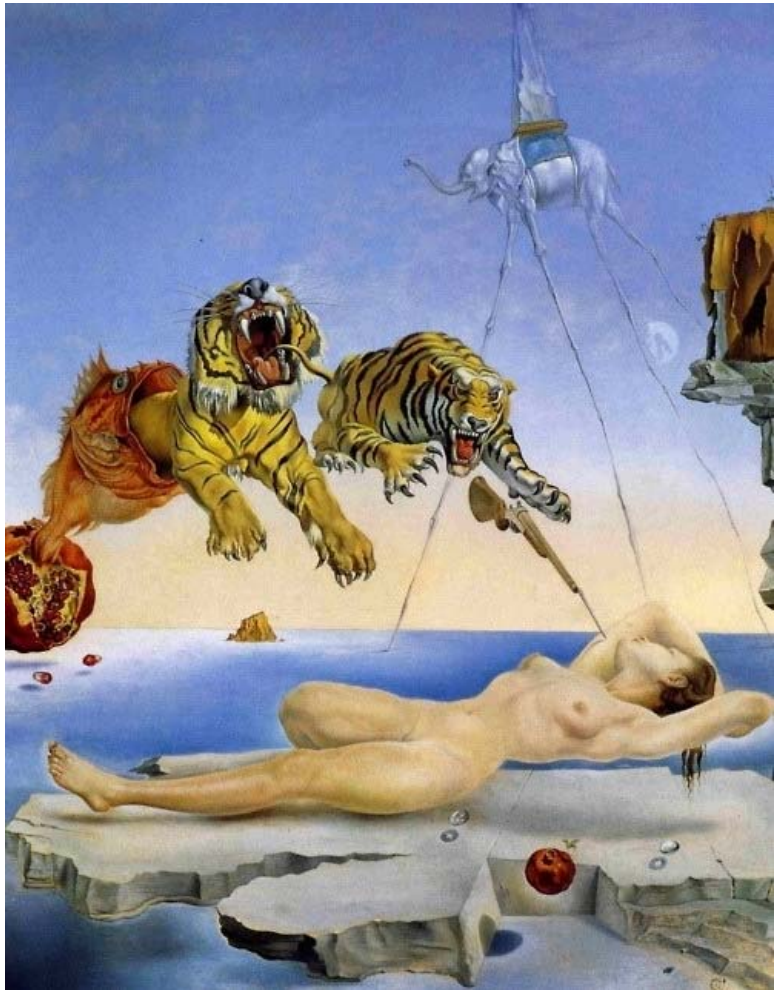
Functional Neurobiology Lecture

Jan 28, 2016

REM Sleep: the Basics & History

Yu Hayashi

Awkward dreams



Dali “Dream Caused by the Flight of a Bee Around a Pomegranate a Second Before Awakening “

Dreams are awkward

How are dreams formed?
Why do we dream?

Discovery of REM sleep

Aserinsky and Kleitman, Science, 1953

During sleep, there is a phase accompanied by rapid eye movement

Rapid Eye Movement Sleep

Discovery of REM sleep

Aserinsky and Kleitman, Science, 1953

Regularly Occurring Periods of Eye Motility, and Concomitant Phenomena, During Sleep[1]

Respiratory & heart rate ↑ , Dreaming ↑

Eugene Aserinsky[2] and Nathaniel Kleitman

Department of Physiology, University of Chicago, Chicago, Illinois

Slow, rolling or pendular eye movements such as have been observed in sleeping children or adults by Pietrusky (*1*), De Toni (*2*), Fuchs and Wu (*3*), and Andreev (*4*), and in sleep and anesthesia by Burford (*5*) have also been noted by us. However, this report deals with a different type of eye movement—rapid, jerky, and binocularly symmetrical—which was briefly described elsewhere (*6*).

Jouvet's group in France

EEG and EMG recording from sleeping cats

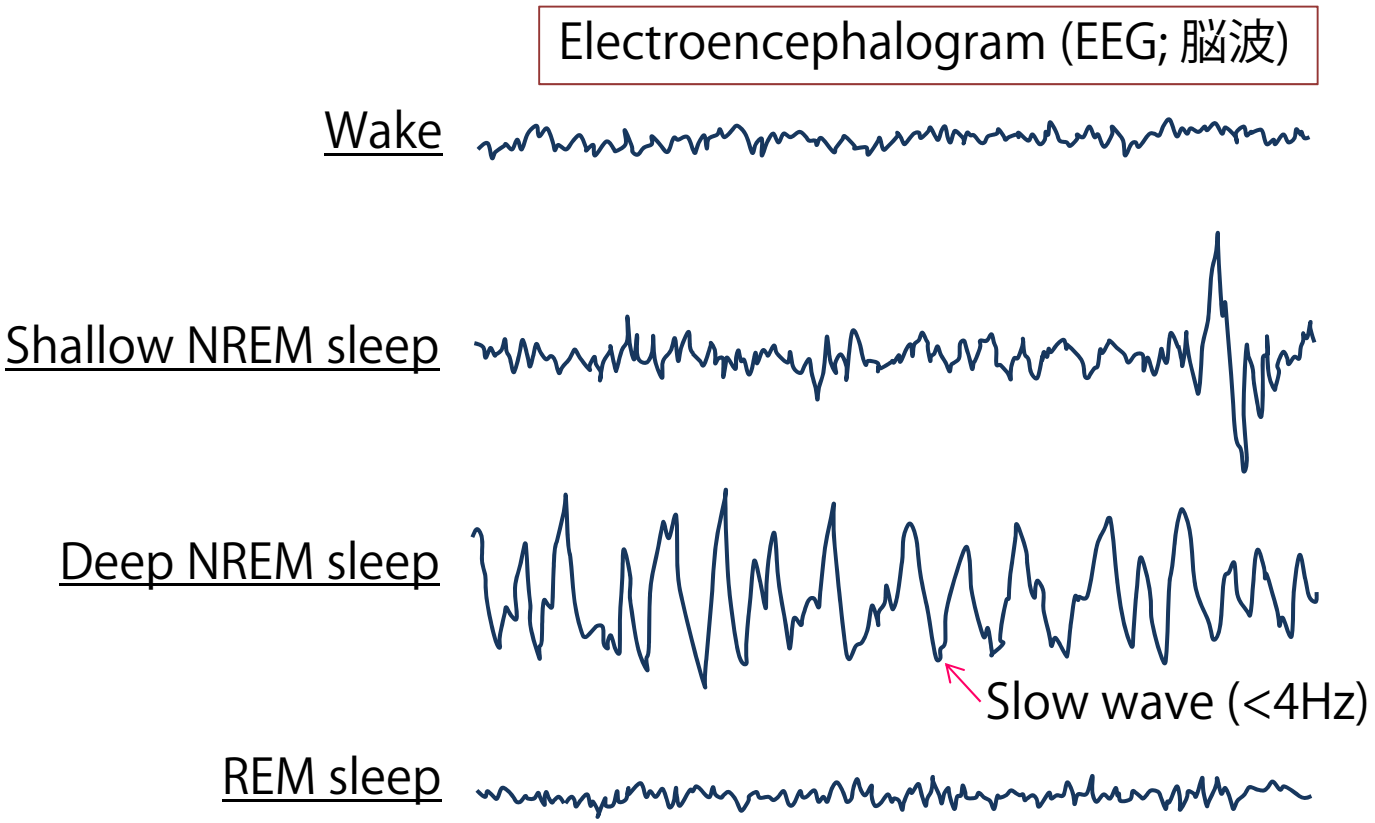
EEG → looks like wake
EMG → totally absent

"Paradoxical sleep (or PS)"

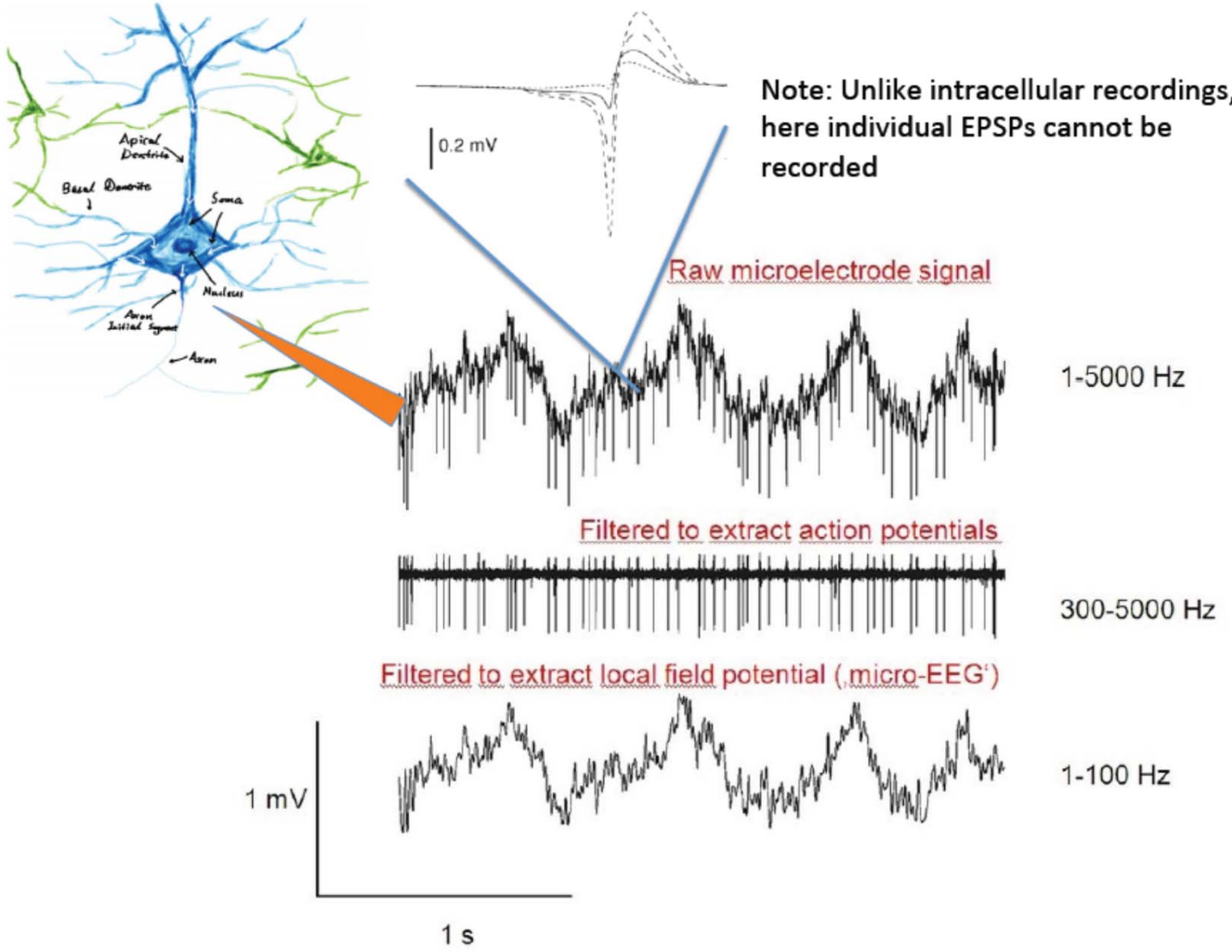
Jouvet et al.
Sur un stade d'activité é]ectrique cérébrale rapide au cours du sommeil physio]ogique. C.R. Soc. Biol. 1959

Jouvet and his students contribute most to the neural mechanism of REM sleep

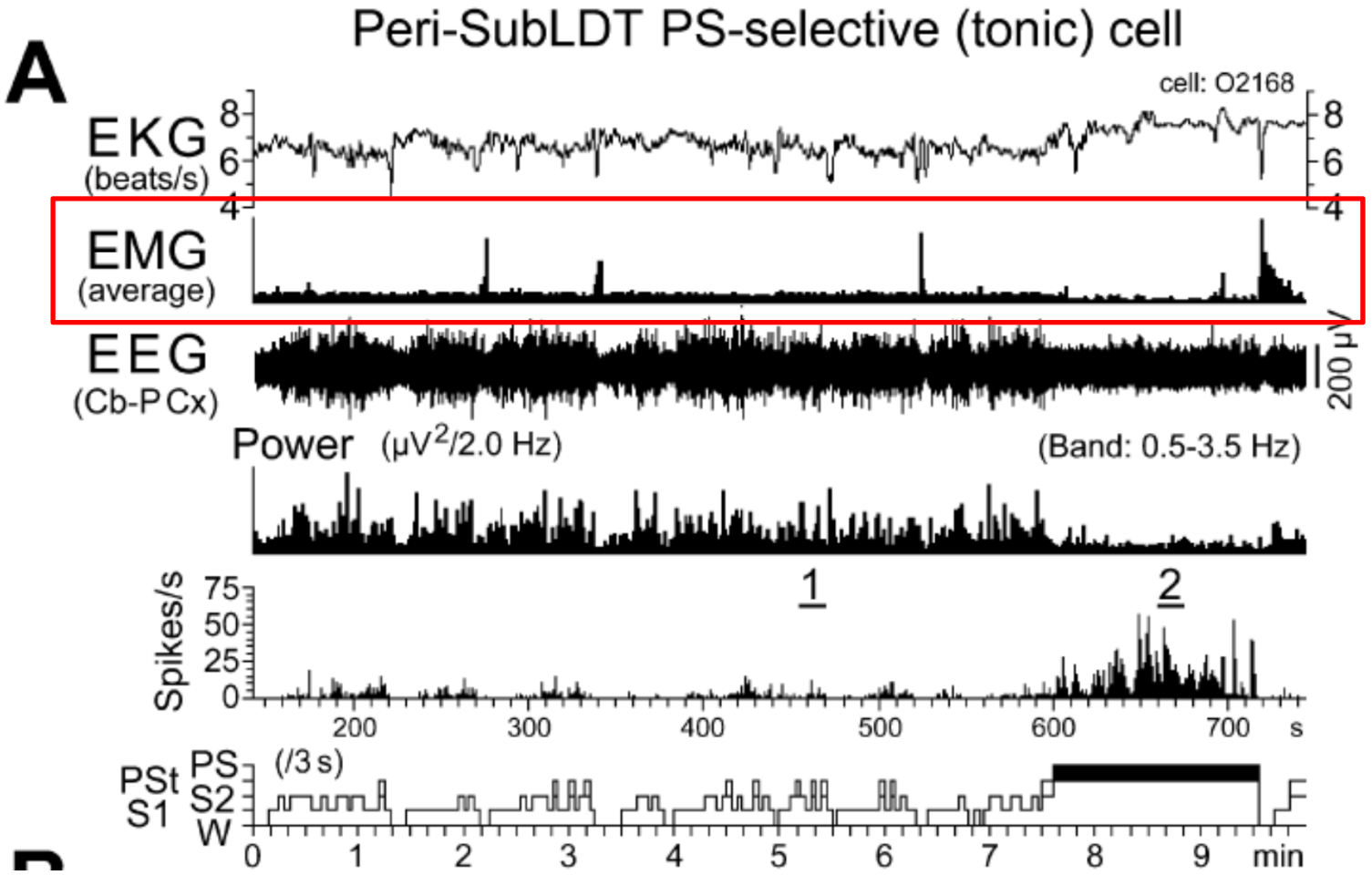
Electroencephalogram recording reveals sleep is not a homogeneous state



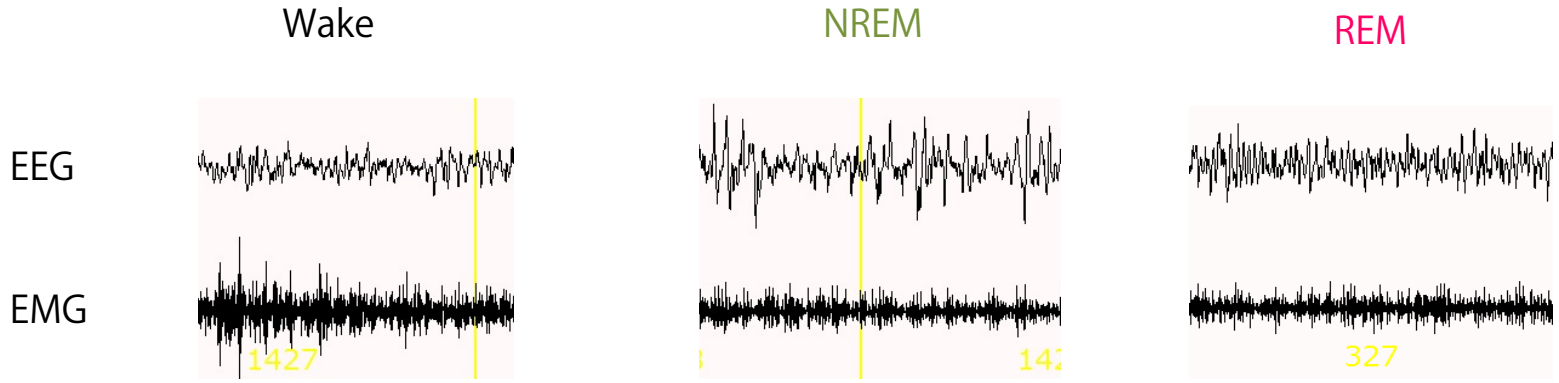
Multi-unit recording and local field potentials (LFP): Similar methods, different analyses



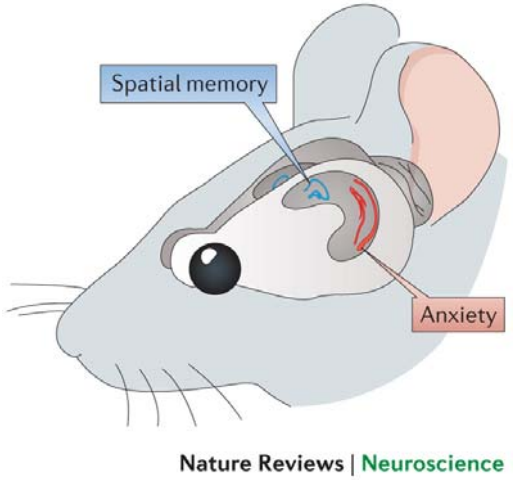
Loss of muscle tone is another important feature of REM sleep



In case of mice, REM sleep can be differentiated from wake by high theta wave

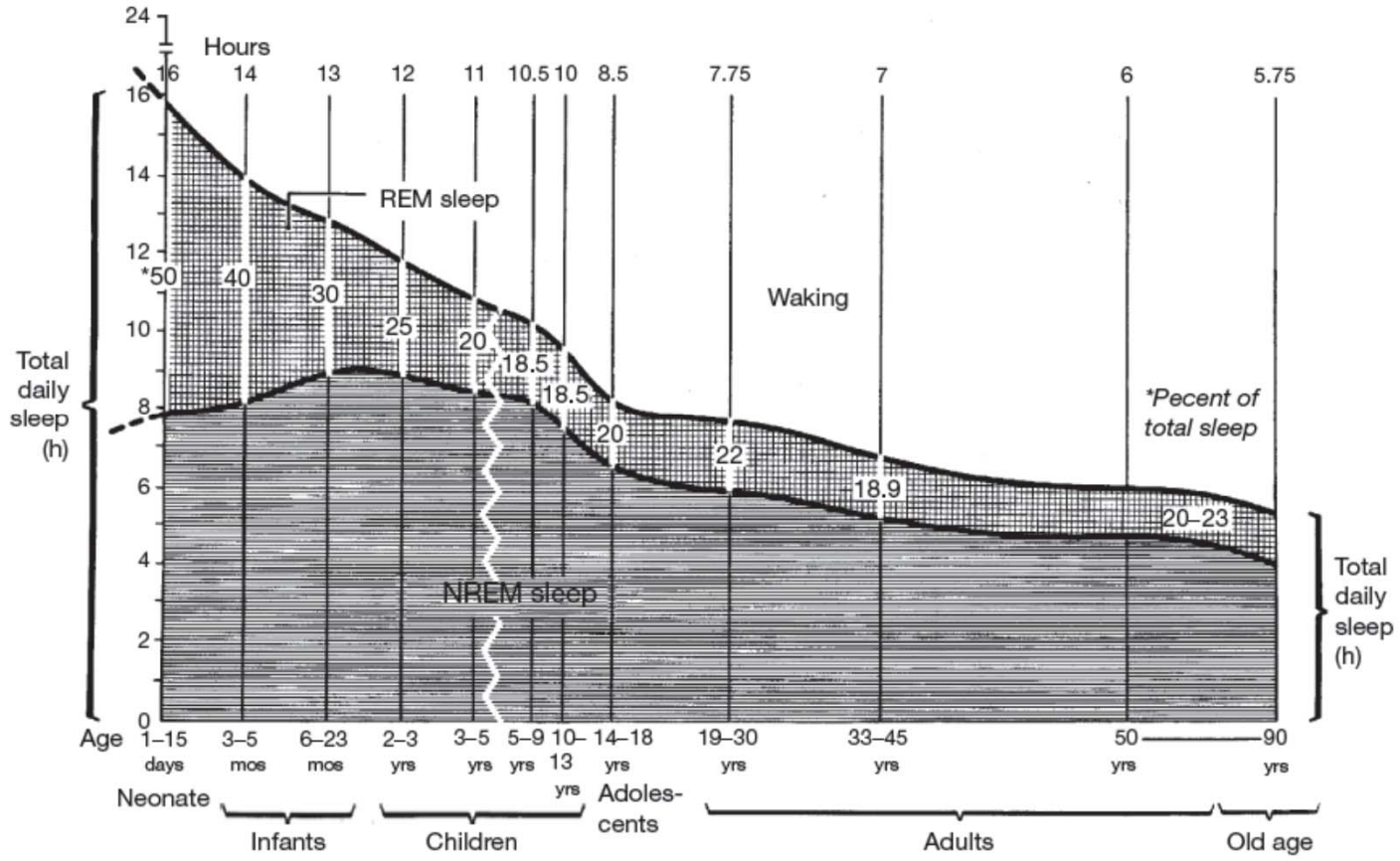


Theta waves are generated in the hippocampus



REM sleep and ontogeny

Roffwarg and Dement, Science (1966)
Ontogenetic development of the human sleep-dream cycle



REM sleep and phylogeny

Siegel, Science (2001)

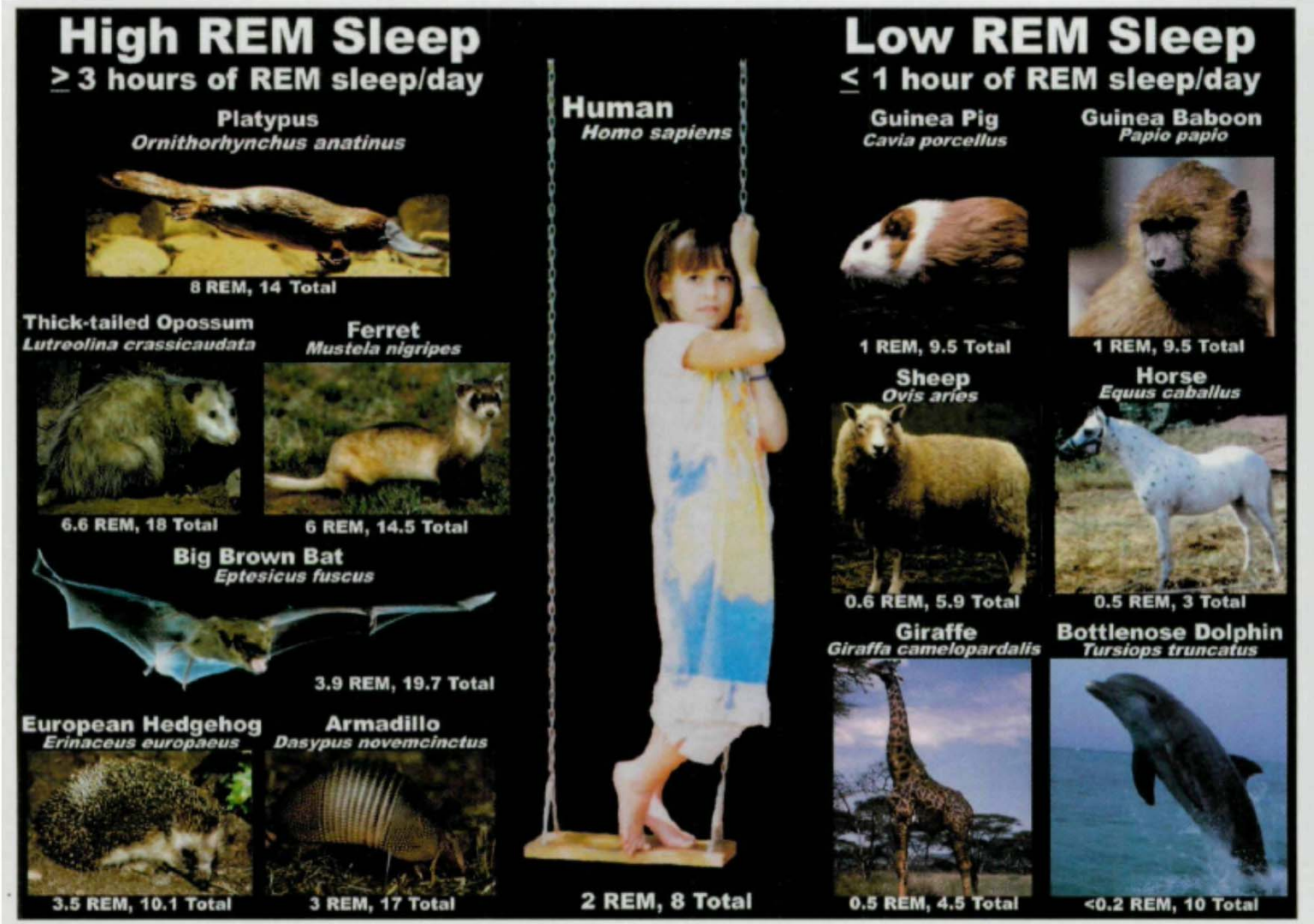
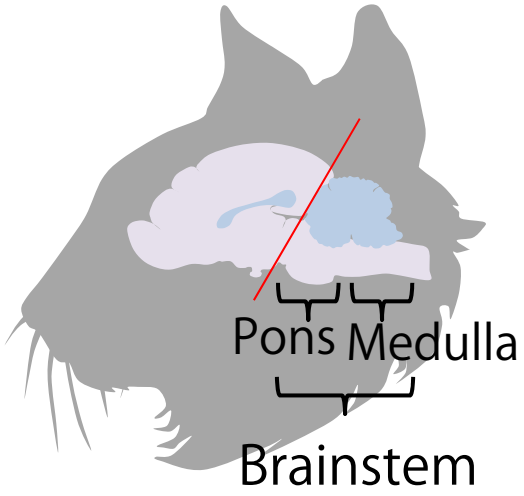
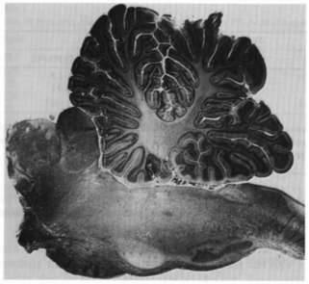


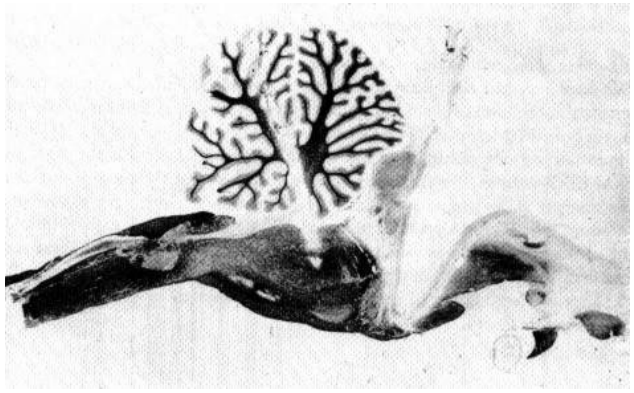
Fig. 1. Sleep durations in representative mammals. Daily REM sleep time in

opossum), Alden M. Johnson, California Academy of Sciences; ferret (photo is of

The “pontine” cat







Keep in an incubator and will survive for several days~weeks

Wake-like: Turning its head towards acoustic stimuli, regular respiration

REM sleep-like: Rapid eye movement, absence of muscle tone, active brainstem LFP

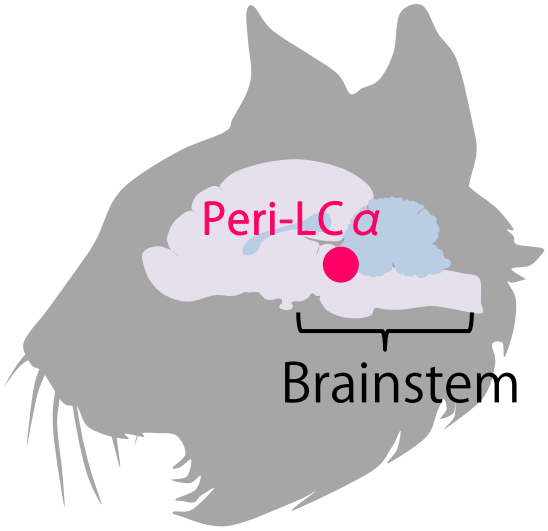
(No NREM sleep-like state)

Further studies narrowed down the REM sleep center to the “Peri-LC α”

The pontine “Peri-LC α”

Injection of carbachol rapidly induces REM sleep

Vanni-Mercier, Sakai K, Lin JS, Jouvet M, Arch Ital Biol, 1989



Is REM sleep primitive sleep?

1. Jouvet called REM sleep as the "rhombencephalic phase of sleep"

   ≒ brainstem

2. The brainstem is highly conserved among vertebrates

3. REM sleep is highly abundant in neonates

The brainstem also strongly regulates NREM sleep

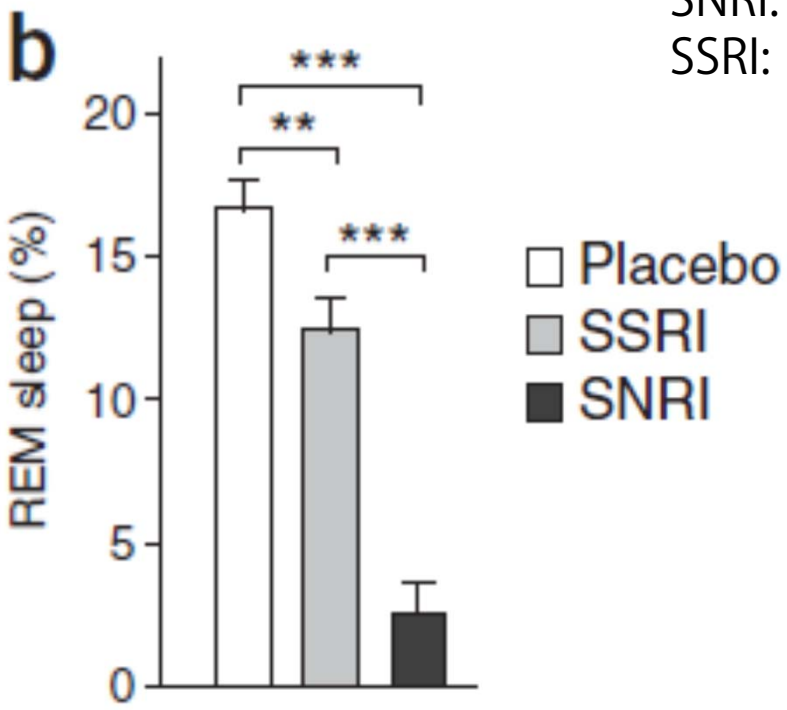
Anaclet et al. Nat Neurosci. 2014

The GABAergic parafacial zone is a medullary slow wave sleep–promoting center

Christelle Anaclet[1], Loris Ferrari[1], Elda Arrigoni[1], Caroline E Bass[2], Clifford B Saper[1], Jun Lu[1] & Patrick M Fuller[1]

Work in animals and humans has suggested the existence of a slow wave sleep (SWS)-promoting/electroencephalogram (EEG)-synchronizing center in the mammalian lower brainstem. Although sleep-active GABAergic neurons in the medullary parafacial zone (PZ) are needed for normal SWS, it remains unclear whether these neurons can initiate and maintain SWS or EEG slow-wave activity (SWA) in behaving mice. We used genetically targeted activation and optogenetically based mapping to examine the downstream circuitry engaged by SWS-promoting PZ neurons, and we found that this circuit uniquely and potently initiated SWS and EEG SWA, regardless of the time of day. PZ neurons monosynaptically innervated and released synaptic GABA onto parabrachial neurons, which in turn projected to and released synaptic glutamate onto cortically projecting neurons of the magnocellular basal forebrain; thus, there is a circuit substrate through which GABAergic PZ neurons can potently trigger SWS and modulate the cortical EEG.

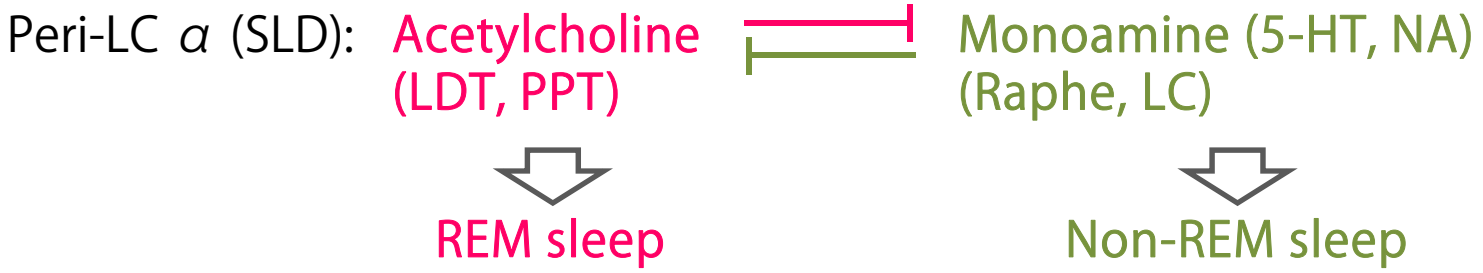
Monoamines negatively regulate REM sleep?



SNRI: selective noradrenalin reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor

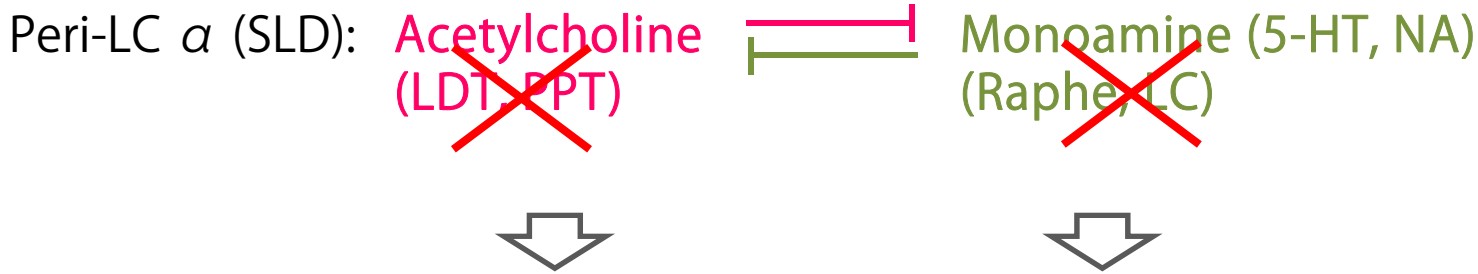
The mutual inhibitory model (Frequently appears in textbooks)

■ Mutual inhibitory model (Hobson, Nat Rev Neurosci, 2009)



Major challenge to the mutual inhibitory model

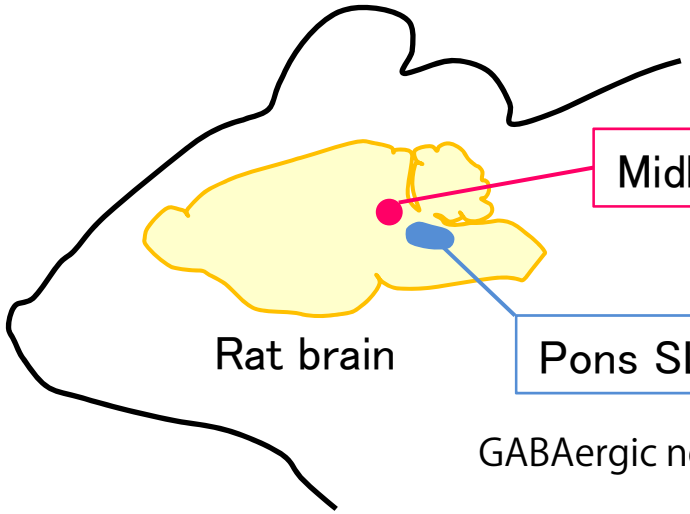
■ Mutual inhibitory model (Hobson, Nat Rev Neurosci, 2009)



(Lu et al., Nature, 2006)

Novel model: Flip-flop switch model

(Lu et al., Nature, 2006)



Midbrain vlPAG: lesion increases REM

Pons SLD: lesion decreases REM

GABAergic neurons in these two areas send axons to each other

■ Flip-flop switch model (Lu *et al.* Nature, 2006)

Peri-LC α = SLD: GABA ⊣⊢ GABA (vlPAG)

GABA → REM sleep

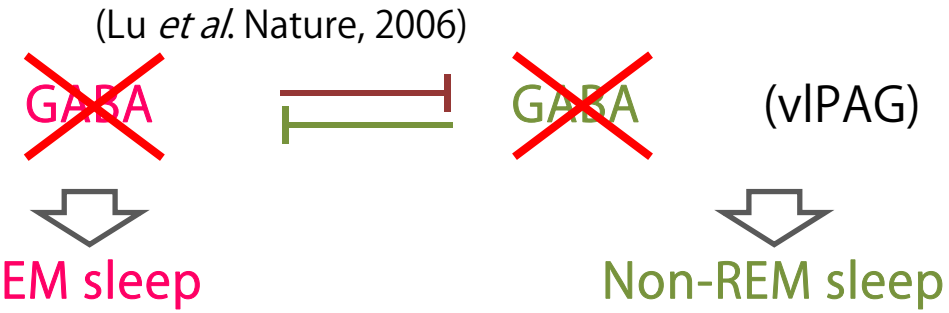
GABA (vlPAG) → Non-REM sleep

A major challenge to the flip-flop switch model

(Lu et al., Nature, 2006)

■ Flip-flop switch model

Peri-LC α = SLD:



No effect on REM sleep!

(Krenzer et al., Plos One, 2011)

Current situation

■ Flip-flop switch model (Lu *et al.* Nature, 2006)

(Krenzer et al., Plos One, 2011)

(Weber et al., Nature, 2015)

(Hayashi et al., Science, 2015)