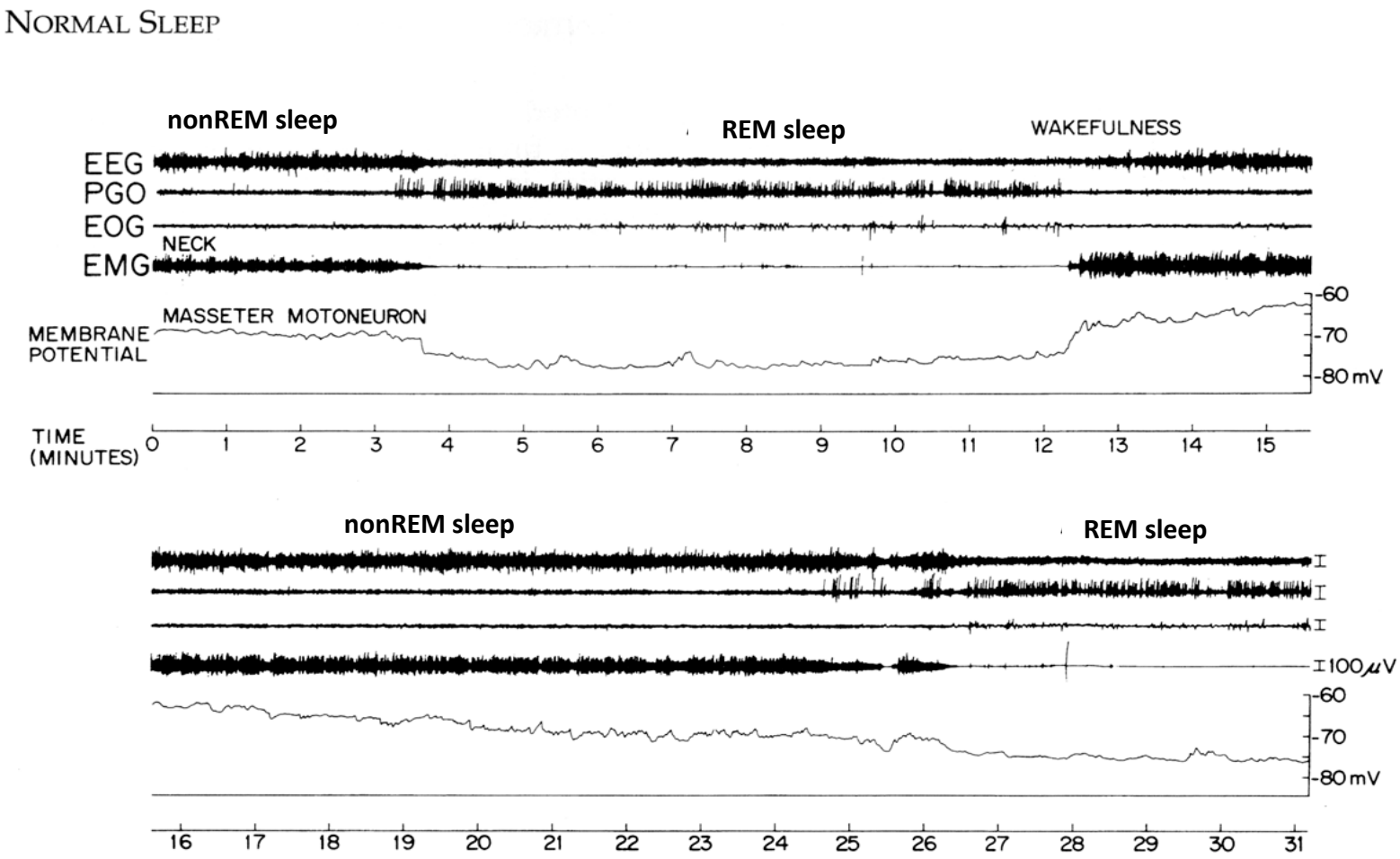
the control of cortex-wide activity patterns in schematic



With reduction in depolarizing input from brainstem reticular neurons and neuromodulatory neurons, thalamic neurons respond to excitation by producing spindle oscillations. During non-REM sleep, when such reductions occur, thalamic reticular neurons are excited en masse by cortical neurons. The resulting spindle oscillations of thalamic reticular neurons entrain cortically-projecting thalamic neurons (of the specific nuclei).



‘PGO’ spikes differentiate the thalamic and cortical patterns of REM sleep and waking



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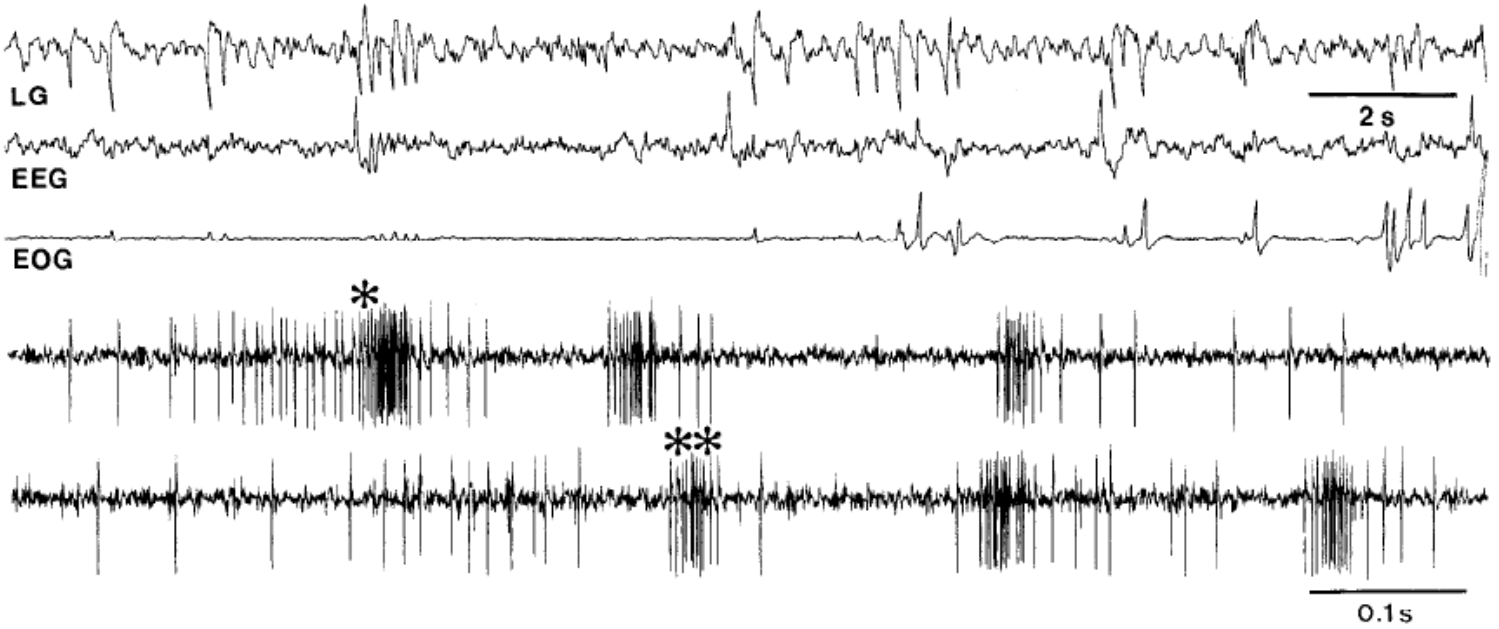

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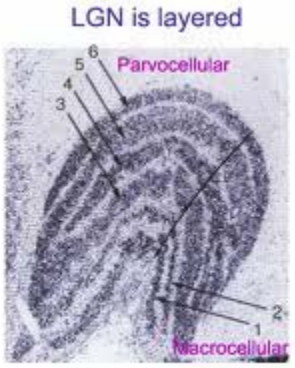

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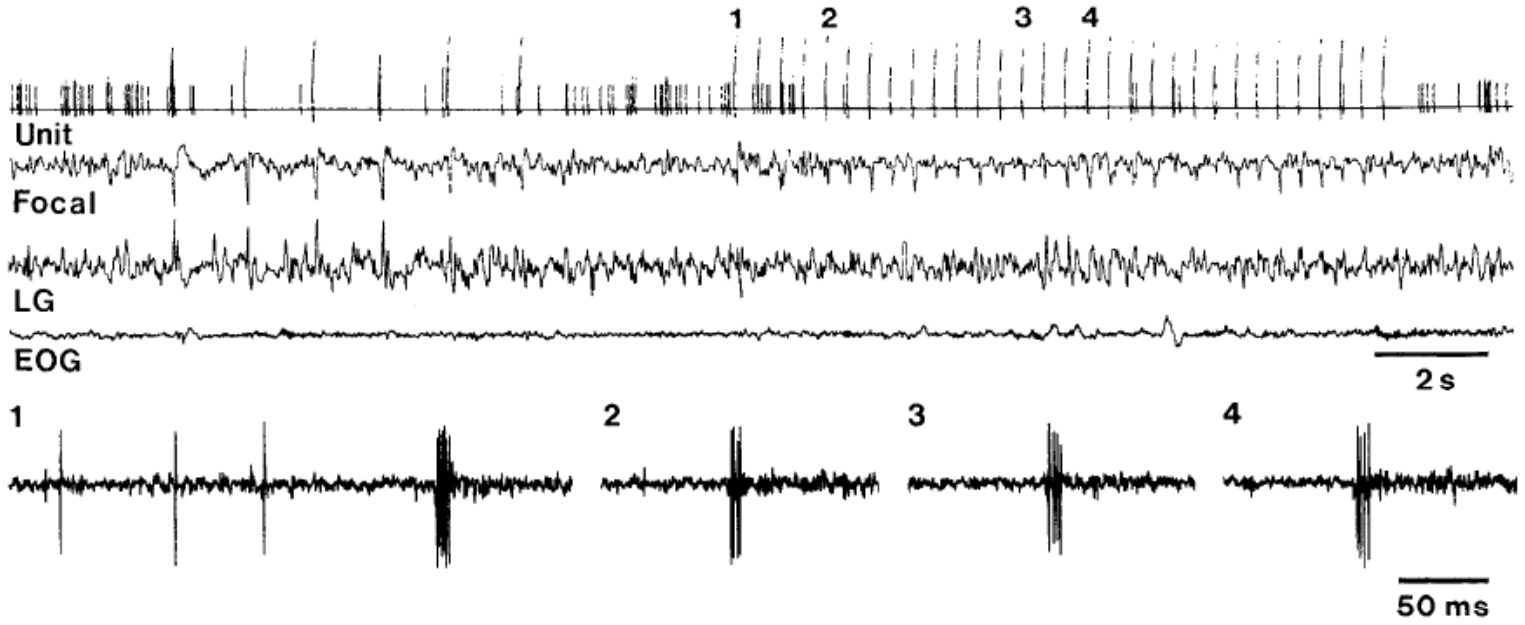

Steriade et al., 1990, J. Neuroscience

But…what makes the brainstem reticular formation and neuromodulatory systems depress to initiate non-REM sleep?

And…what makes REM sleep a ‘sleep’ state?

from sleep to attention – lecture 4 – April 9, 2012

control of sleep/wake state production II

"From the moment of my birth, the angels of anxiety, worry, and death stood at my side, followed me out when I played, followed me in the sun of springtime and in the glories of summer. They stood at my side in the evening when I closed my eyes, and intimidated me with death, hell, and eternal damnation. And I would often wake up at night and stare widely into the room: Am I in Hell?" - Edvard Munch

themes –

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At the core of changes in the form of cortical EEG/LFPs that accompany changes in sleep/wake state (wake, non-REM sleep stages 1-4, REM sleep), are changes in the activity of brainstem reticular and thalamic reticular neurons.

Changes in thalamo-cortical activity patterns (as measured through cortical EEG) are brought about by changes in the activity of brainstem reticular neurons and neuromodulatory neurons (ACh, NE, HA, DA, 5-HT, orexin).

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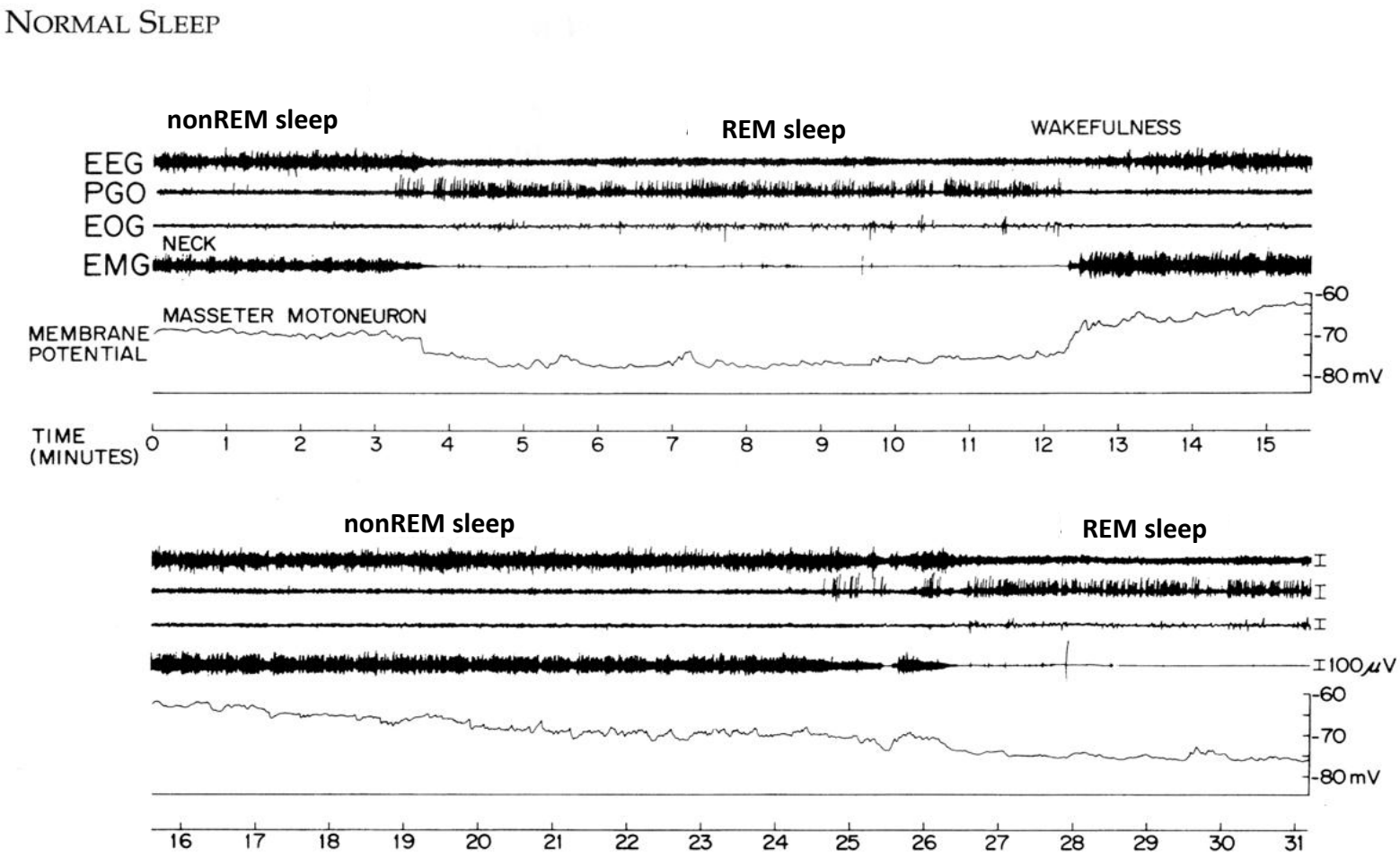

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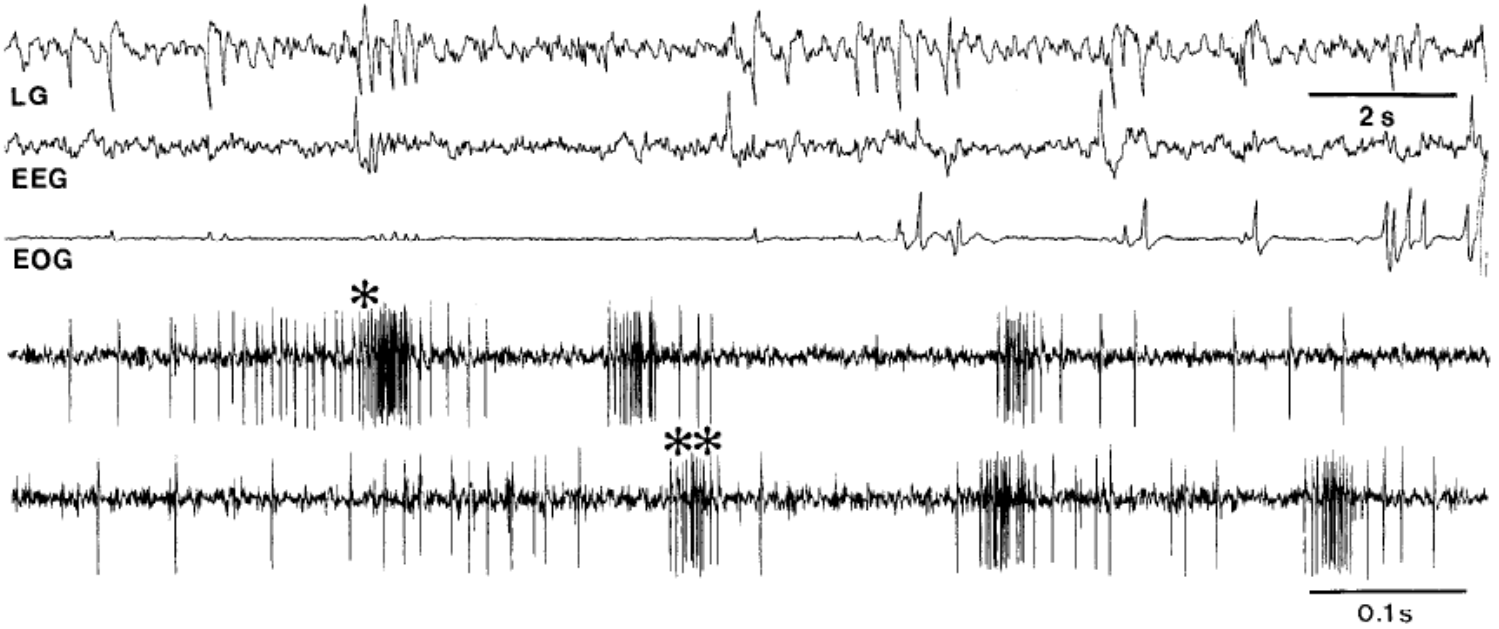

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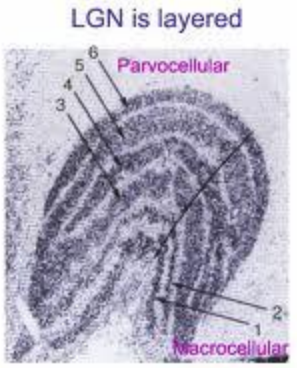

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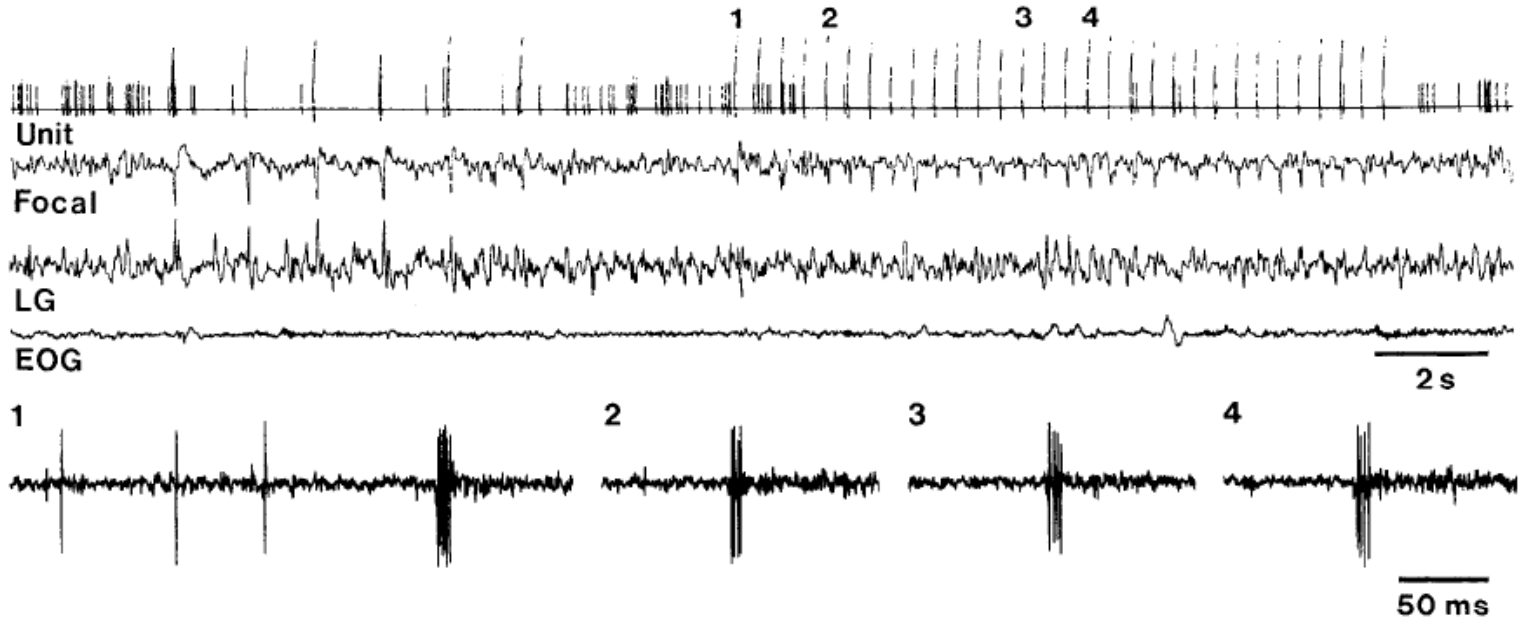
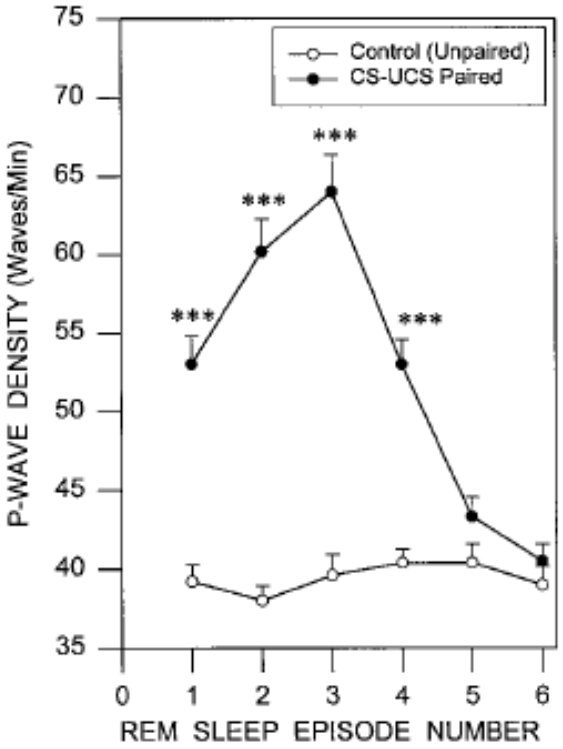
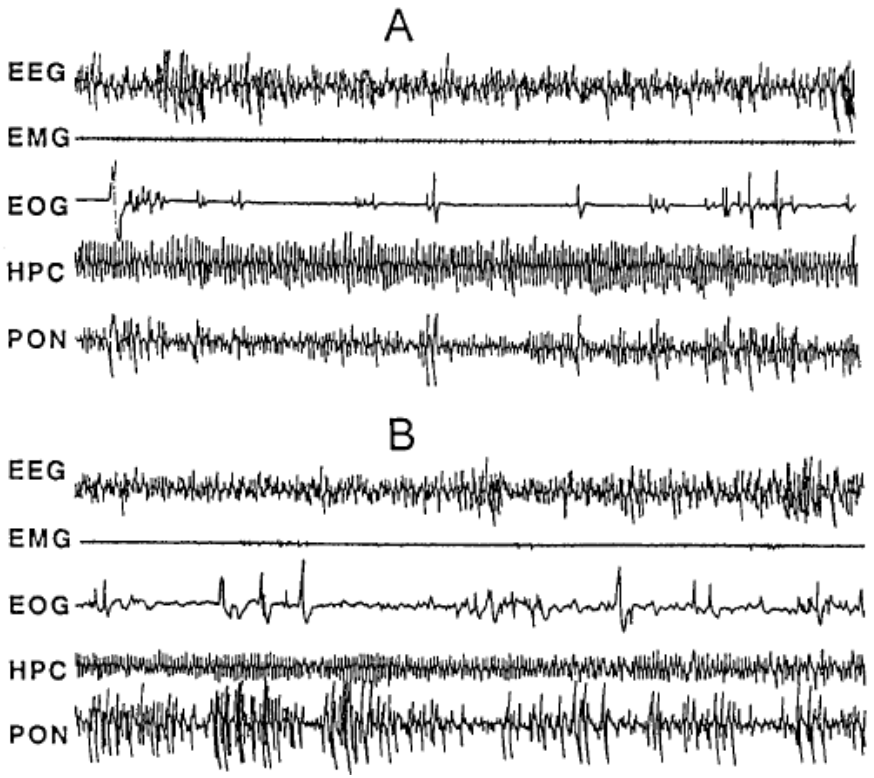


Steriade et al., 1990, J. Neuroscience

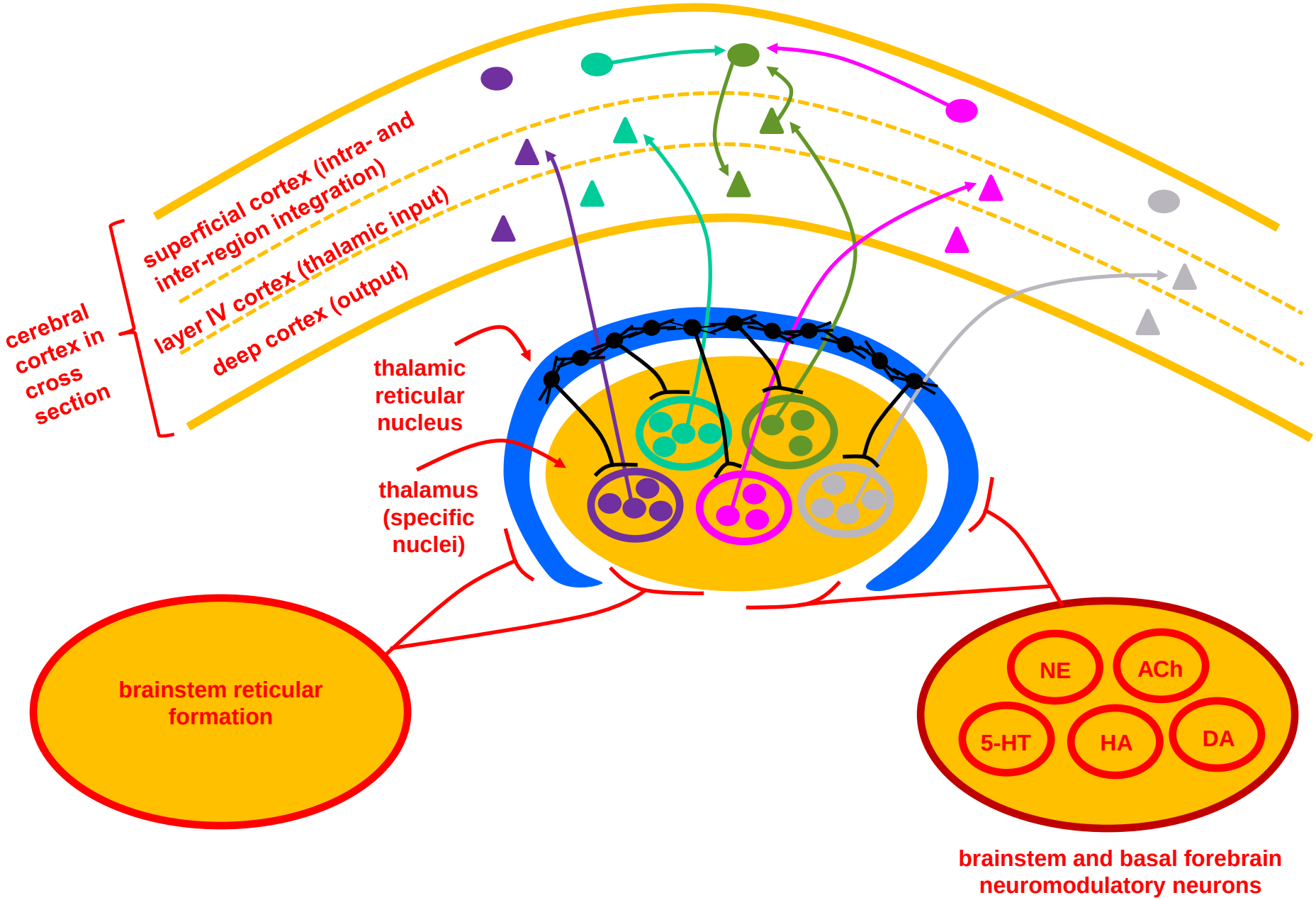
shock avoidance training increases PGO spike density in subsequent sleep





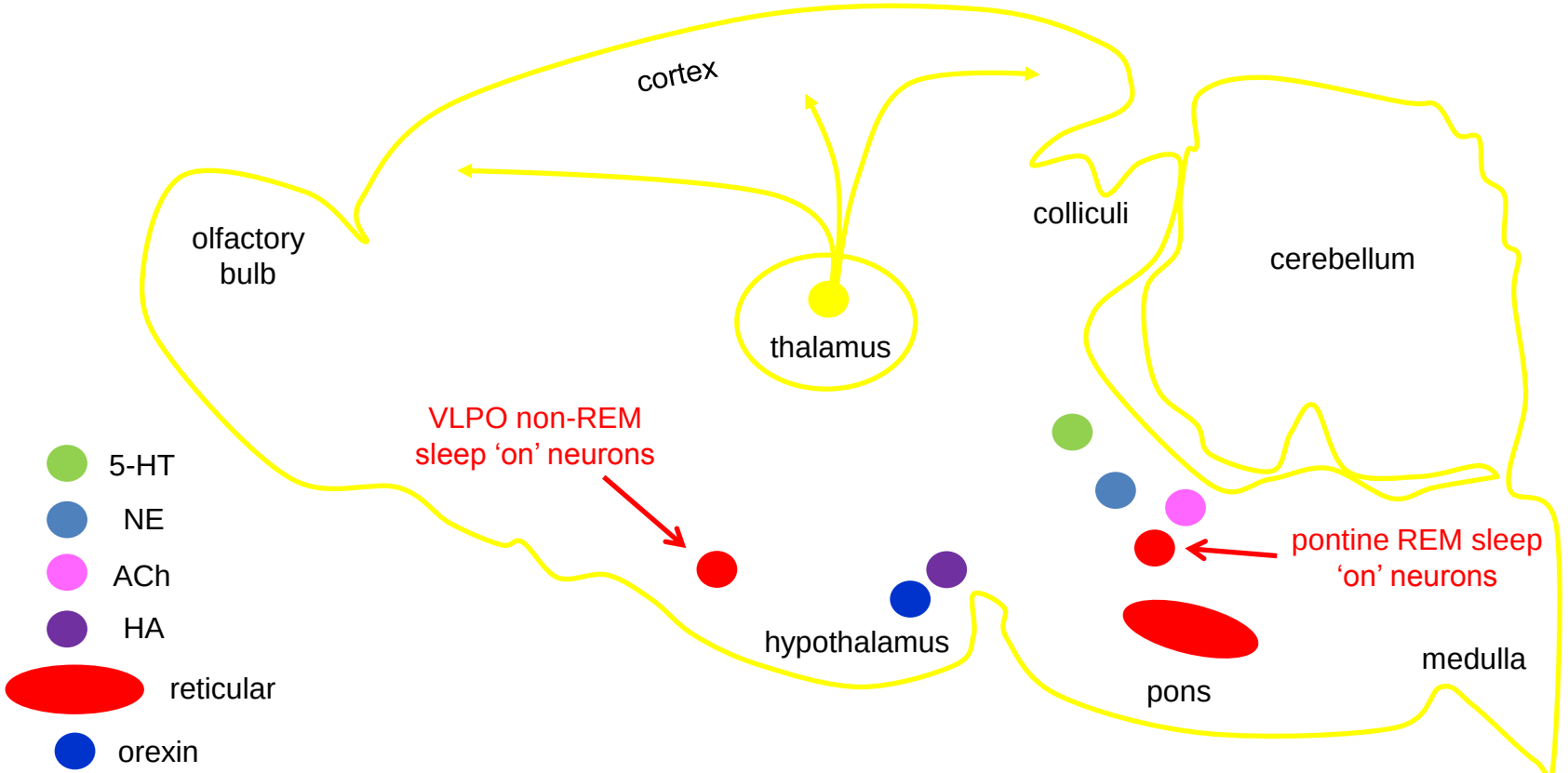
Datta, 2000 J. Neuroscience

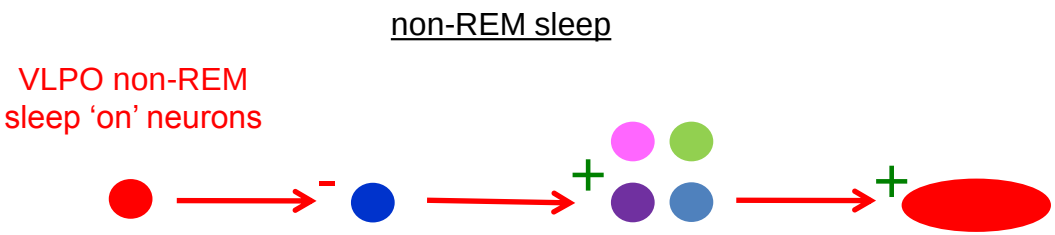
the control of cortex-wide activity patterns in schematic

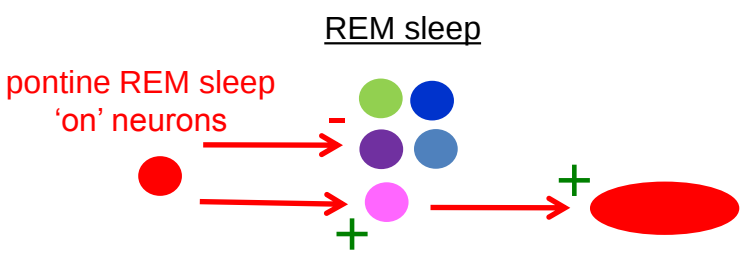


Q: What alters the activity of brainstem reticular neurons and neuromodulatory neurons to yield the patterns of thalamic and cortical activity that accompany wake, non-REM sleep, and REM sleep?

A: hypothalamic 'non-REM sleep on' and pontine 'REM sleep on' neurons
A: absence of movement and absence of environmental stimuli







	waking	NREM	REM
cortical EEG / LFP	fast/low-amp/irregular	slow-waves/spindles	fast/low-amp/irreg
trunk muscle tone	high	minimal	absent (paralysis)
eye movements	frequent	none	frequent
heart rate	high/variable	low/regular	high/variable
breathing rate	high/variable	low/regular	high/variable
mentation	vivid	minimal / transient	vivid
hippo. LFP	theta rhythm	slow-waves	theta rhythm
PGO spikes	few	none	frequent
arousal thresholds	low	highest	variable
cortex/thalamus	fast/irregular	slower/burst-pause	fast/irregular
ACh neurons	high rate	lowest rate	highest rate
NE neurons	high rate	very low rate	inactive (REM-off)
5-HT neurons	high rate	low rate	inactive (REM-off)
HA neurons	high rate	very low rate	inactive (REM-off)
DA neurons	moderate rate	moderate rate	moderate rate
VLPO neurons	inactive	highest rates	inactive
REM-on neurons	inactive	inactive	high rate
orexin neurons	high rate	low rate	low rate

* red coloring denotes major distinctions between wake and REM

so…a dream has to originate somewhere doesn't it?