

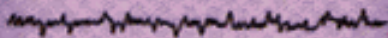
CEREBRAL
CORTEX

THALAMUS

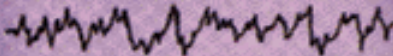
PONS

SPINAL CORD

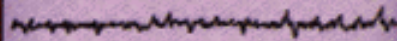
AWAKE

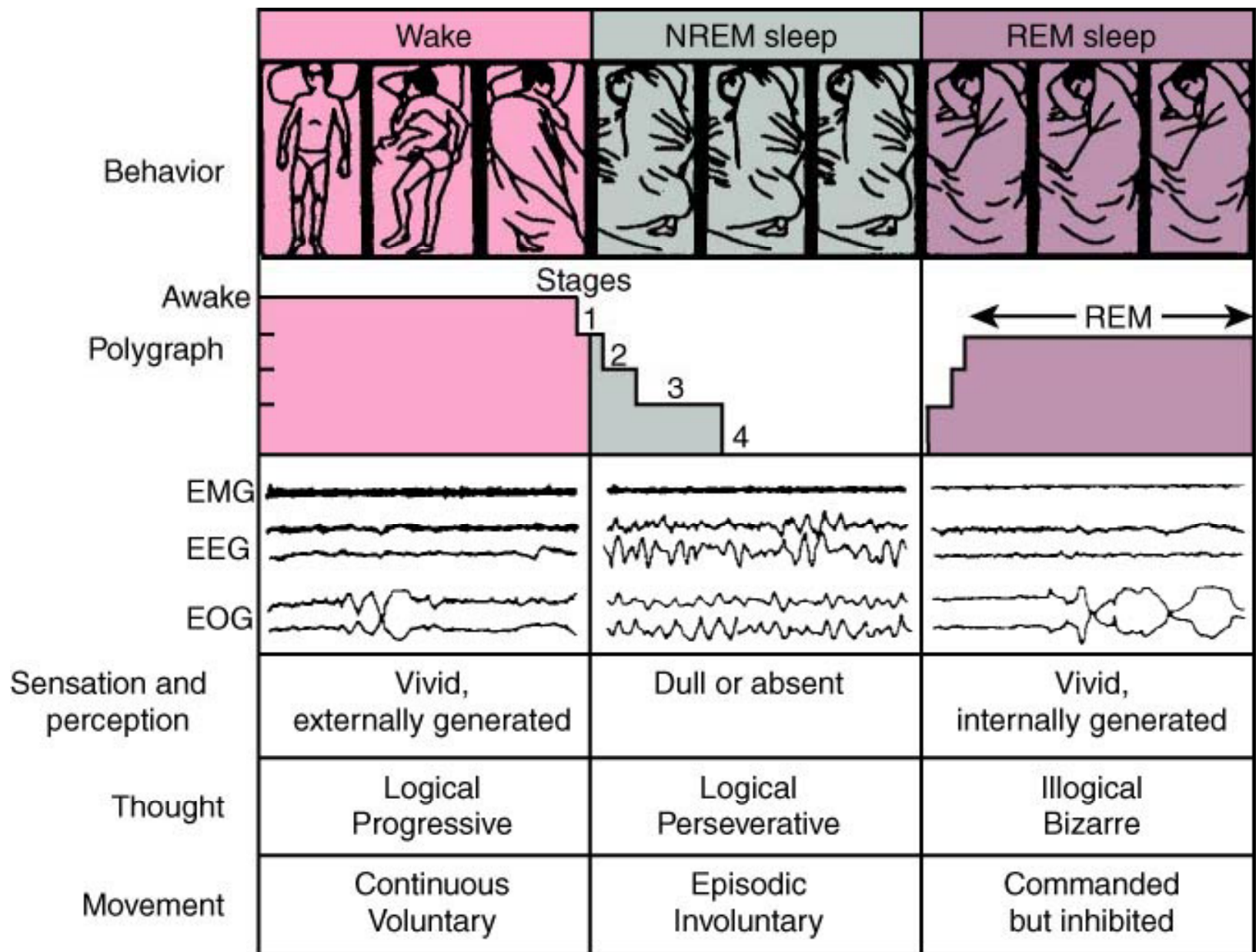


NON REM

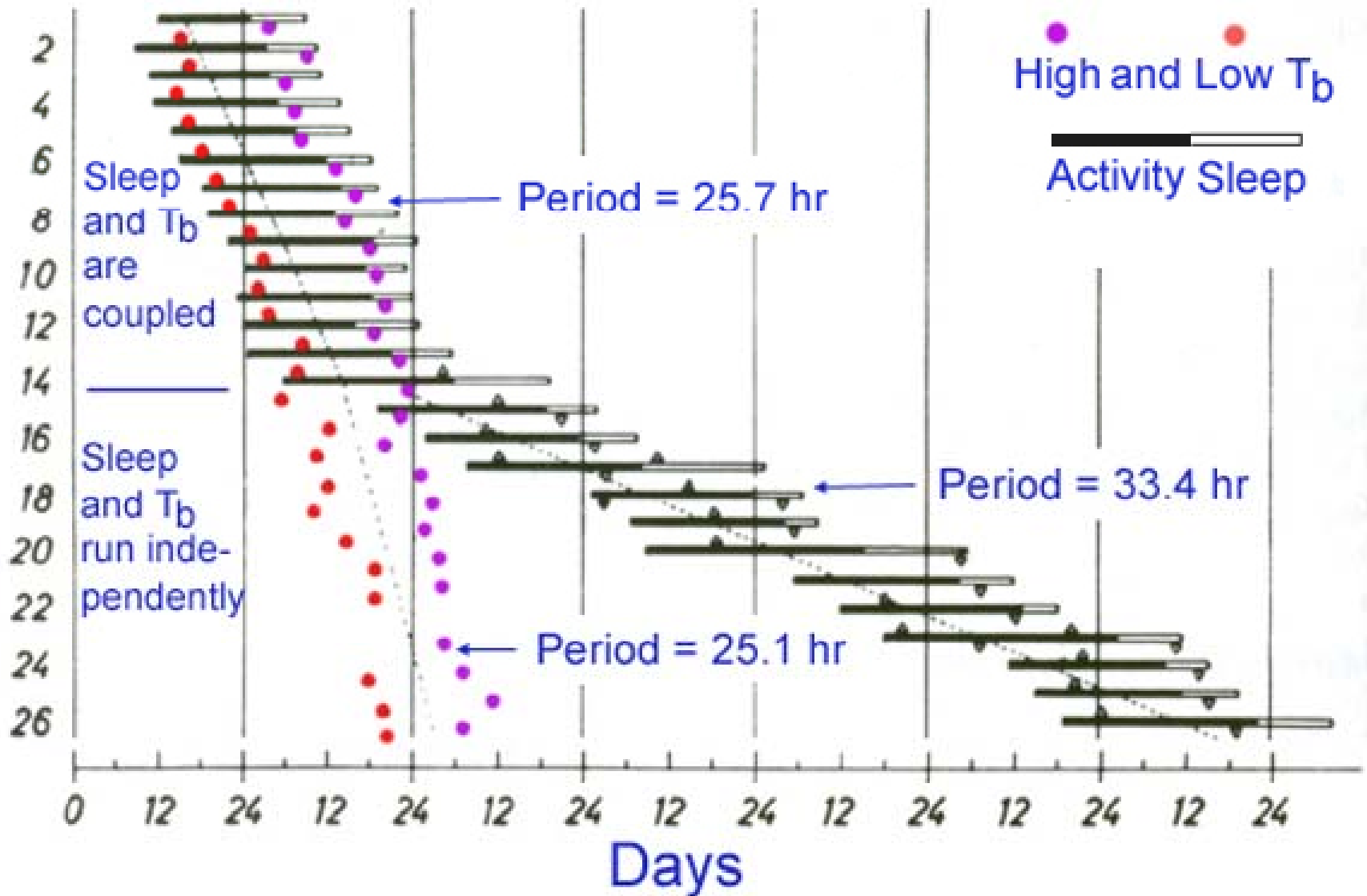


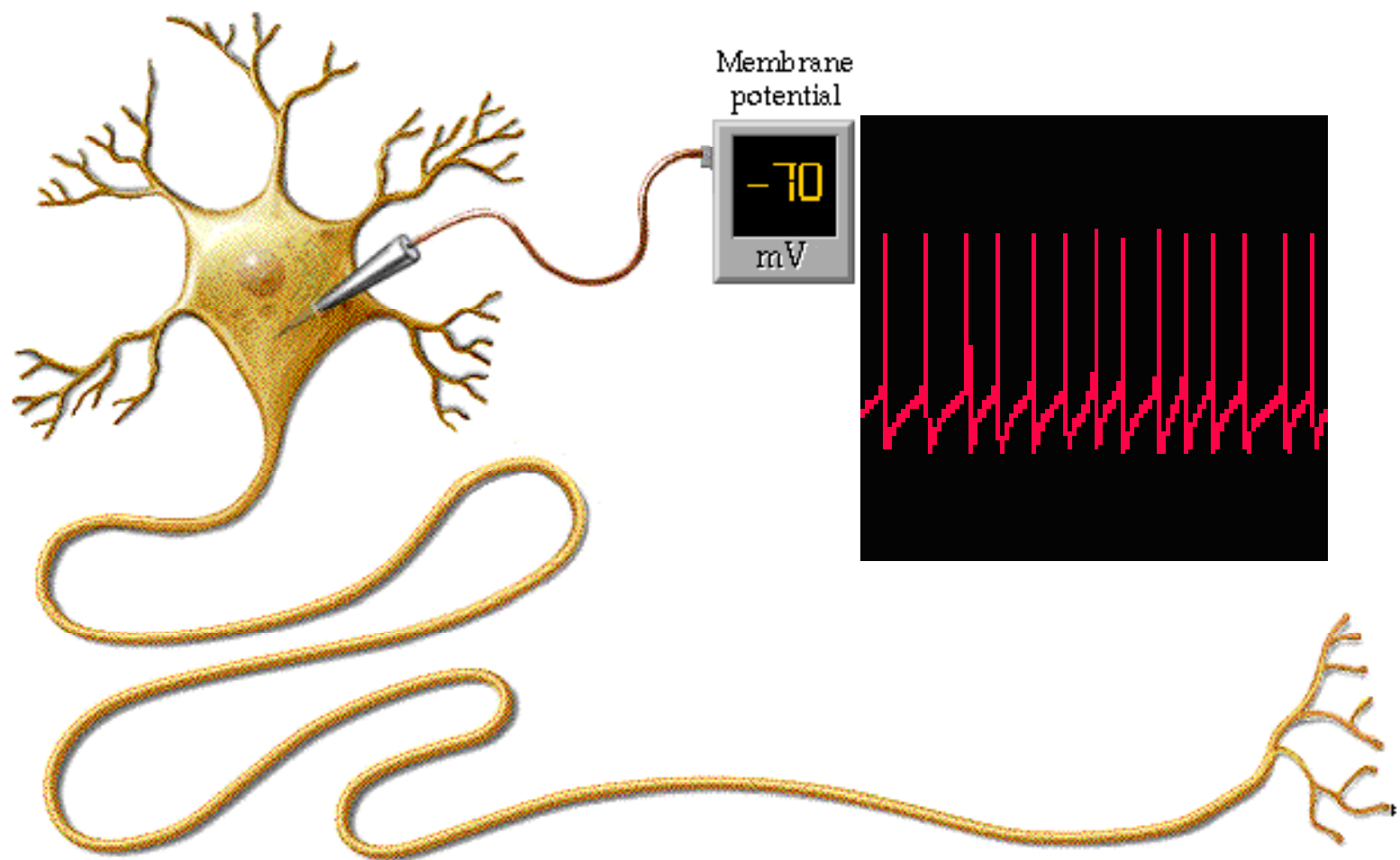
REM





Free-running Sleep and Temperature (T_b) Rhythms

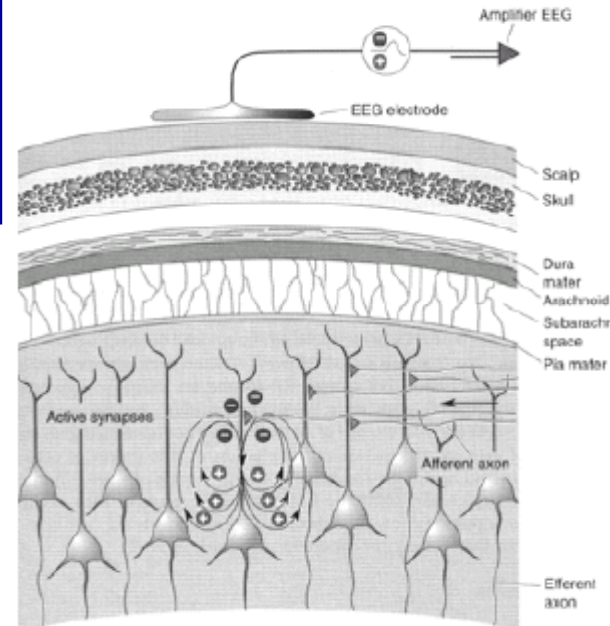
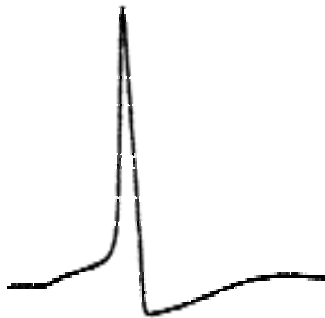
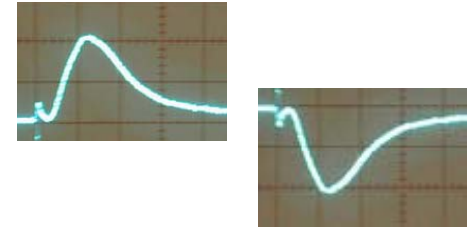
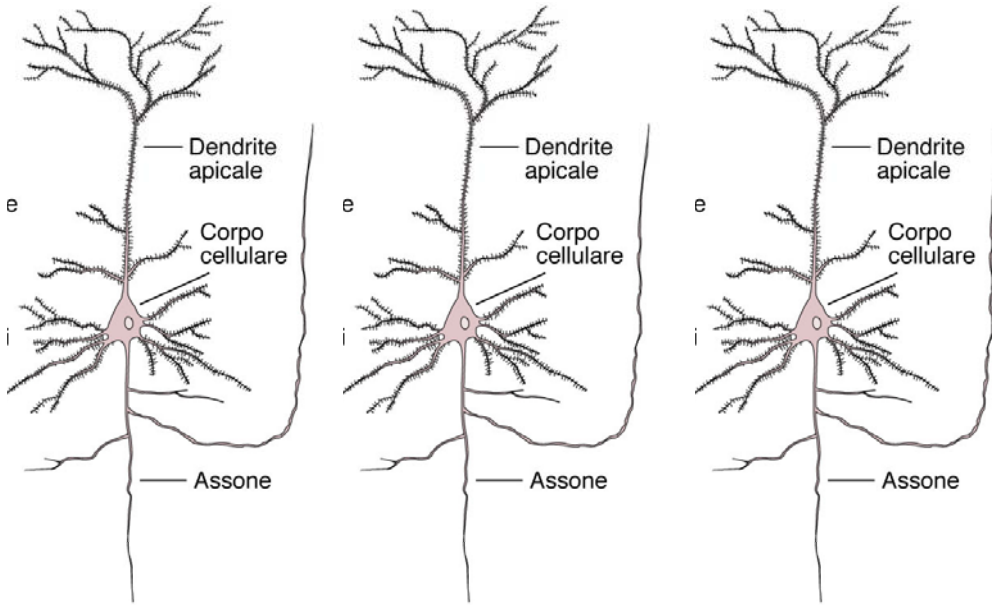






cranio

meninge



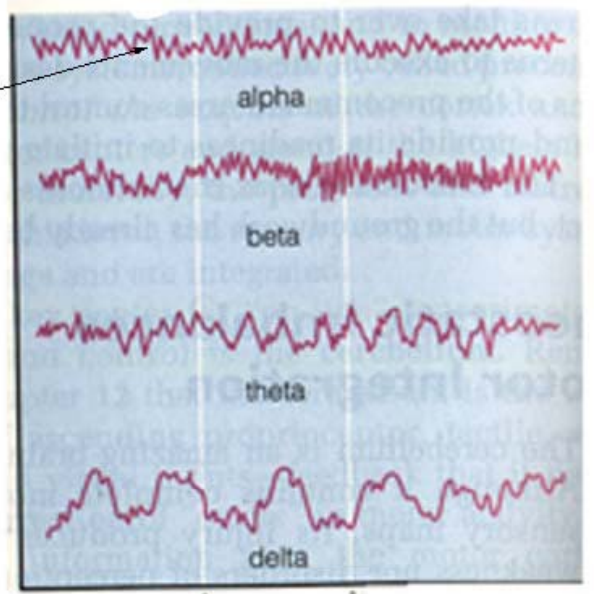


Relaxed Wake/
Stage I/REM
"sawtooth"
Awake, Alert

Stage 2

Stage 3/4

(a)



(b) 1 second interval

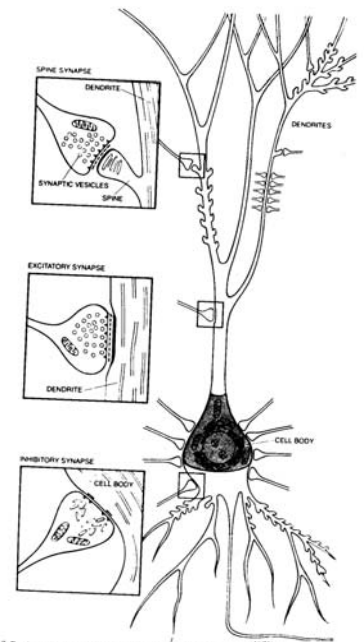
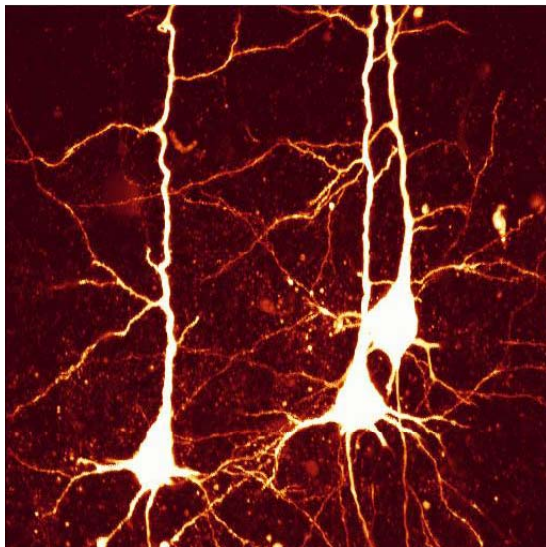
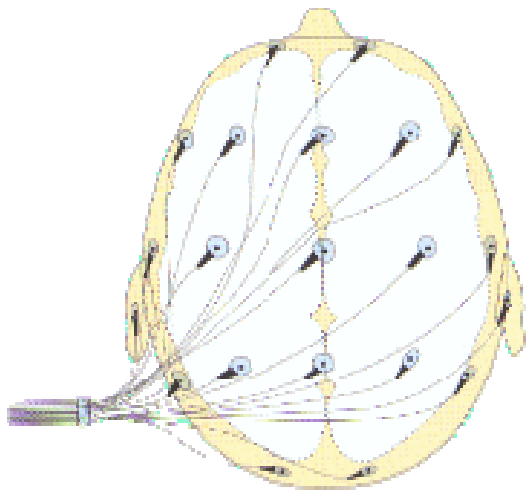
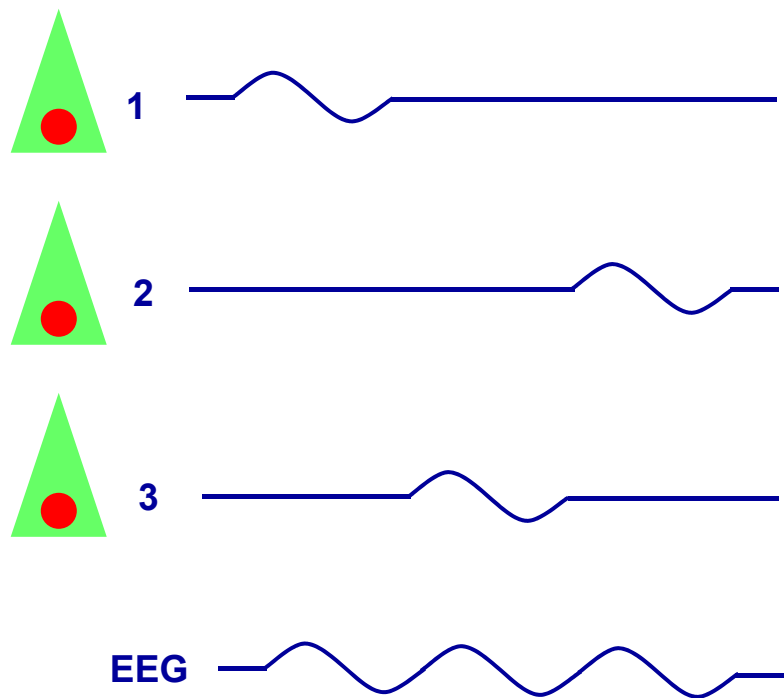


Fig. 3-5. A pyramidal cell and several synapses.



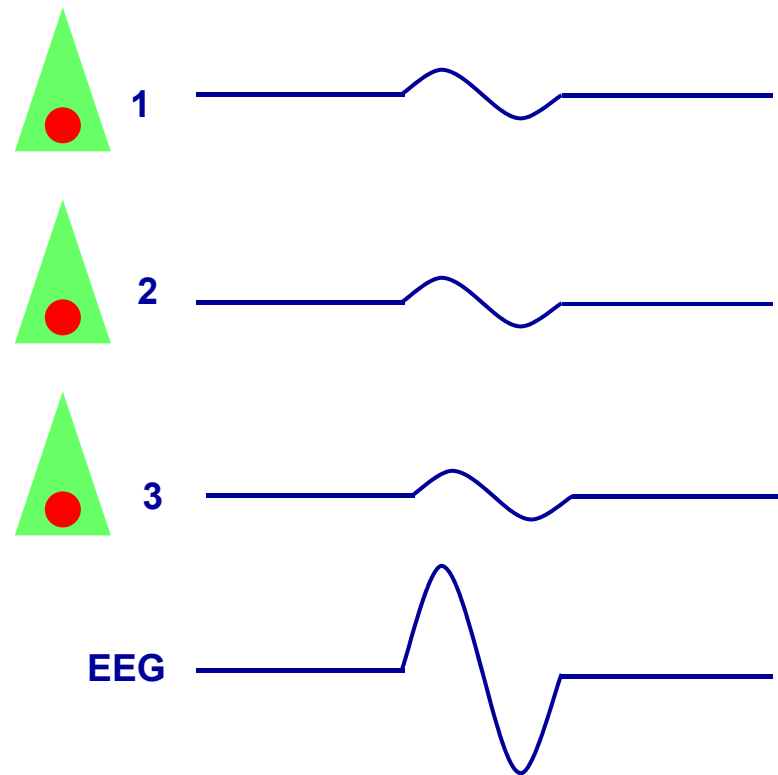
attività corticale desincronizzata

EEG:

alta frequenza

bassa ampiezza

Awake: low voltage-random, fast



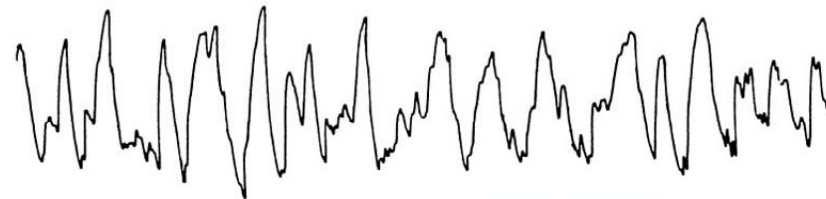
attività corticale sincronizzata

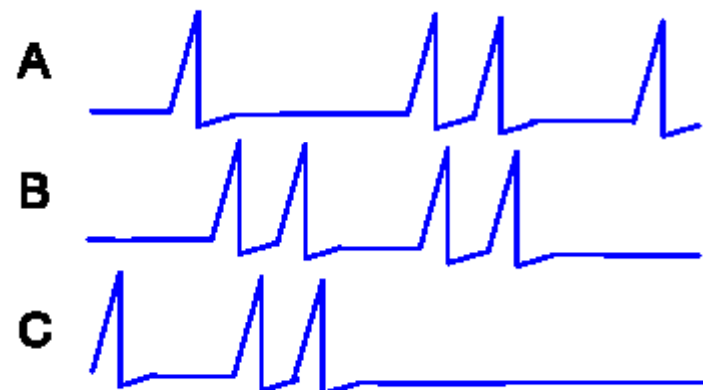
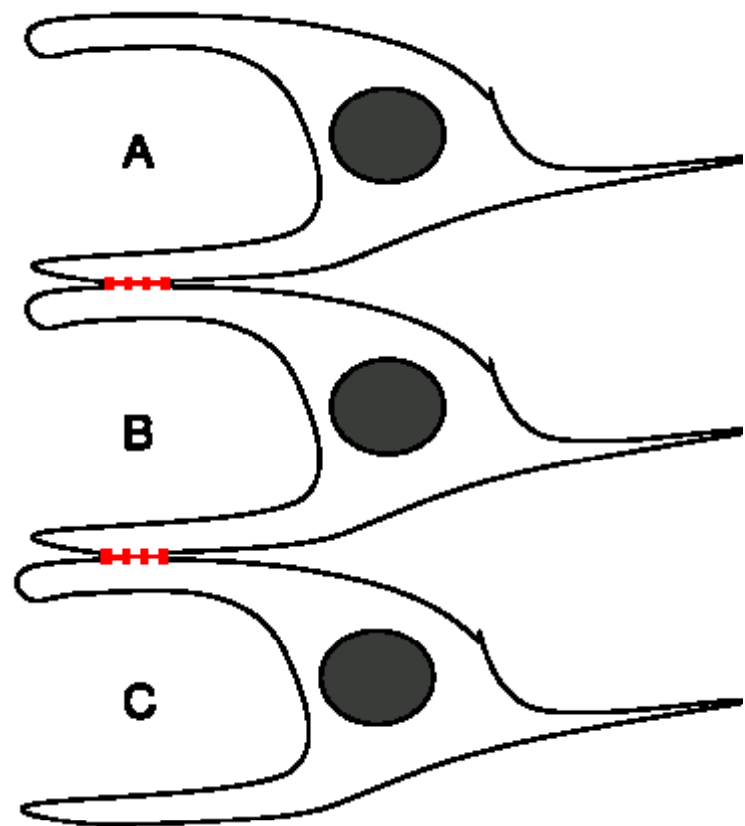
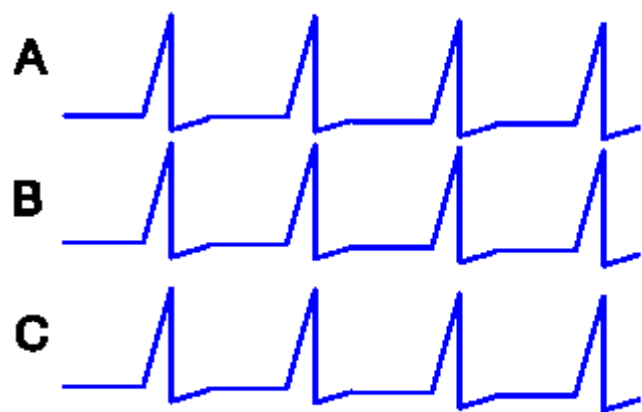
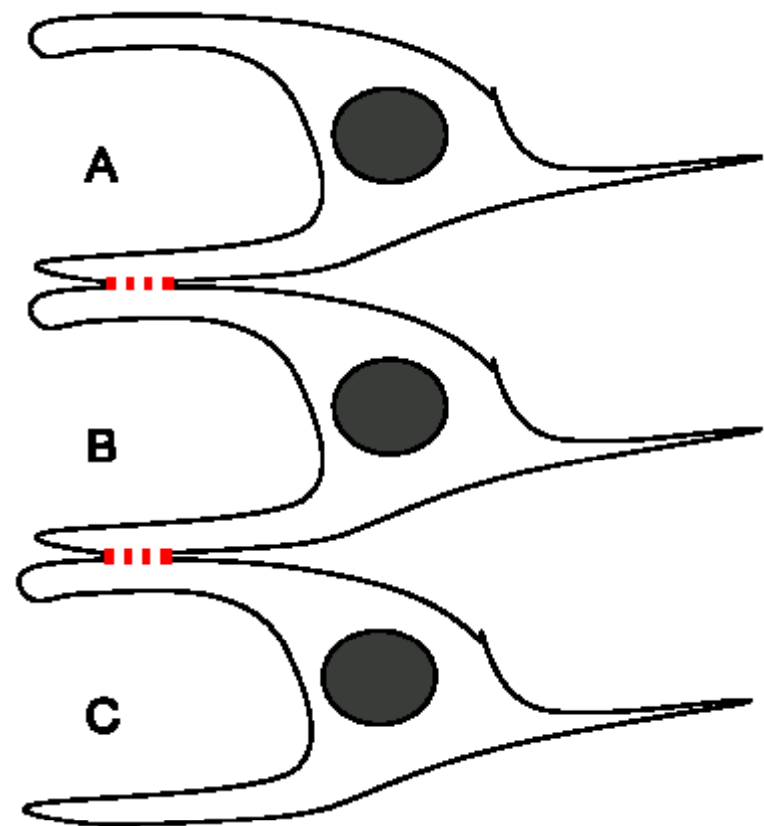
EEG:

bassa frequenza

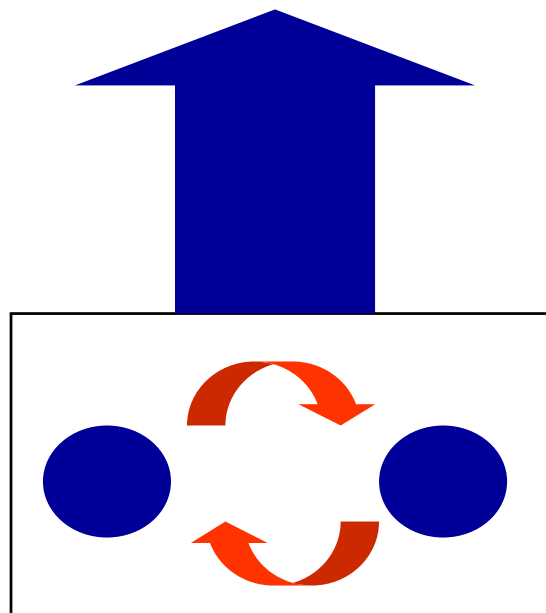
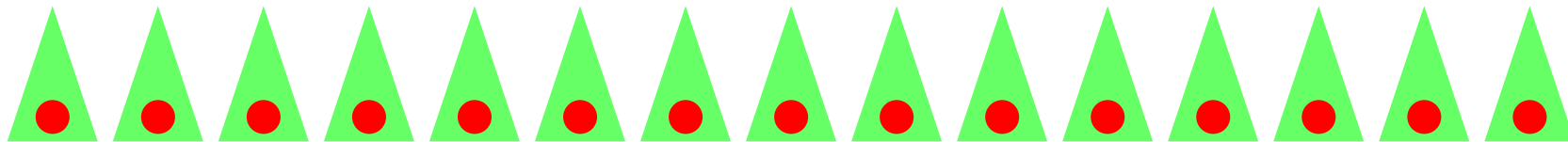
alta ampiezza

Deep sleep: 1/2 to 2 cps- delta waves >75 μ V





Corteccia cerebrale



**Talamo
(ritmatore)**

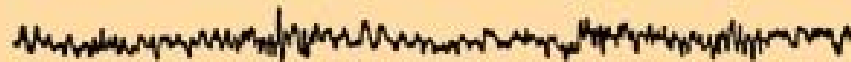
Awake with eyes open



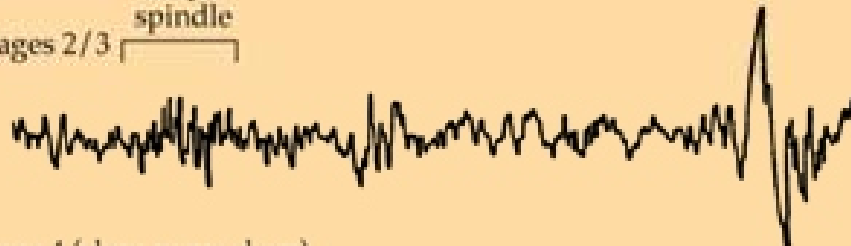
Awake with eyes closed



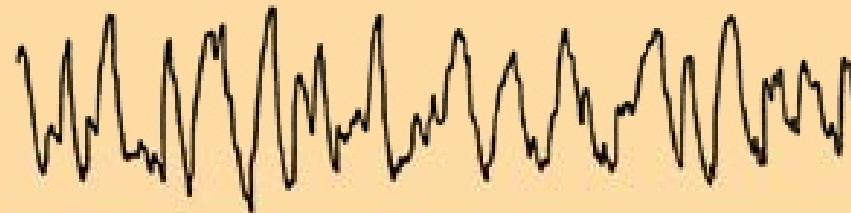
Non-REM sleep
Stage 1



Stages 2/3
Sleep spindle

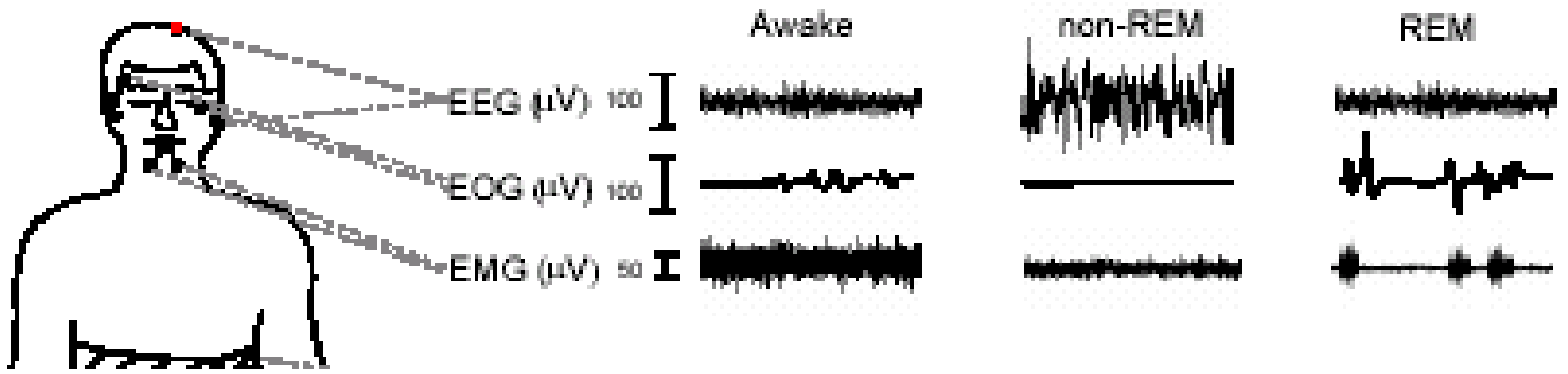
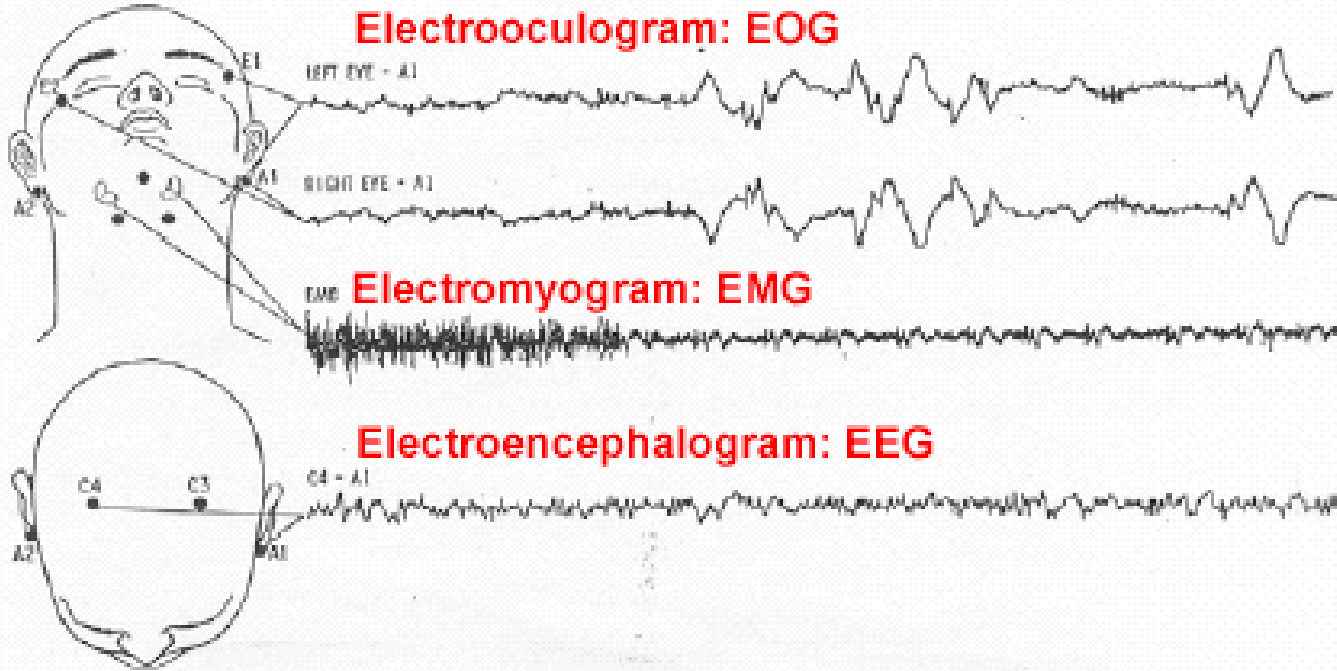


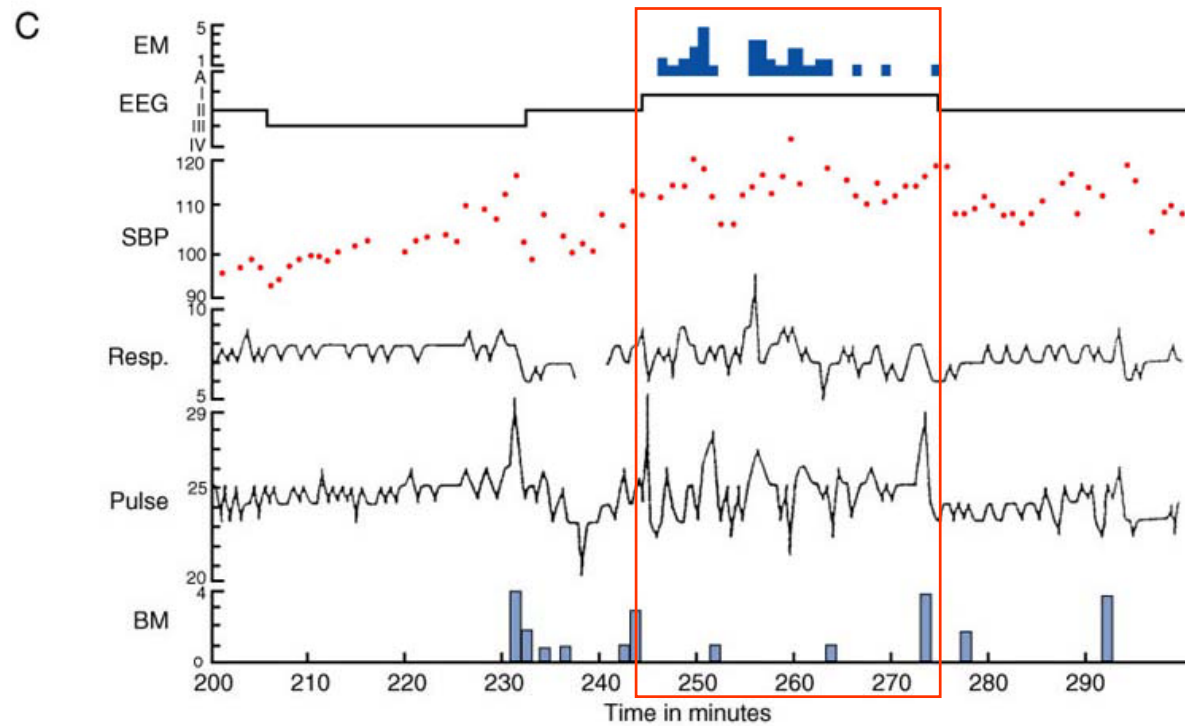
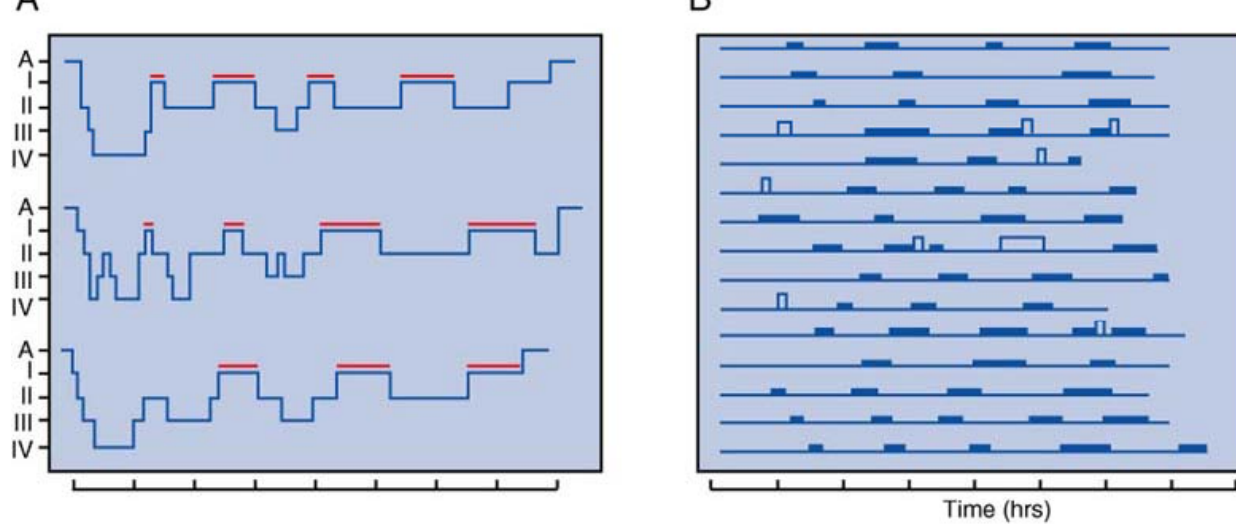
Stage 4 (slow-wave sleep)

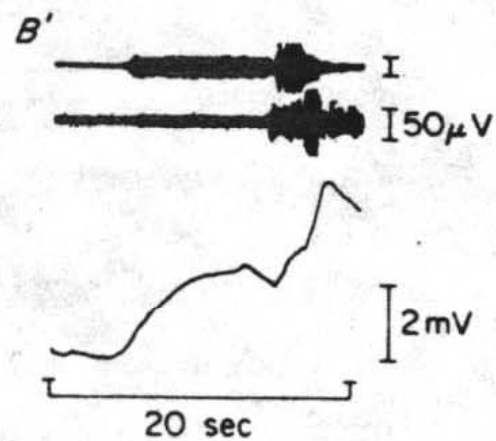
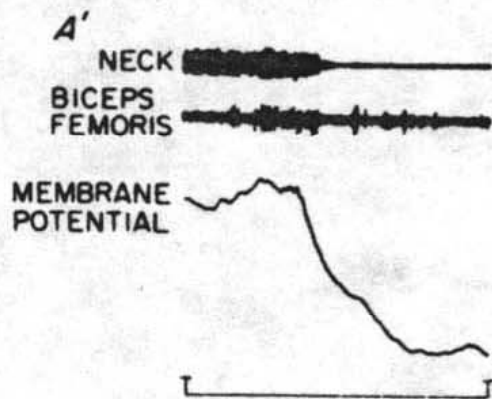
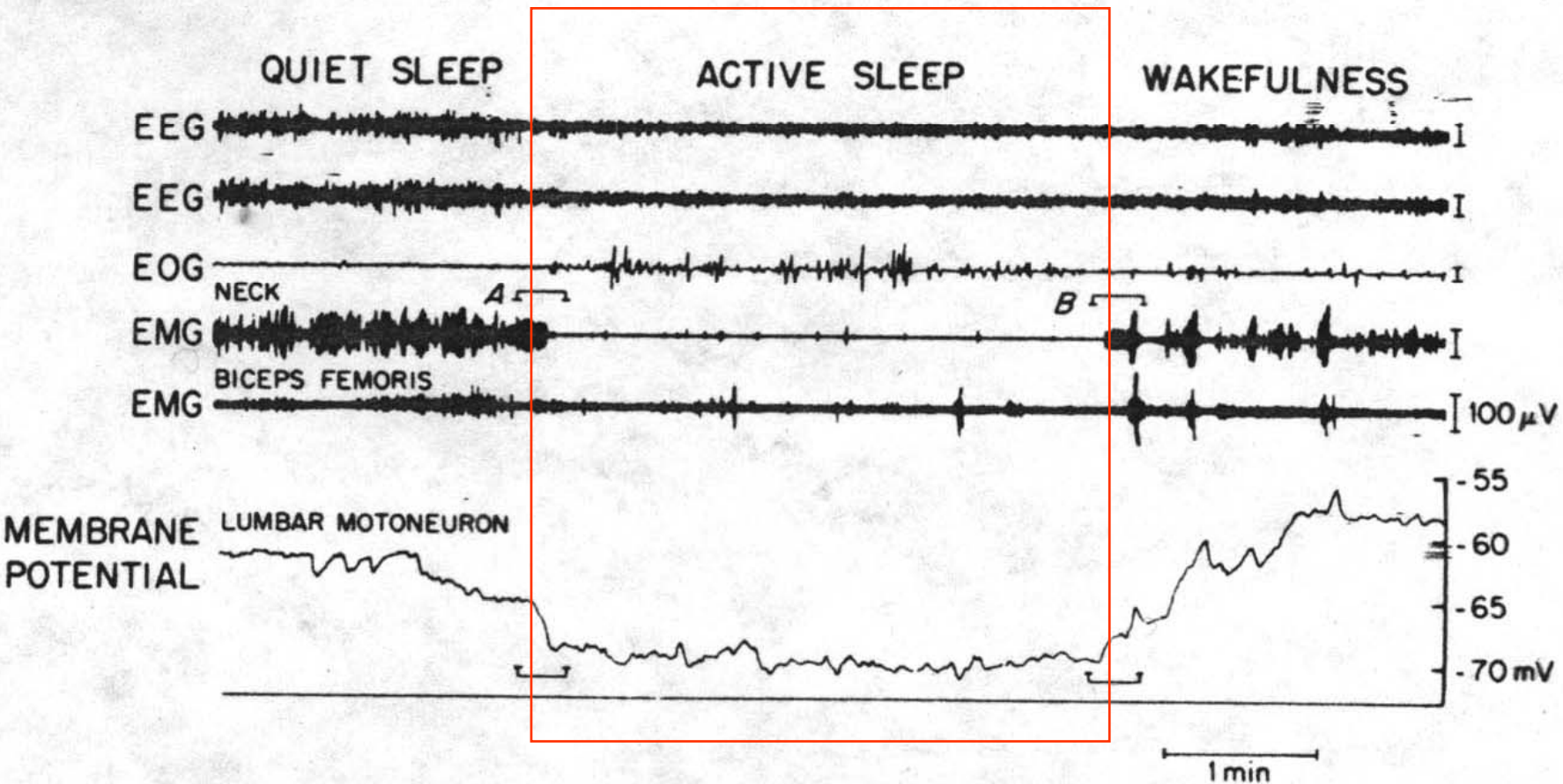


REM sleep





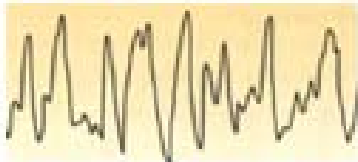




Characteristics of REM and Non-REM Sleep

Non-REM

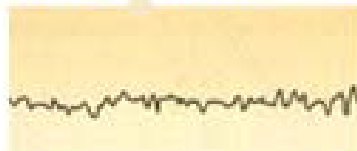
Slow EEG



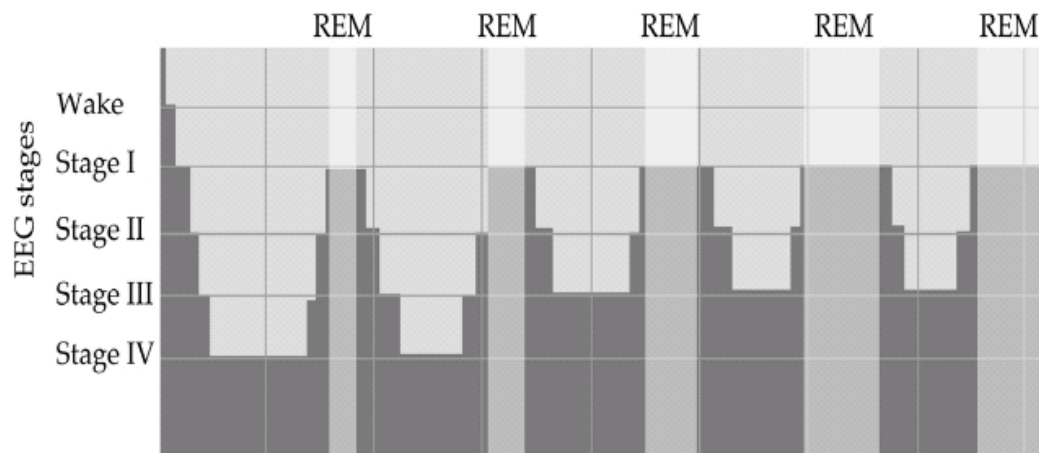
Muscular activity
Dreaming rare
Easily awakened
80% of sleep time

REM (Paradoxical)

EEG similar to awake person



No movement
Dreaming common
Hard to arouse easily
20% of sleep time



SWS and REM alternate during the total sleep period.

SWS precedes REM.

Sleep Cycle

1

Interim between
consciousness
and sleep

Move to Stage 2
after 5-15 mins

2

Heart rate slows,
brain does less
complicated tasks

After another 15 mins,
move into non-REM sleep,
the Delta stage

3

Body makes
repairs

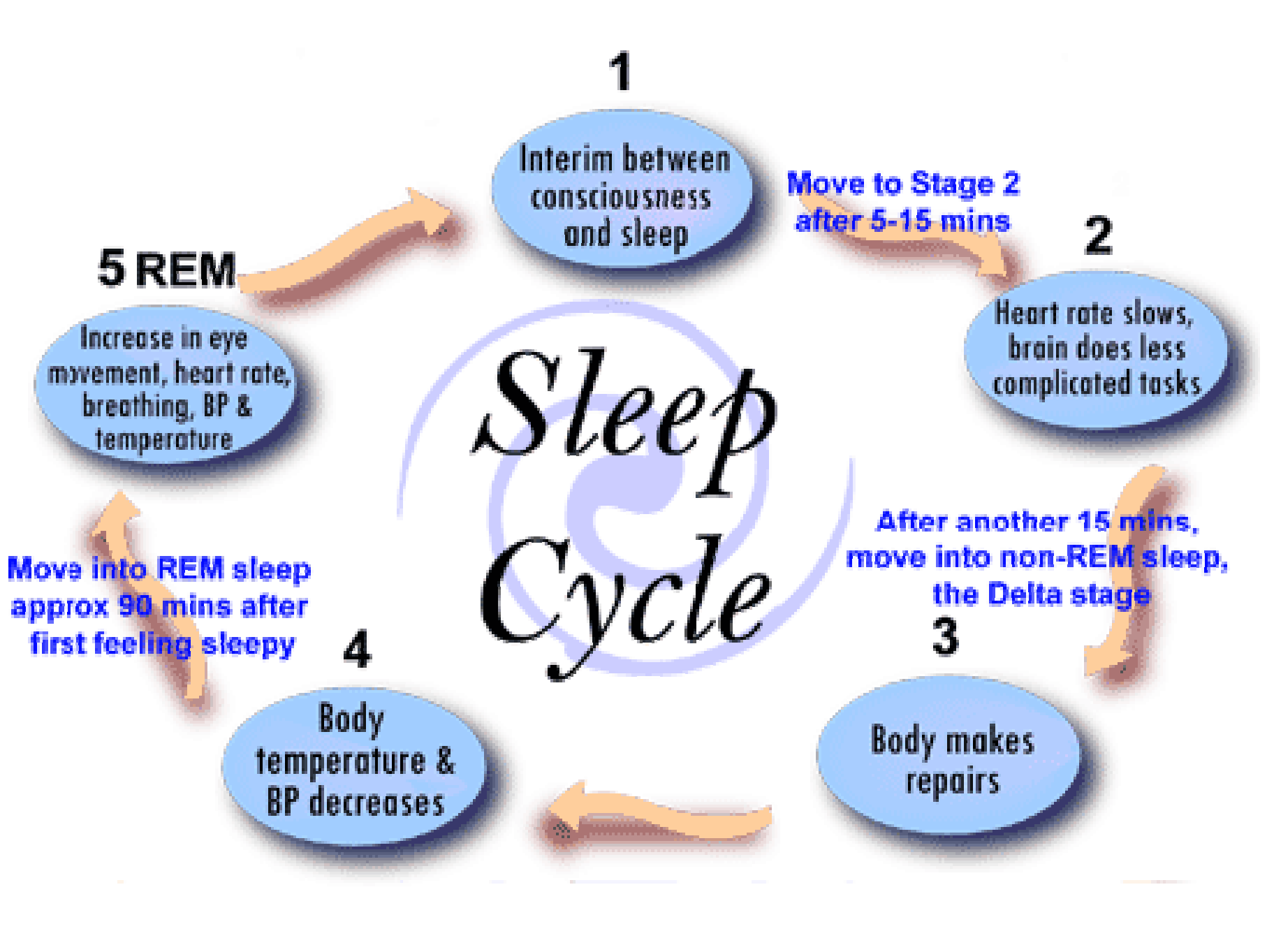
4

Body
temperature &
BP decreases

5 REM

Increase in eye
movement, heart rate,
breathing, BP &
temperature

Move into REM sleep
approx 90 mins after
first feeling sleepy



COMA IS NOT DEEP SLEEP

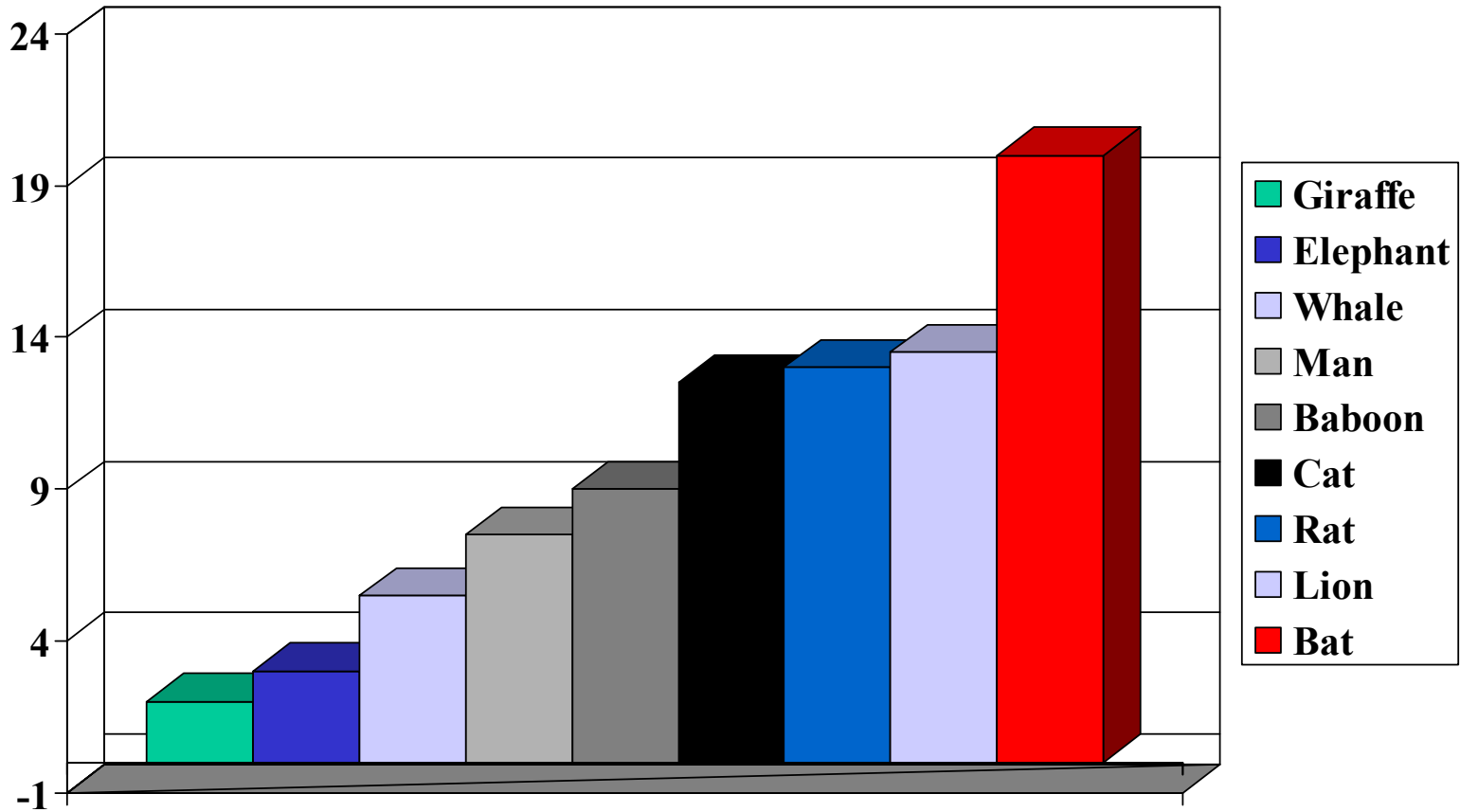
- 1. Animal cannot be aroused from a coma, but can be aroused from sleep.**
- 2. The comatose brain does not cycle through the different stages of sleep.**
- 3. Cerebral oxygen consumption is decreased in the comatose brain, but may be increased during REM sleep.**

Filogenesi del sonno

- **Reptiles, amphibians, fish - sleep is usually determined by behavioral criteria.**
- **"Sleep" is present throughout the animal kingdom - including insects.**
- **REM sleep is rarely, if ever present, in reptiles.**

- **Mammals - all mammals sleep, and all except one have the cyclical alternation between REM and NREM sleep.**
- **Birds - have alternating REM/NREM (very short: 9 sec/2.5 min).**
- **REM sleep in birds and mammals developed independently.**

Ore di sonno nelle 24 ore in diverse specie di mammiferi



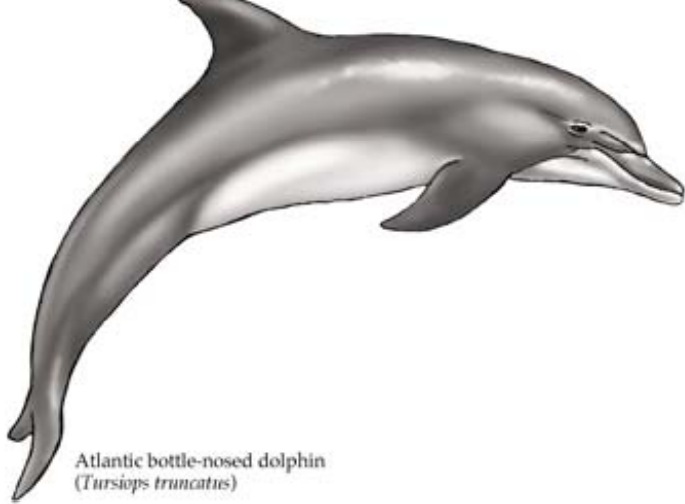
% of Total Sleep as REM

<u>Species</u>	<u>Neonate</u>	<u>Adult</u>
Ruminants	17	7
Rodents	55	15
Carnivores	50	20
Humans	50	20

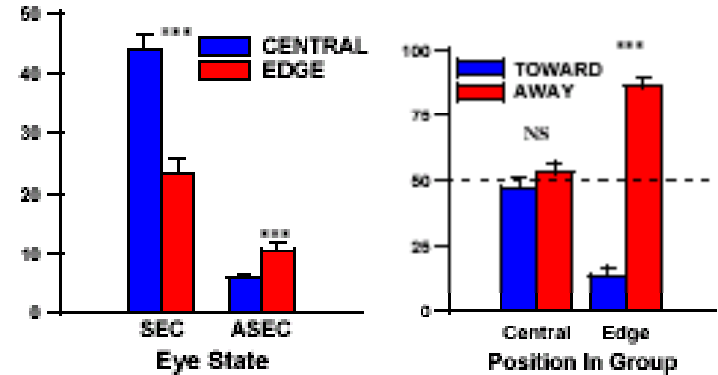
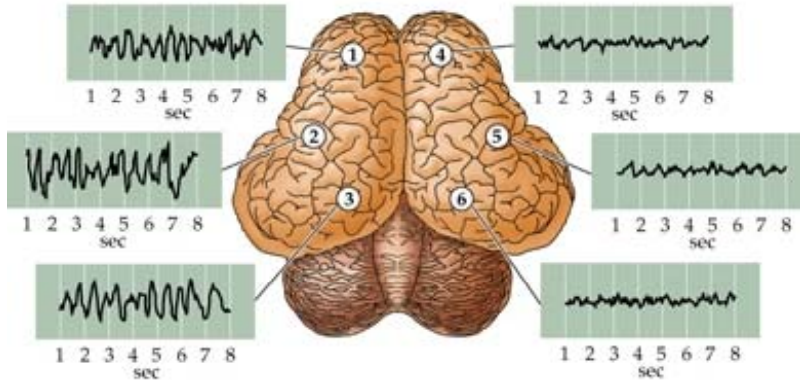
Platypus - 8hrs REM/day!!!!



Dormire con un occhio (emisfero) solo

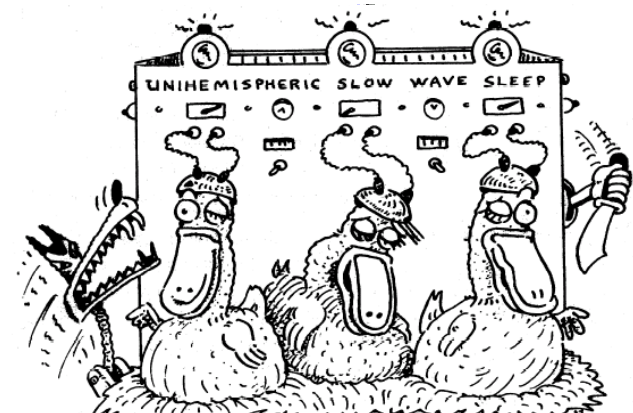
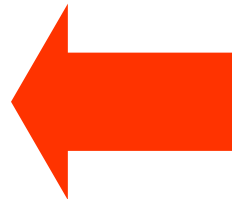


Atlantic bottle-nosed dolphin
(*Tursiops truncatus*)

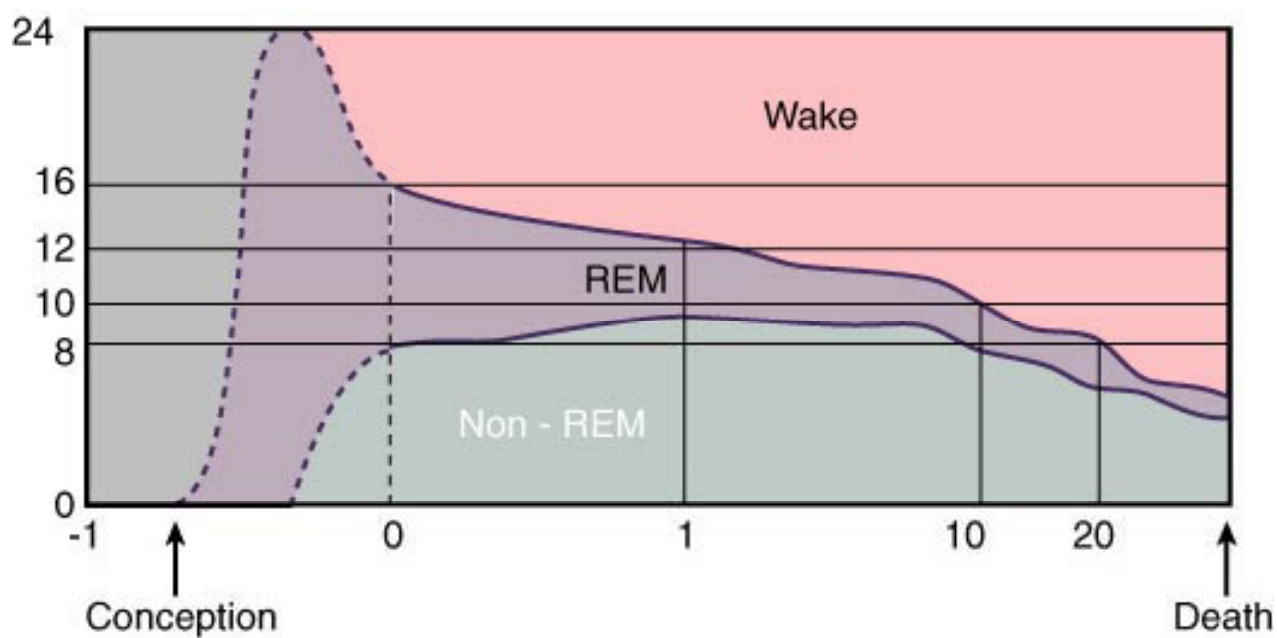


Visual Test Results

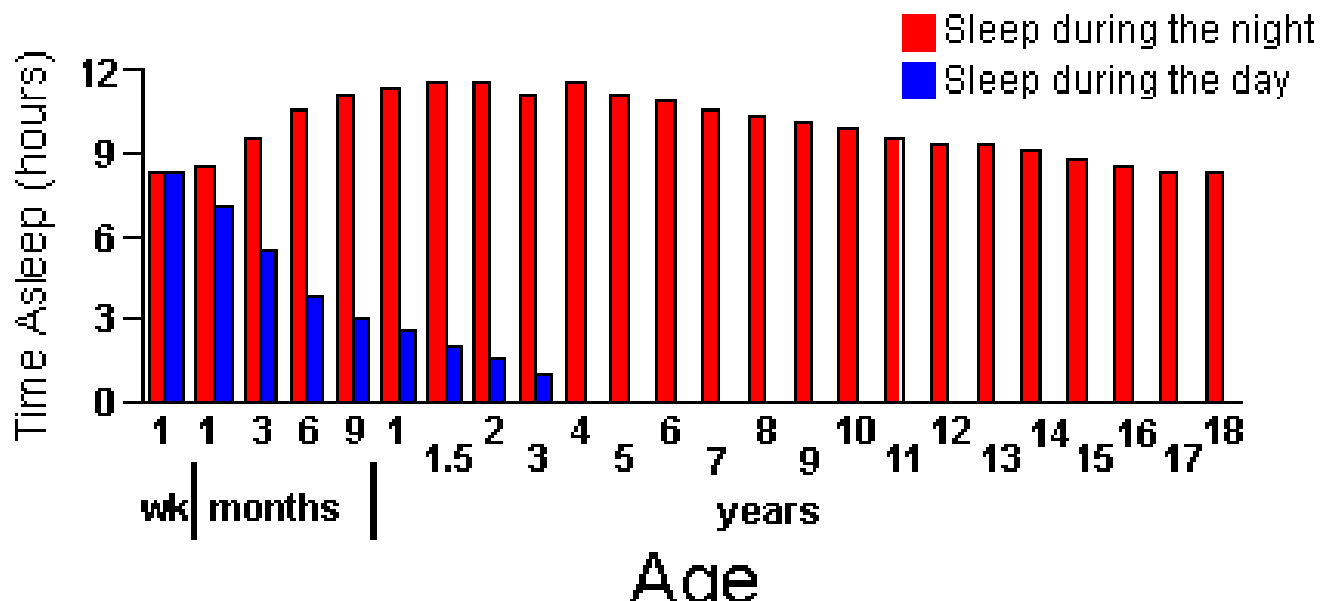
USWS Reaction Time =
 0.165 ± 0.006 sec.
(range 0.133 - 0.183 sec)



Hemisphere *is* functionally awake.



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The Sleep Rhythm Develops Gradually

Week

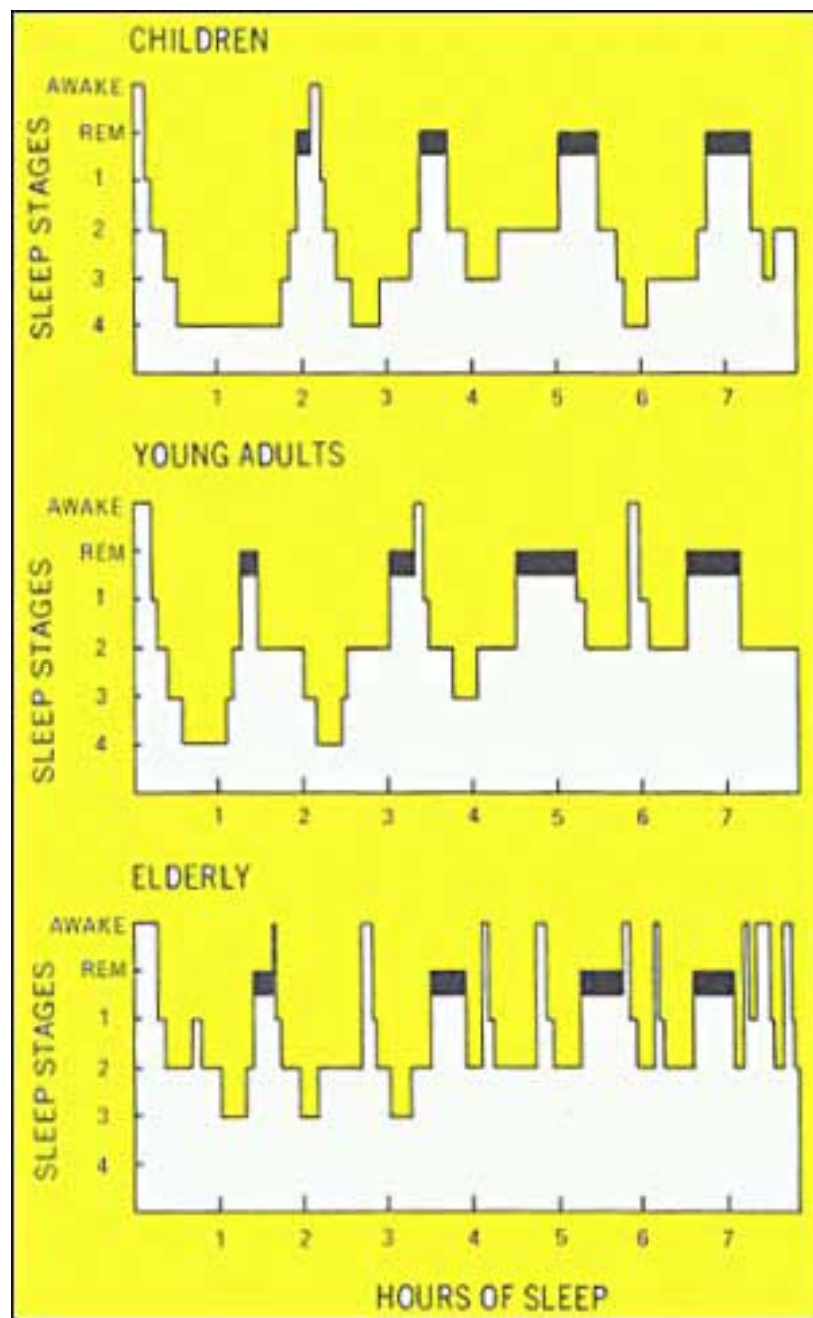
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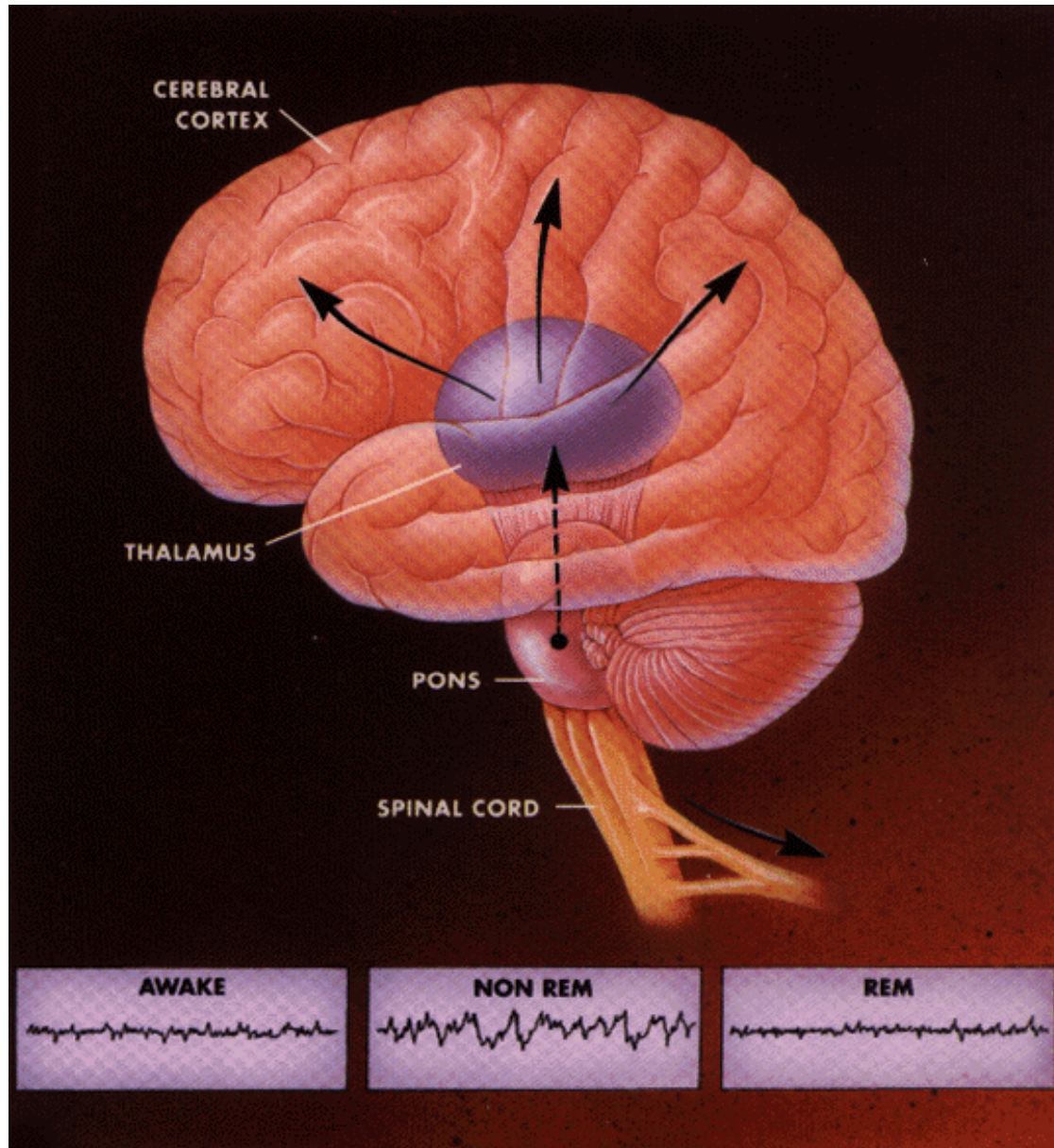
12

24

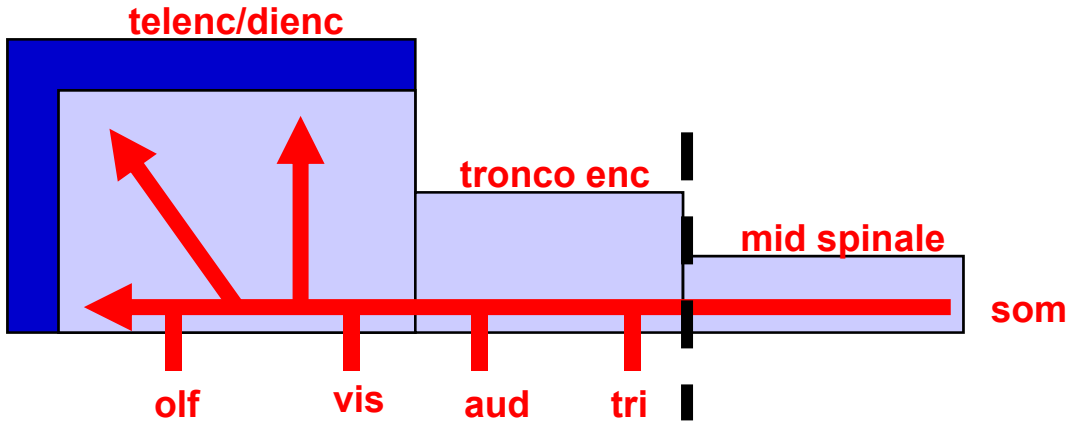
Sonno sismico e sonno REM



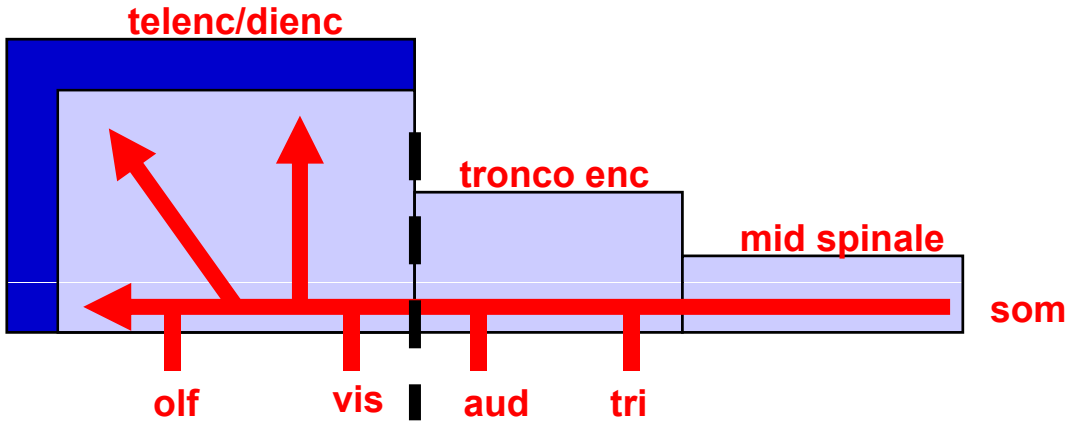
Neurofisiologia del sonno



Bremer: il sonno passivo

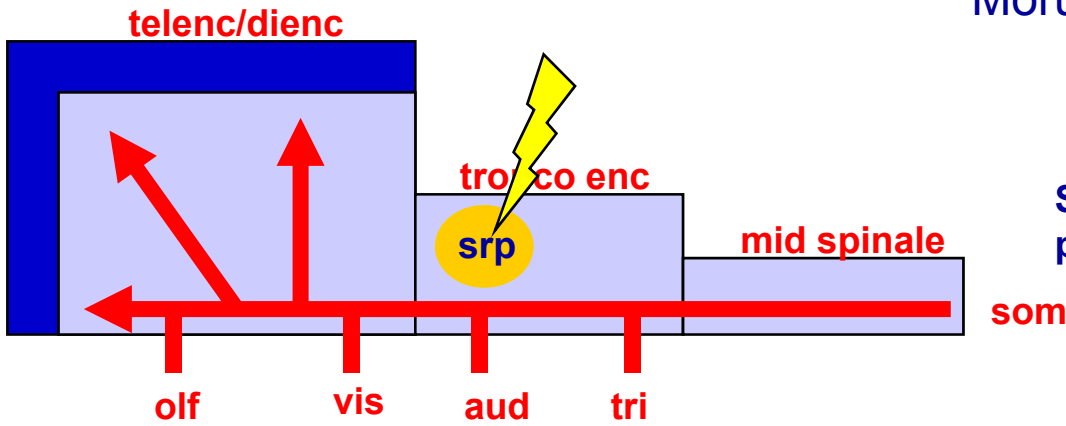


encefalo isolato: sonno-veglia

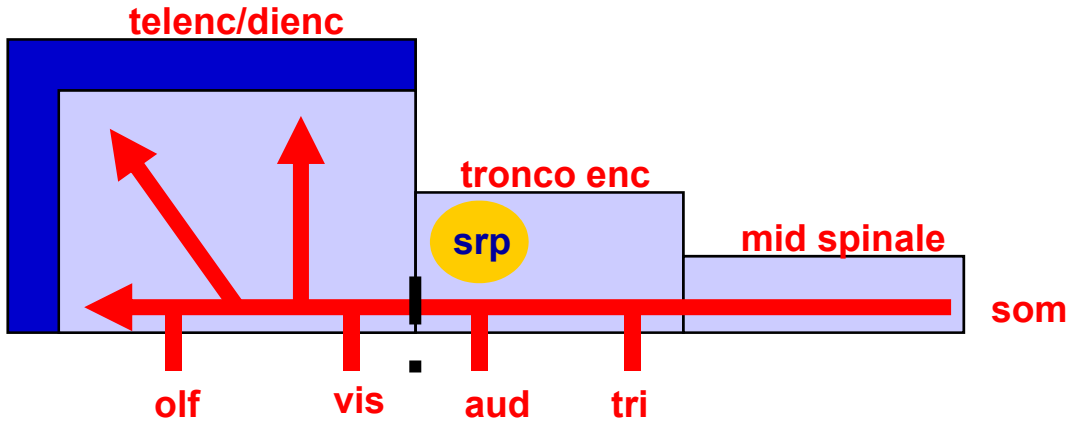


cervello isolato: dorme sempre

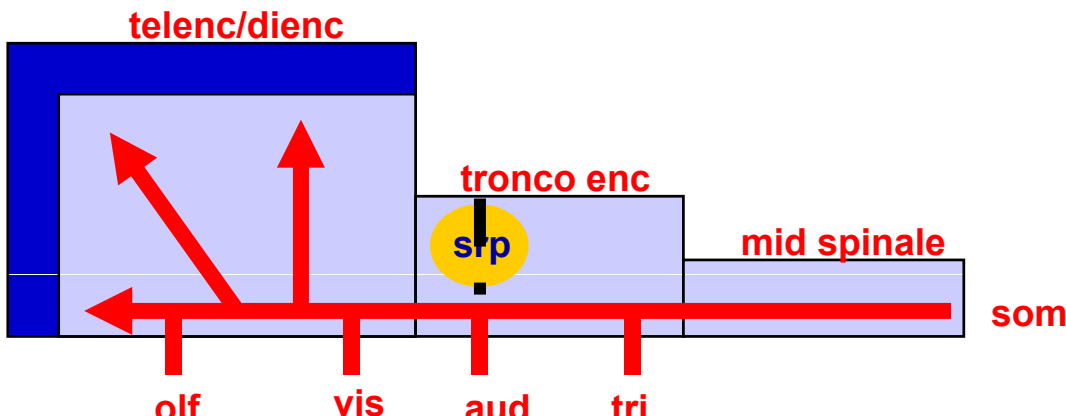
Moruzzi & Magoun: il sonno attivo



Stimolazione della sostanza reticolare pontina (srp) induce la veglia

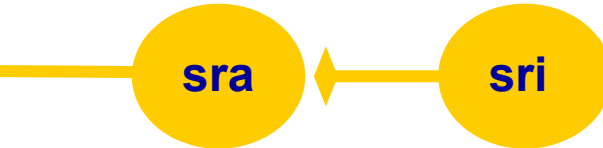
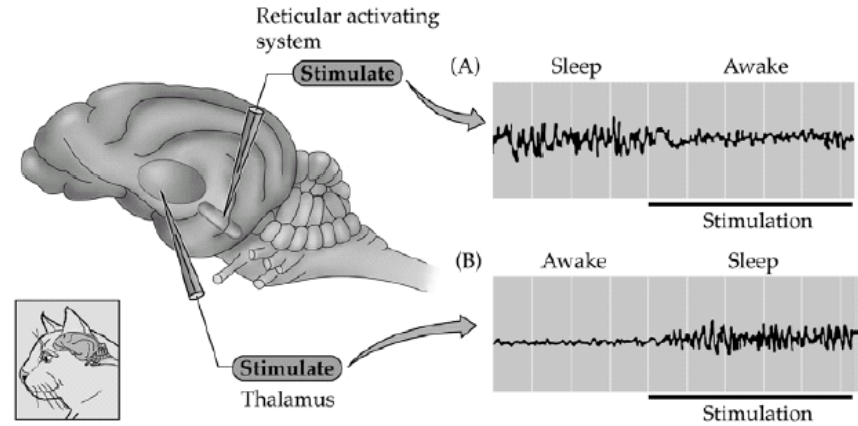
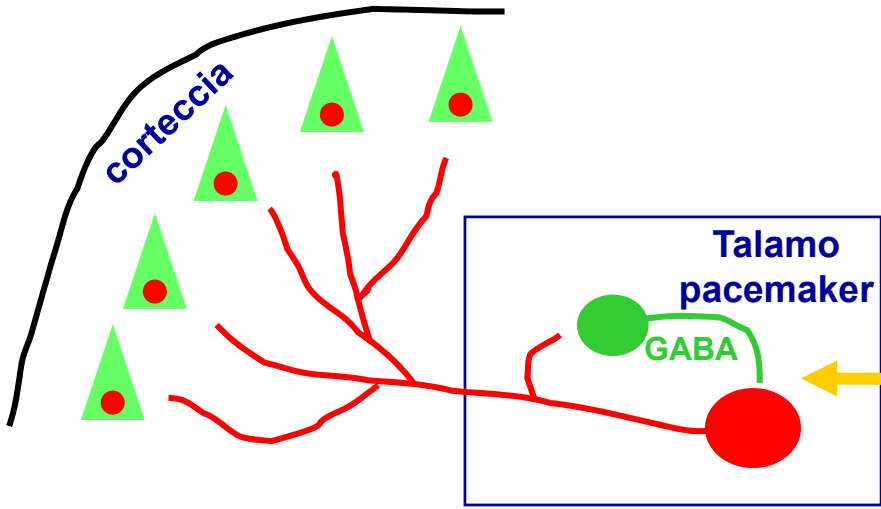
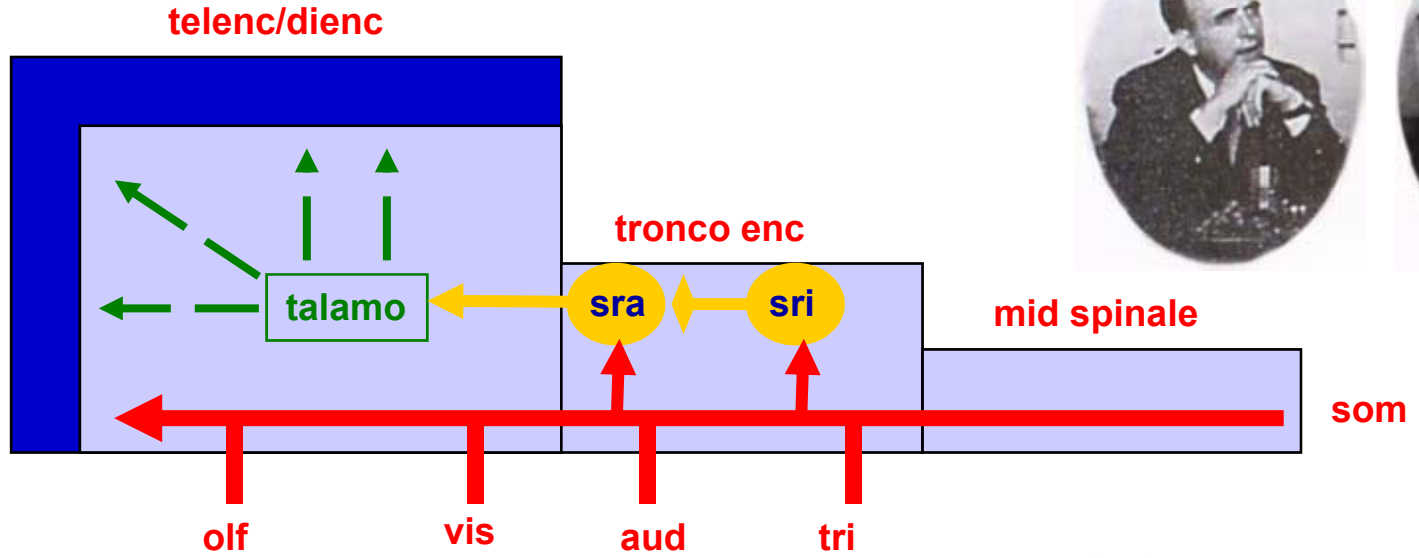


Sezione delle sole vie sensoriali non altera il ciclo sonno-veglia

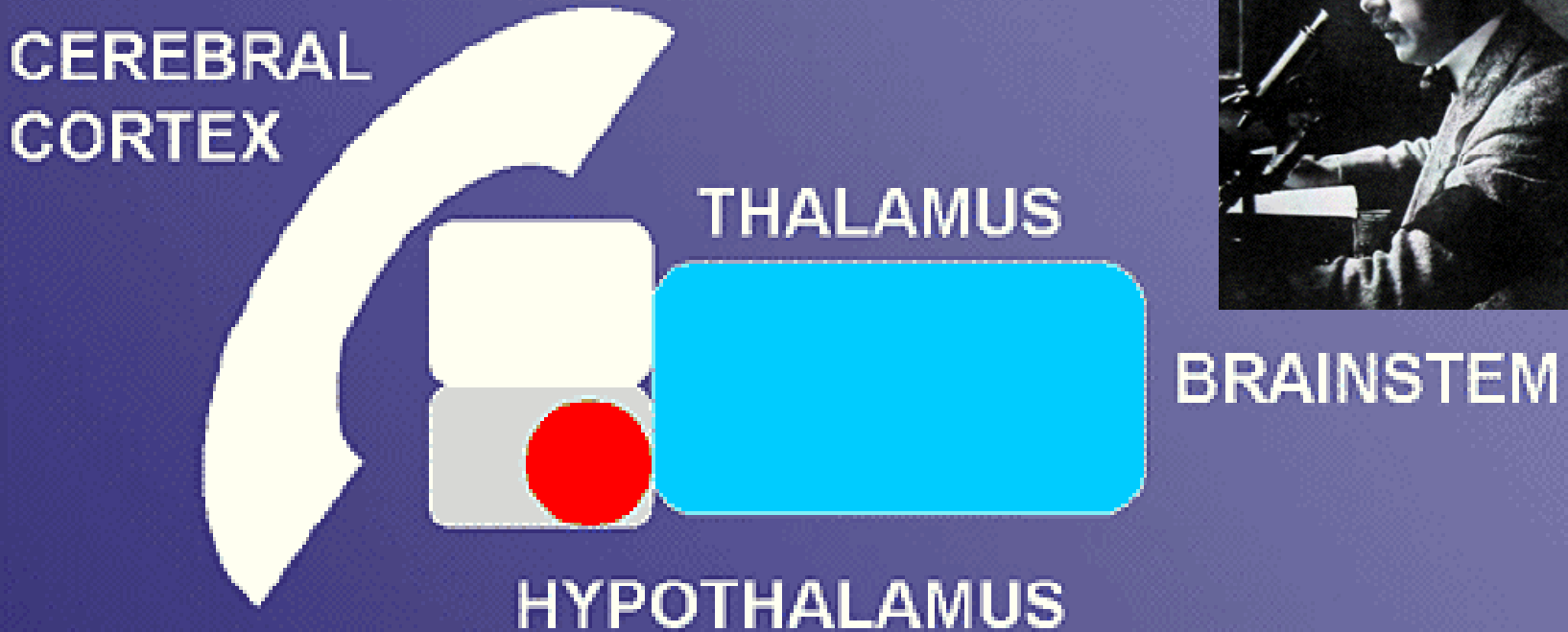


lesione medio-pontina abolisce il sonno

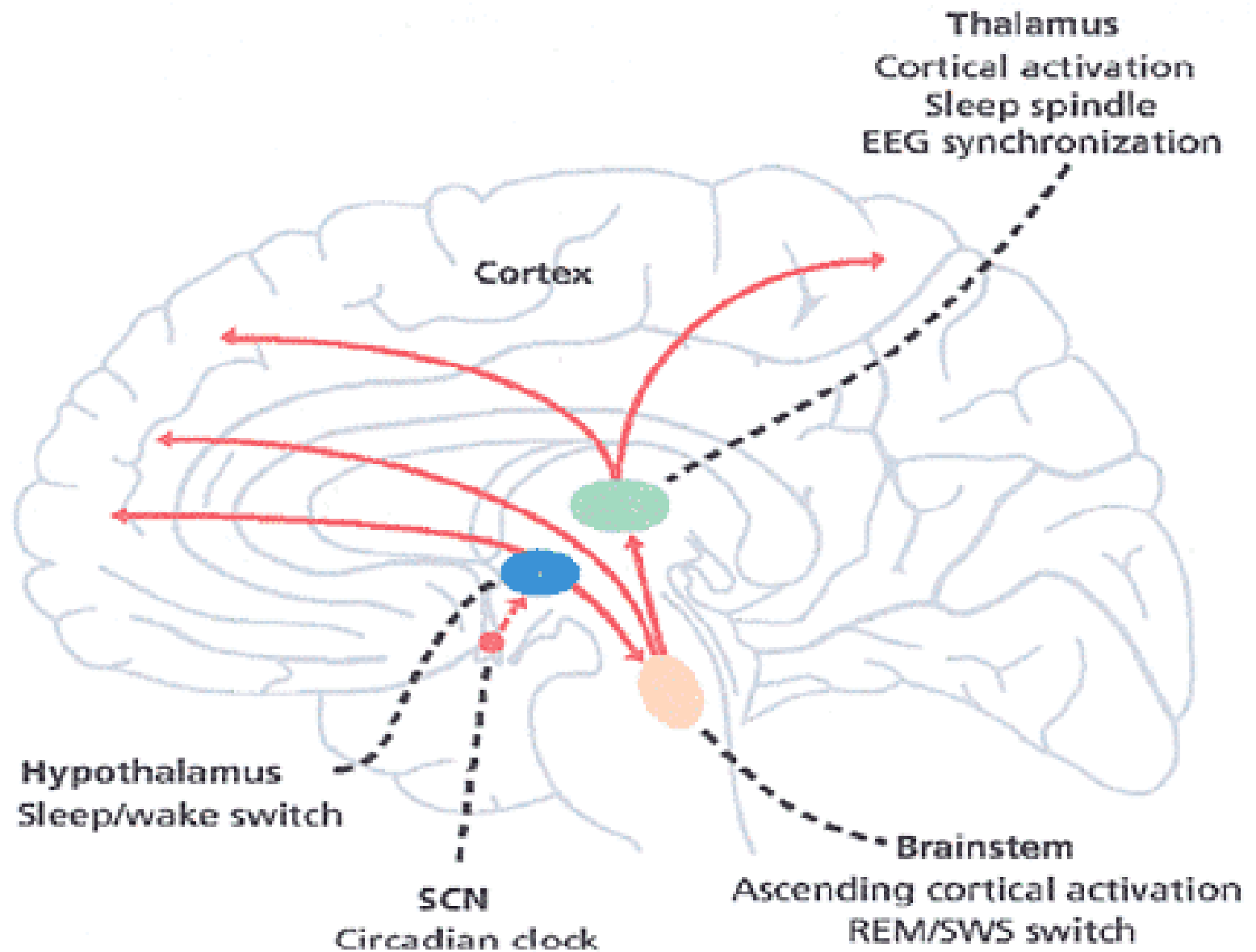
Modello di Moruzzi & Magoun



THE WAKING STATE REQUIRES THE POSTERIOR HYPOTHALAMUS



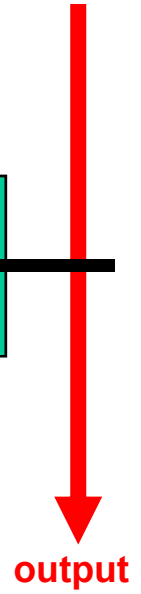
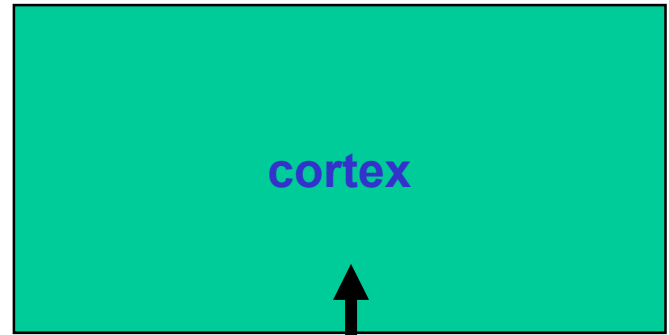
Ipotalamo anteriore centro del sonno
Ipotalamo posteriore centro della veglia



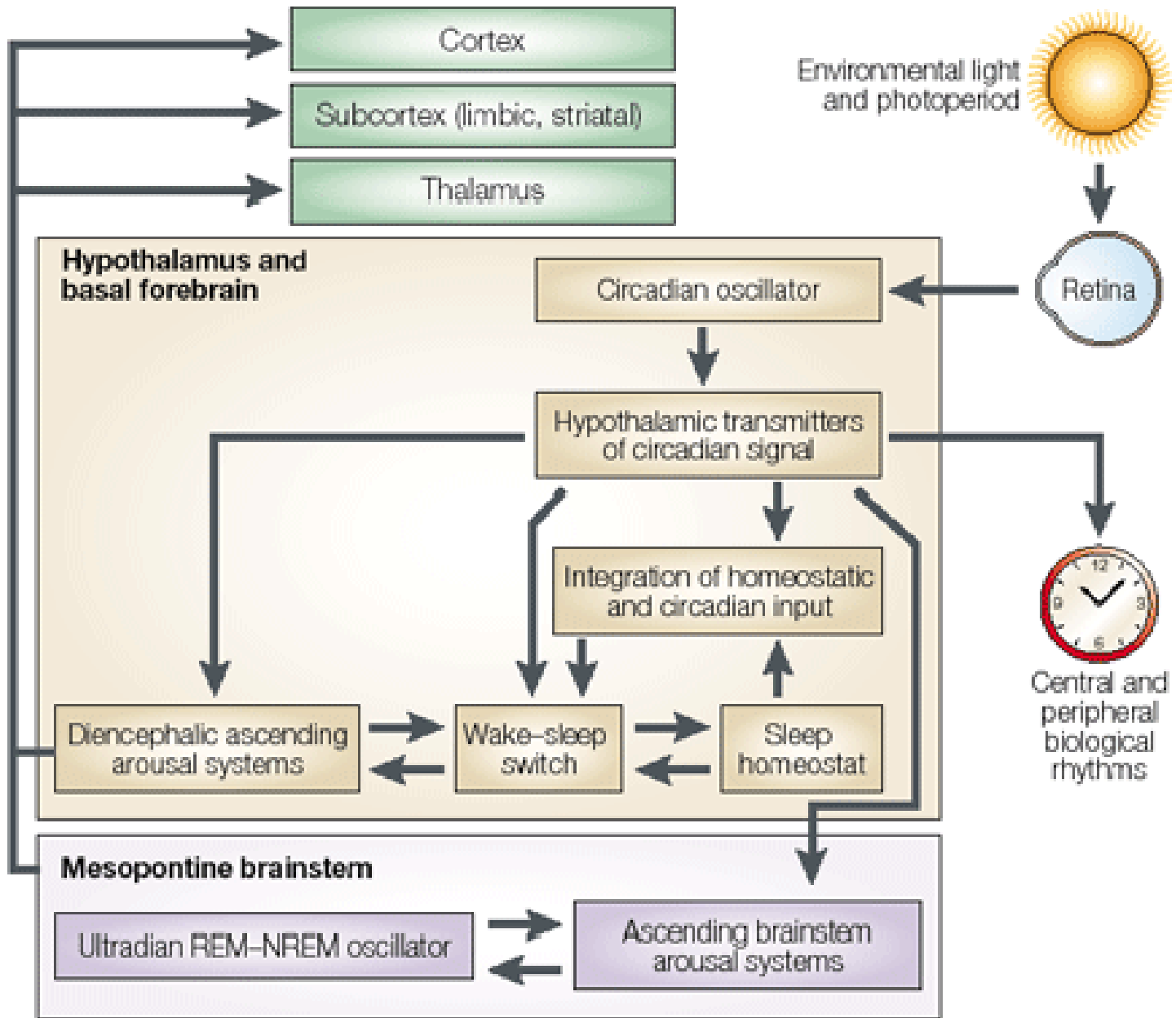
veglia



sonno

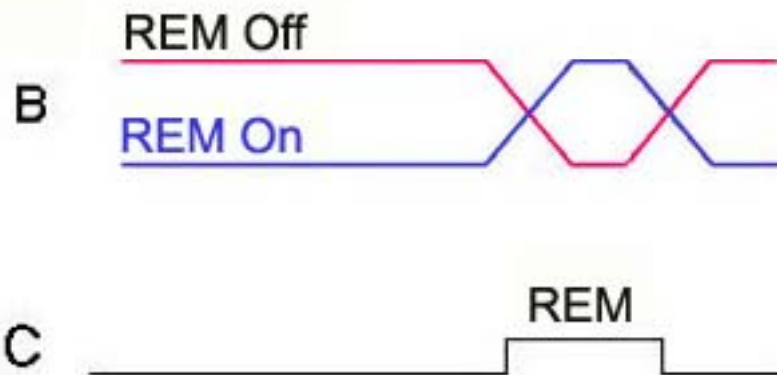
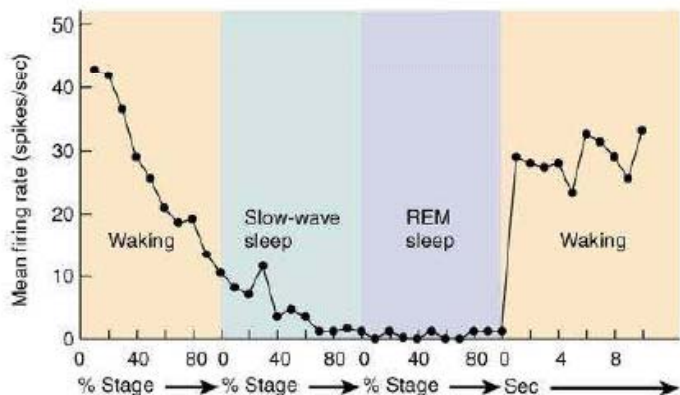
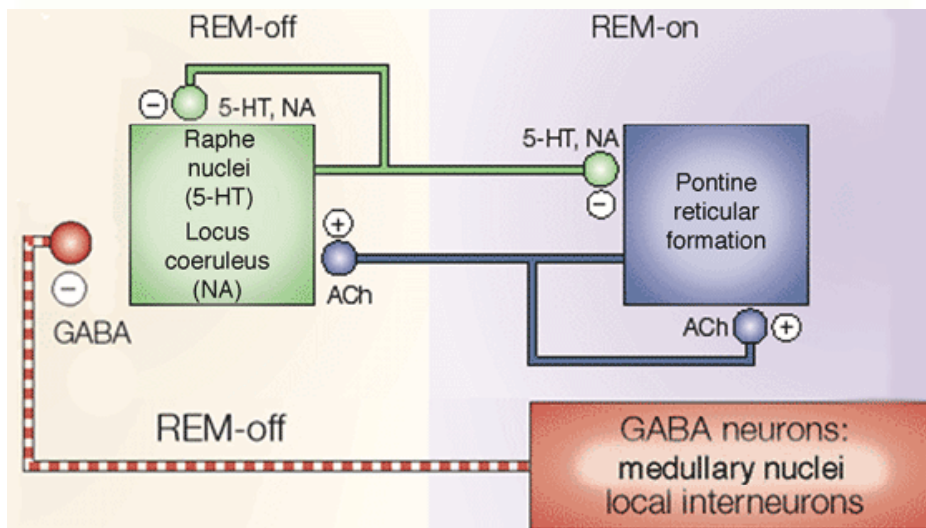


Sleep-wake control systems



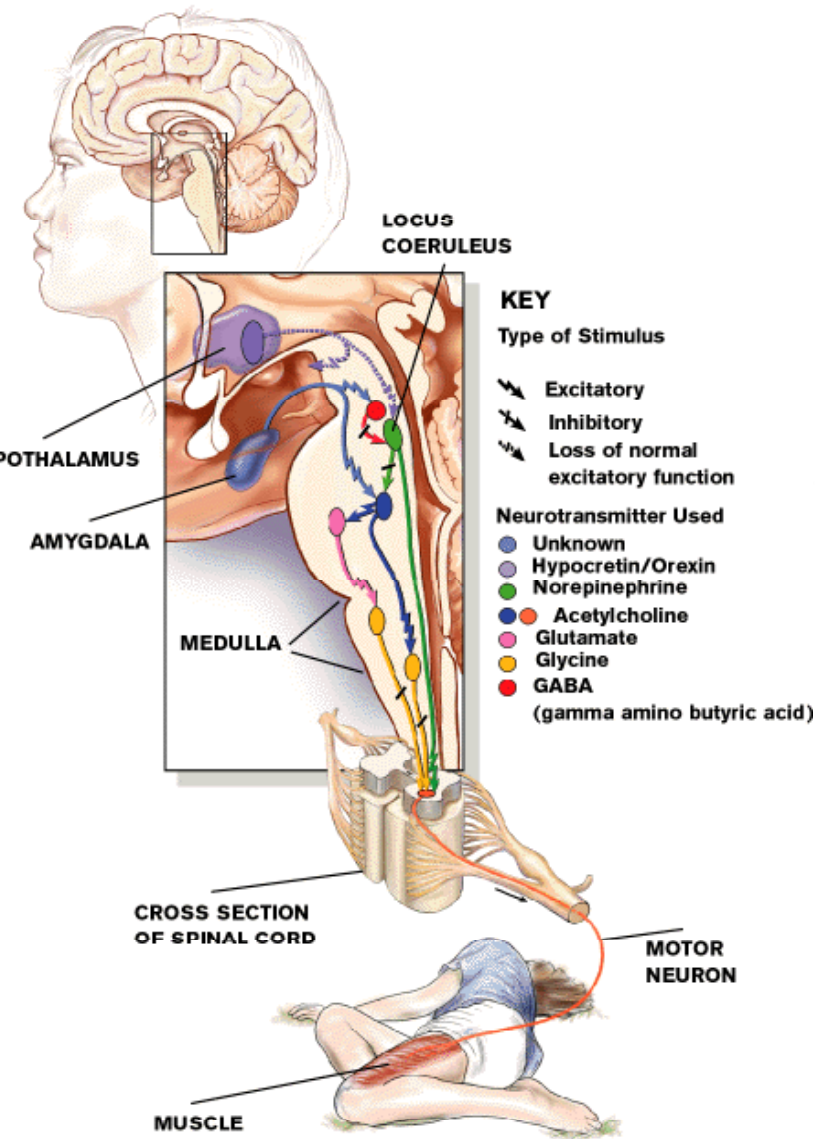
Phases	
Period	90 - 100 minutes
Brain locus of clock	
Cellular mechanism	Reciprocal interaction of cholinergic and aminergic neurons
Function	Sets "state" of organism

Neurotransmitters and REM Sleep

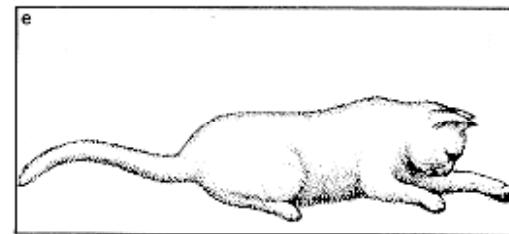
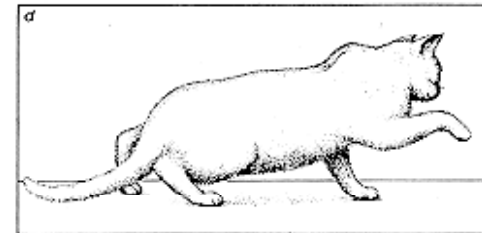
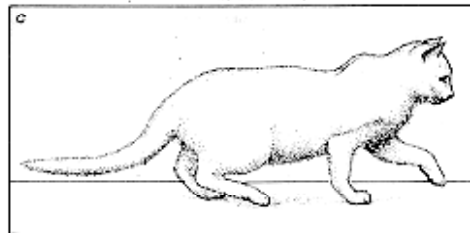
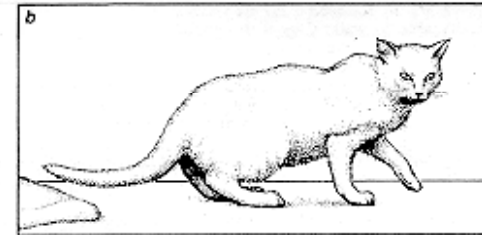
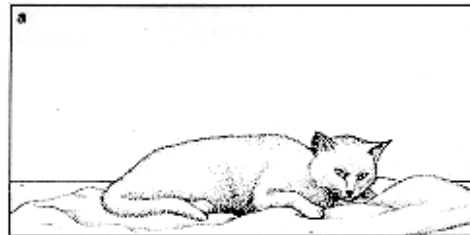
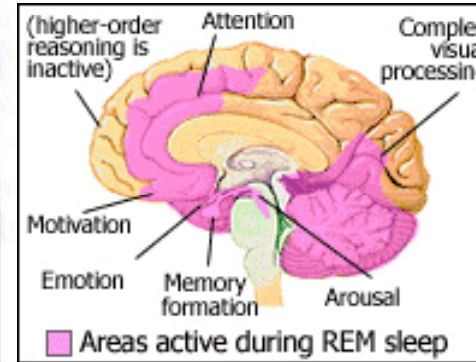
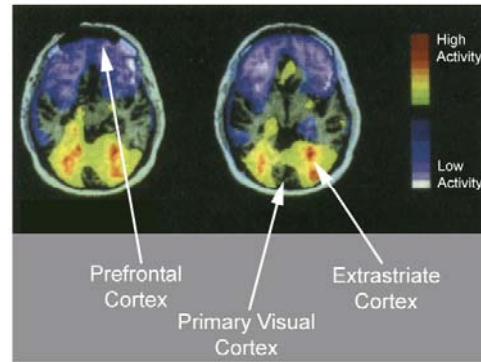


Summary of the Cellular Mechanisms of Sleep and Wakefulness

Brainstem nuclei	Activity state	Transmitter
Wakefulness		
Cholinergic nuclei	Active	ACh
Locus coeruleus	Active	NE
Raphe nuclei	Active	5-HT
Non-REM sleep		
Cholinergic nuclei	Inactive	ACh
Locus coeruleus	Inactive	NE
Raphe nuclei	Inactive	5-HT
REM sleep on		
Cholinergic nuclei	Active (PGO waves)	ACh
Raphe nuclei	Inactive	5-HT
REM sleep off		
Locus coeruleus	Active	NE



BLOOD FLOW DURING REM SLEEP



Characteristics of Mental Activity During REM and Slow-Wave Sleep

	Sleep Stage		
	Slow-wave (SWS)	Ascending	Rapid eye move- ment (REM)
Features present:			
Dreaming content	51%	51%	82%
Thinking content	19%	23%	5%
Emotion felt	28%	29%	50%
Visual	73%	62%	90%
Shift in scene	28%	38%	63%
Recall makes sense to dreamer in terms of recent experience	69%	75%	48%
Median reported duration of mental experience	5 min	5 min	5 min
Anxiety	0.71	1.00	1.19
Violence/Hostility	0.12	0.59	0.71
Distortion	1.12	0.41	1.68

Funzioni del sonno - teorie

Sonno non REM

Teorie organismiche (le cause e-o le funzioni del sonno sono all'interno dell'organismo)

- a. Teorie **ristoratrici**: il sonno serve a ristorare il cervello
- b. Teorie **protettrici**: il sonno protegge il cervello da un eccesso di veglia (ipnotossine)
- c. Teorie **economiche**: il sonno permette di risparmiare energie

Teorie ecologiche (il sonno è regolato secondo le necessità dell'individuo e della specie)

- **Orologio biologico predittivo**
- **Necessità di alternare periodi** di veglia e periodi di sonno
- **Veglia dominante** per la sopravvivenza dell'individuo e della specie
 - periodi di sonno subordinati alle necessità di veglia
 - sonno localizzato**
 - sonno di lusso e di necessità**

Sonno REM

Sonno REM sentinella

Apprendimento, memoria, oblio

Crescita e rinforzo strutturale e funzionale dei circuiti nervosi

Funzioni del sonno

1. Risparmio/recupero energetico (scorte di glicogeno SNC)

Ratti deprivati di sonno:

Fase 1: aumento assunzione cibo con perdita di peso

Fase 2: perdita di termoregolazione (heat-seeking behavior)

Fase 3: morte per sepsi (immunodeficienza)

Animali di taglia piccola hanno bisogno di più ore di sonno rispetto a quelli di taglia più grande (con minore necessità energetica relativa per termoregolazione e attività motoria)

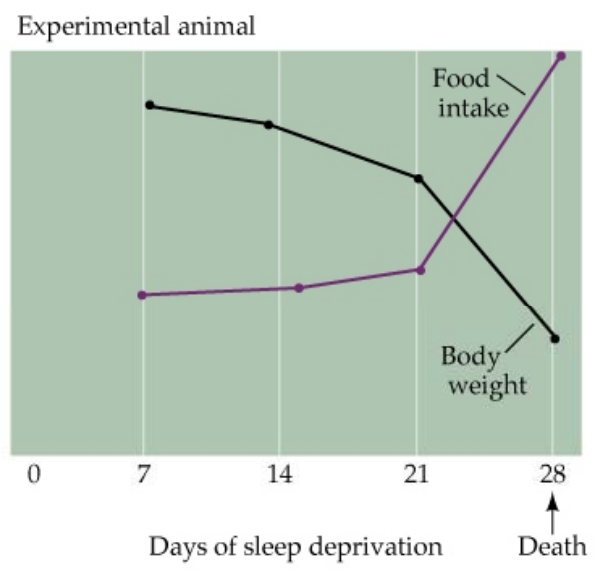
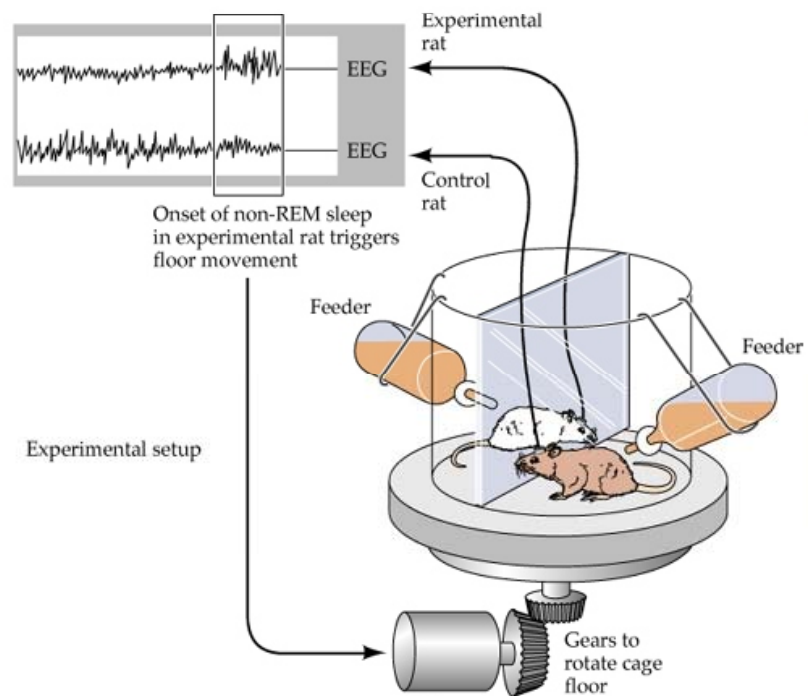
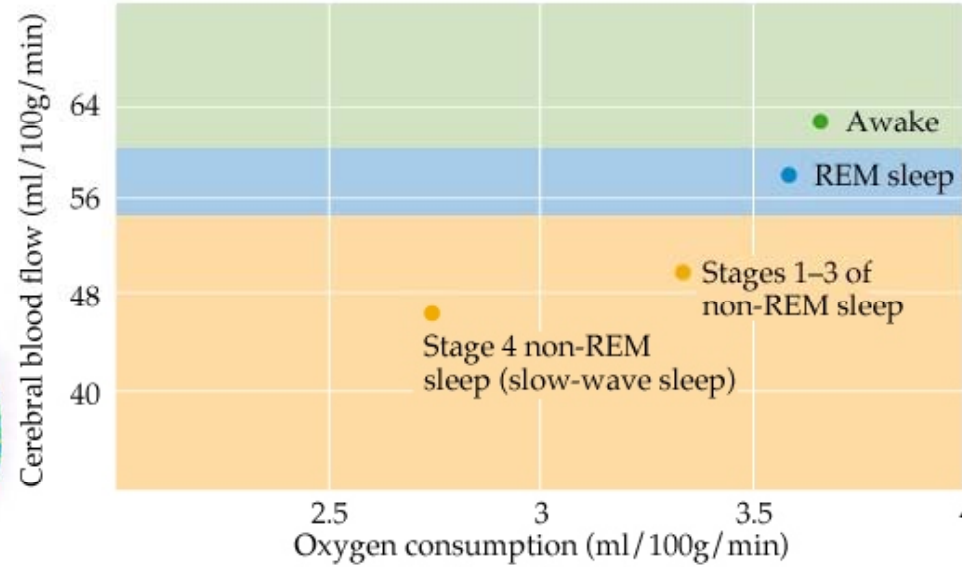
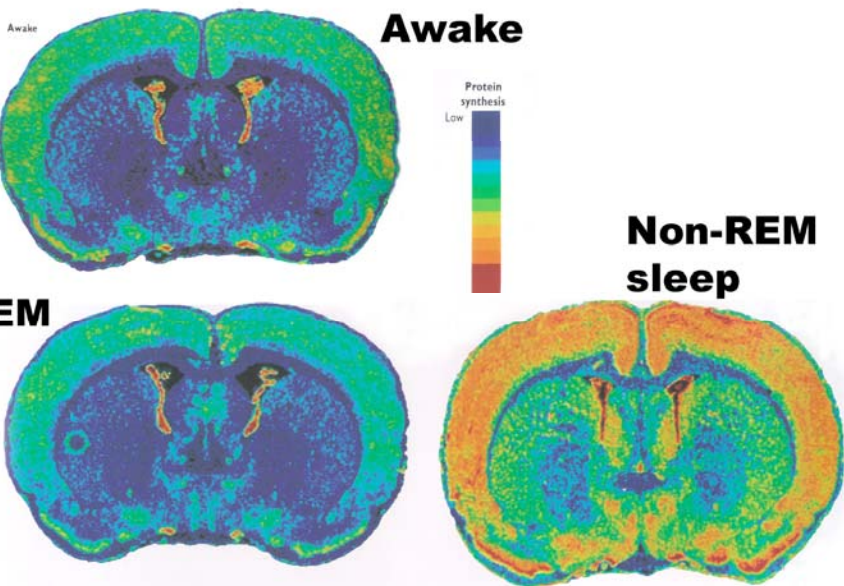
2. Sviluppo/crescita dell'organismo

Cambiamento composizione del sonno (REM/NREM) durante lo sviluppo

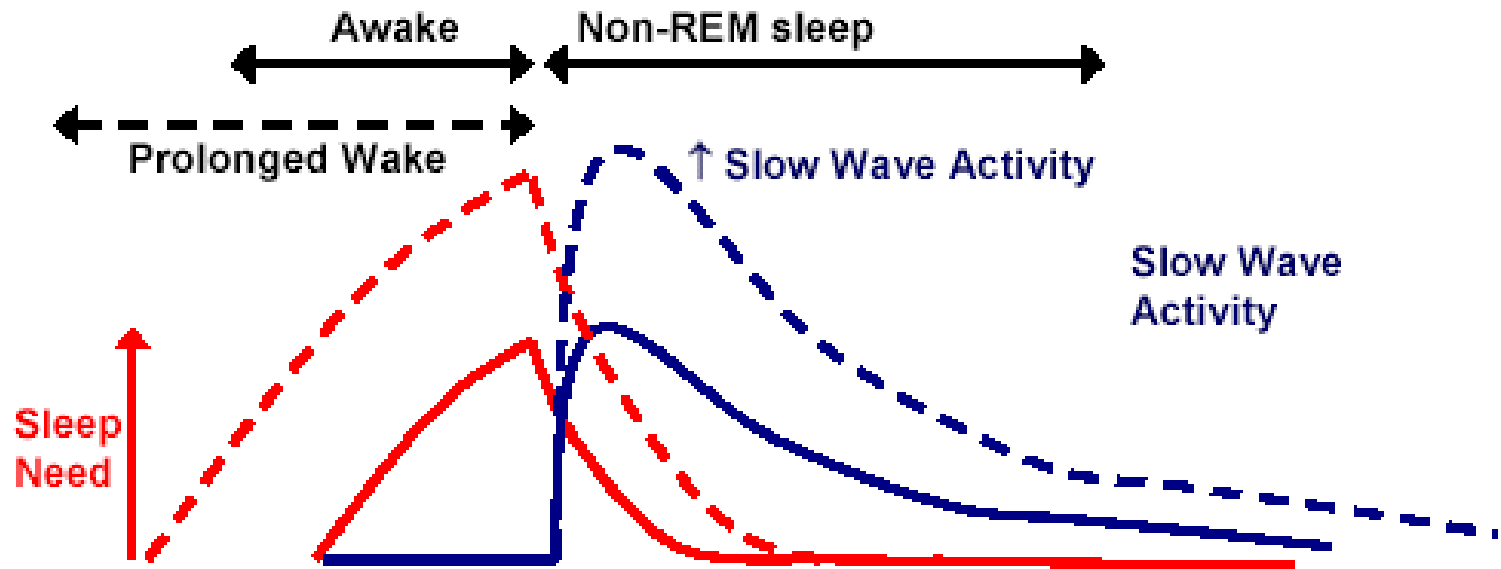
Pattern di attivazione cerebrale (REM)

Secrezione ormonale (ormone della crescita, gonadotropine ipofisarie)

3. Consolidamento tracce mnemoniche



Sleep Need Accumulates in Wakefulness and Dissipates in non-REM sleep



Concept:

High Voltage slow wave activity is a marker of homeostatic sleep need

Homeostatic Principle:

The more we have been awake the more we must sleep

Figure 2. Effect of 72 Hours of Total Sleep Deprivation on Cognitive Performance

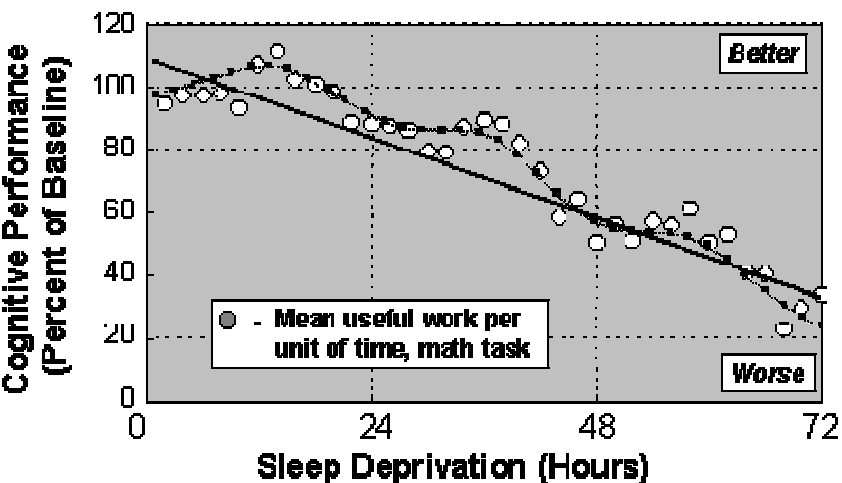


Figure 6. Cognitive Performance during Total Sleep Deprivation vs. with Daily 30-minute Nap

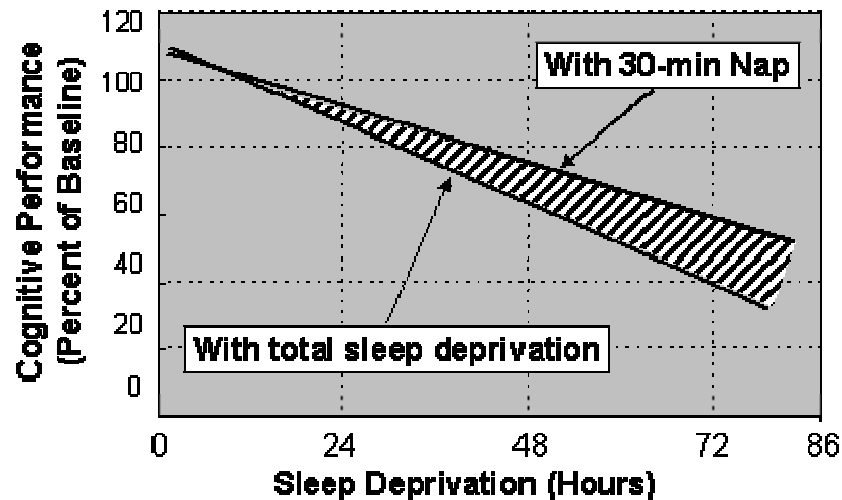
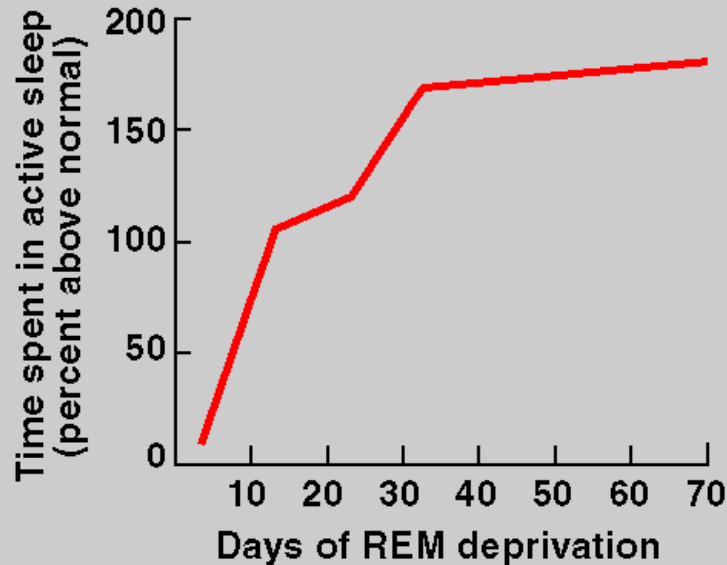
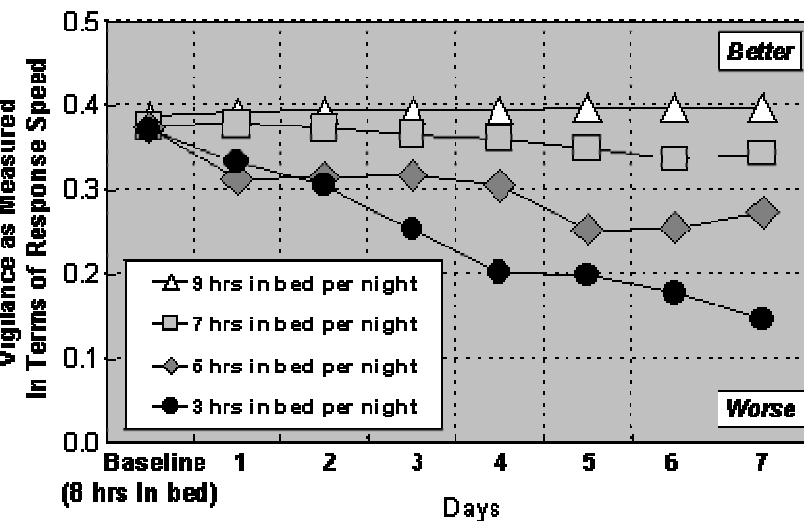
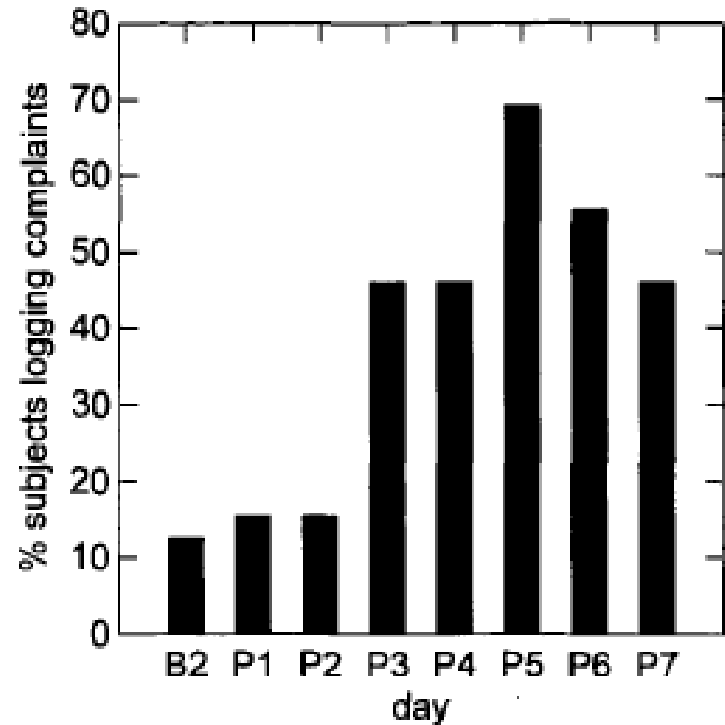
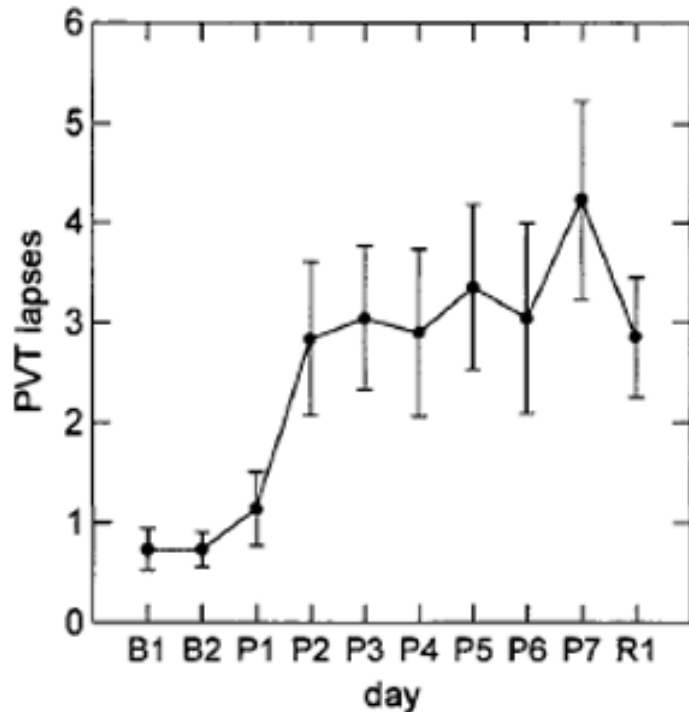


Figure 3. Seven Days of Restricted Sleep: Effects on Vigilance



Gruppo di giovani adulti: sonno ridotto a 5 ore/notte (invece di 7,5/notte)



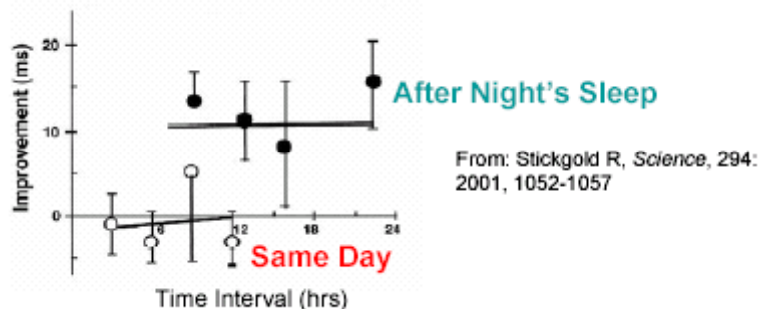
Subjects reported or showed:

- Increasing feelings of sleepiness, fatigue, mental exhaustion and confusion
- Mood effects such as increased irritability, tension and anxiety
- Worsening of performance on a psychomotor vigilance task (PVT) that measured sustained attention
- Increased complaints of sleepiness, somatic problems and cognitive and emotional problems

Sample Experiment:

Discrimination task in normal subjects

Trained and re-tested: **3 to 12 hours later on same day**
8 to 24 hours after night's sleep



So: Improvement Not Seen Until After Post-Training Sleep

Then found: Overnight improvement in learning correlated with:

- (a) amount of non-REM sleep at beginning night
- (b) amount of REM sleep at end of night

addestramento



N-REM stabilizzazione



REM rinforzo



apprendimento

The normal non-REM to REM sleep cycle is important

This normal alternation of states adjusts neural connections that may allow memories to be stored, retrieved and even deleted

3 Step-Model of Learning: R. Stickgold (Harvard)

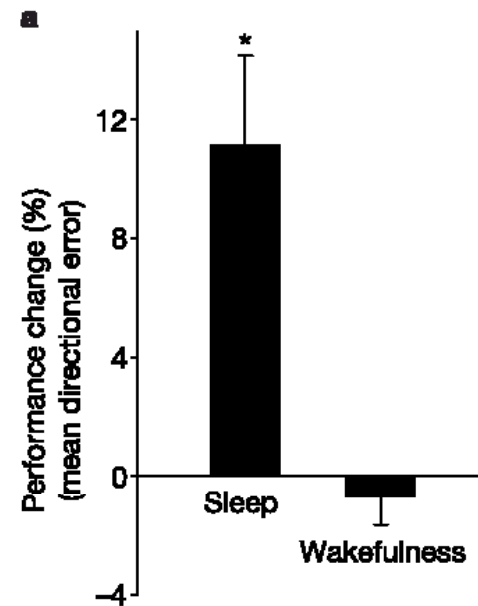
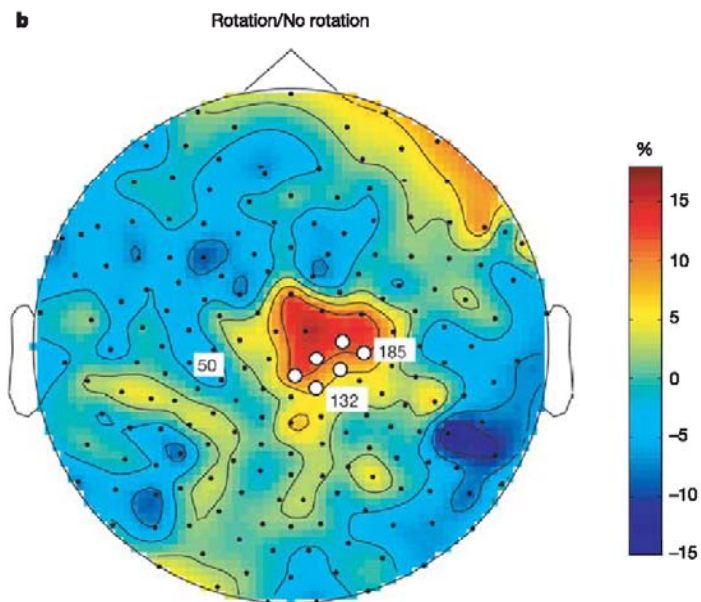
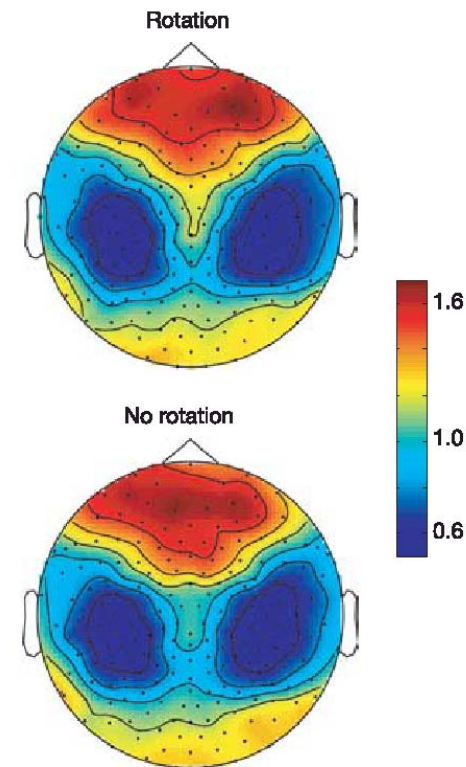
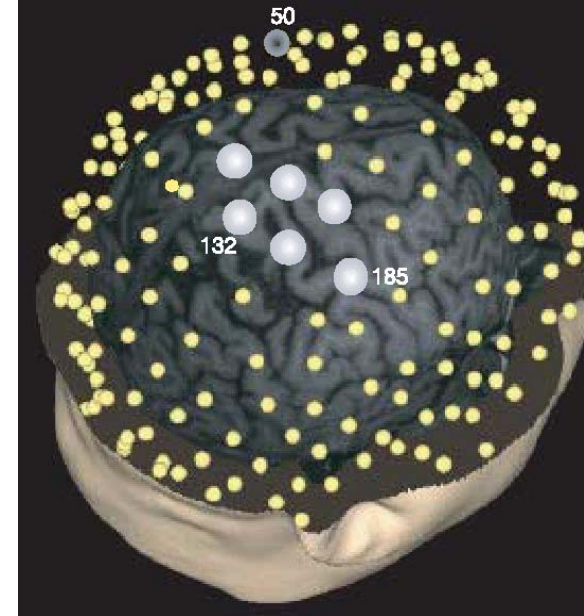
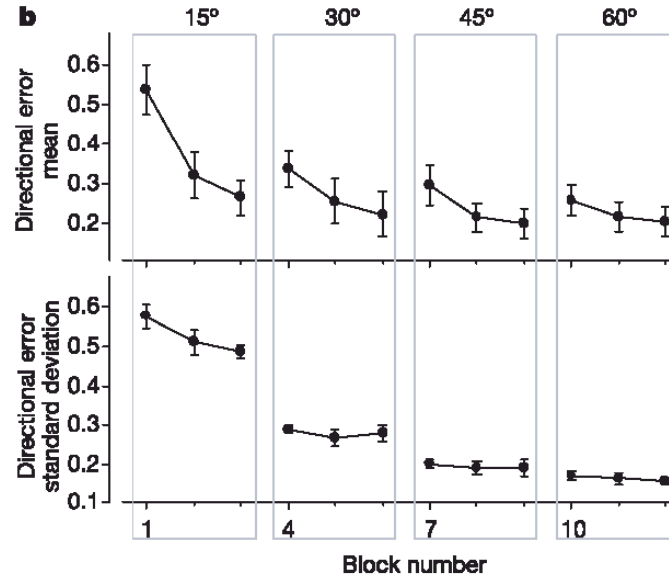
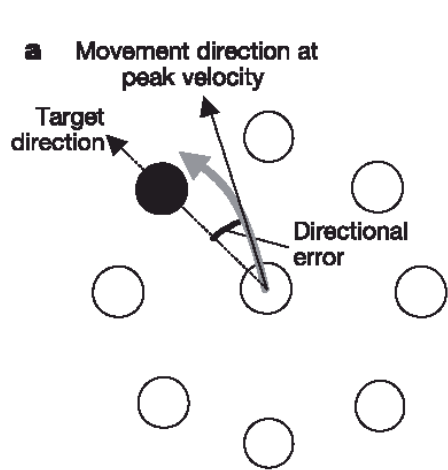
Training initiates learning process

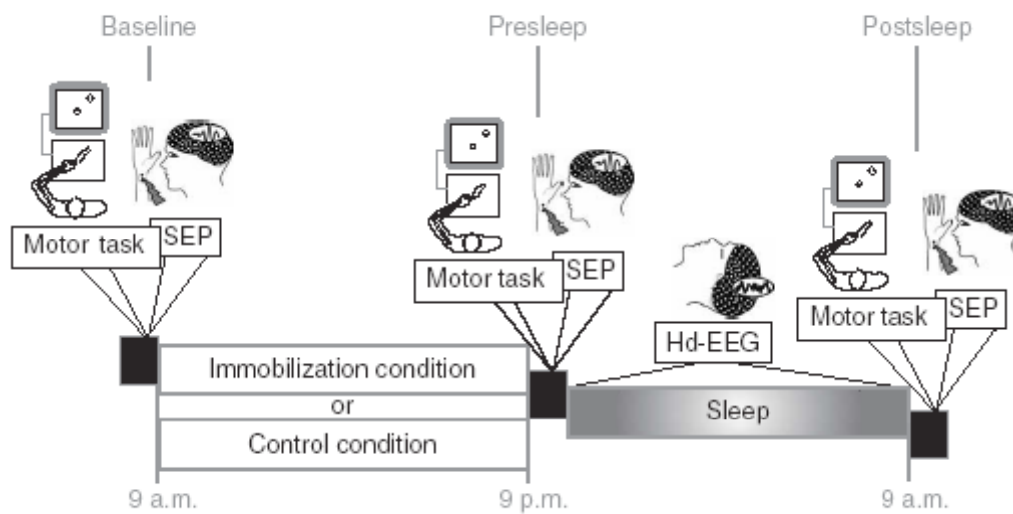
Step 1: Non-REM sleep stabilizes learning process

Step 2: REM sleep enhances learning process

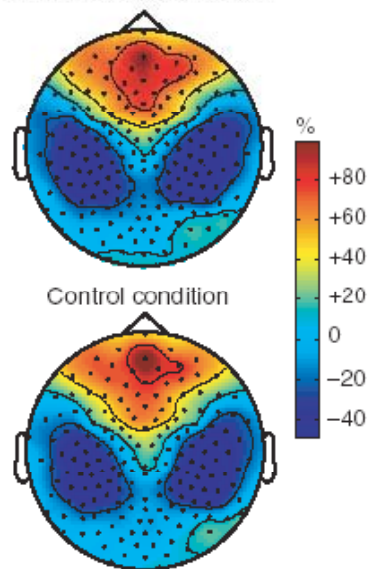
Step 3: Learning

So, would you expect staying up late cramming for exams is a good idea?

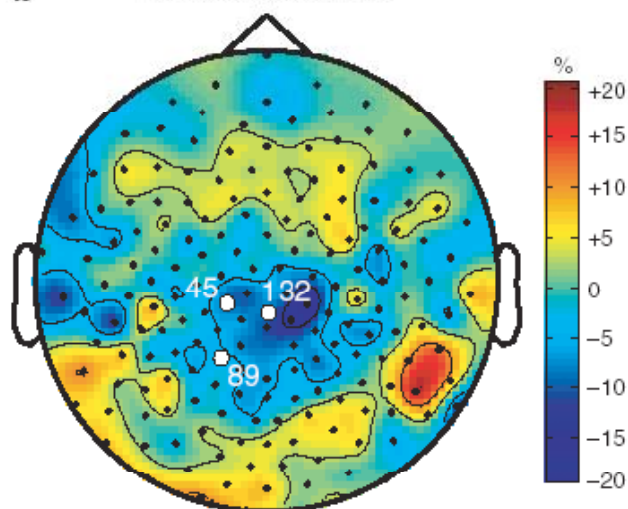




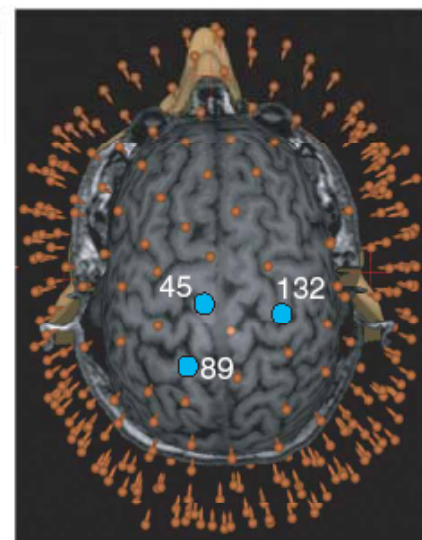
a Immobilization condition



b Immobilization/control



c



Patologia del ciclo sonno/veglia

Eccesso di sonno

Narcolessia

OSAS (Obstructive Sleep Apnea Syndrome)

Sindrome da insufficienza cronica di sonno

Eccesso di veglia

Insomnia (transitoria/cronica)

Alterazioni parziali dello stato di sonno o veglia

parasonnie

REM behavior disorder

Sonnambulismo

Pavor nocturnus

Enuresi notturna

Sonniloquio

Dyssomnias

Intrinsic sleep disorders

Psychophysiologic insomnia
Sleep state misperception
Idiopathic insomnia
Narcolepsy
Recurrent hypersomnia
Idiopathic hypersomnia
Posttraumatic hypersomnia
Obstructive sleep apnea syndrome
Central sleep apnea syndrome
Central alveolar hypoventilation syndrome
Periodic limb movement disorder
Restless legs syndrome

Extrinsic sleep disorders

Inadequate sleep hygiene
Environmental sleep disorder
Altitude insomnia
Adjustment sleep disorder
Insufficient-sleep disorder
Limit-setting sleep disorder
Sleep-onset association disorder
Food allergy insomnia
Nocturnal eating (drinking) syndrome
Hypnotic-dependent sleep disorder
Stimulant-dependent sleep disorder
Alcohol-dependent sleep disorder
Toxin-induced sleep disorder

Circadian rhythm sleep disorders

Time-zone change (jet lag) syndrome
Shift-work sleep disorder
Irregular sleep-wake pattern disorder
Delayed-sleep-phase syndrome
Advanced-sleep-phase syndrome
Non-24 hr sleep-wake disorder

Parasomnias

Arousal disorders

Confusional arousals
Sleepwalking
Sleep terrors

Sleep-wake transition disorders

Rhythmic movement disorder
Sleep starts
Sleep talking
Nocturnal leg cramps

Parasomnias usually associated with REM sleep

Nightmares
Sleep paralysis
Impaired sleep-related penile erections
Sleep-related painful erections
Impaired sleep-related sinus arrest
REM sleep behavior disorder

Other Parasomnias

Sleep bruxism
Sleep enuresis
Sleep-related abnormal swallowing syndrome
Nocturnal paroxysmal dystonia
Sudden unexplained nocturnal death syndrome
Primary snoring
Infant sleep apnea
Congenital central hypoventilation syndrome
Sudden infant death syndrome
Benign neonatal sleep myoclonus

Sleep Disorders Associated with Medical/Psychiatric Disorders

Psychiatric disorders

Psychoses
Mood disorders
Anxiety disorders
Panic disorders
Alcoholism

Neurologic disorders

Cerebral degenerative disorders
Dementia
Parkinsonism
Fatal familial insomnia
Sleep-related epilepsy
Electrical status epilepticus of sleep
Sleep-related headaches

Other medical disorders

Sleeping sickness
Nocturnal cardiac ischemia
Chronic obstructive pulmonary disease
Sleep-related asthma
Sleep-related gastroesophageal reflux
Peptic ulcer disease
Fibrositis syndrome (*Fibromyalgia*)

Narcolessia

20-45 su 100.000 (USA) - inizio 25-30 anni – familiarità (fino al 90%)

Segni caratteristici:

1. Episodi di sonno incoercibile durante il giorno

sonnolenza debilitante (perdita capacità di lavoro)
attacchi incoercibili simili a lunga deprivazione
sonno entro 2-3 minuti (normalmente 10-15)
fase REM all'inizio del sonno (entro 15 min)

2. Cataplessia

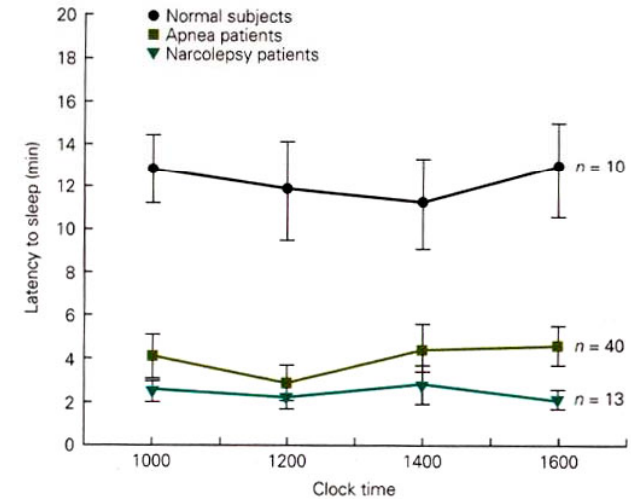
perdita del tono muscolare improvvisa e reversibile
spesso scatenata da un'emozione
durante l'attacco il pz è cosciente

3. Paralisi del sonno

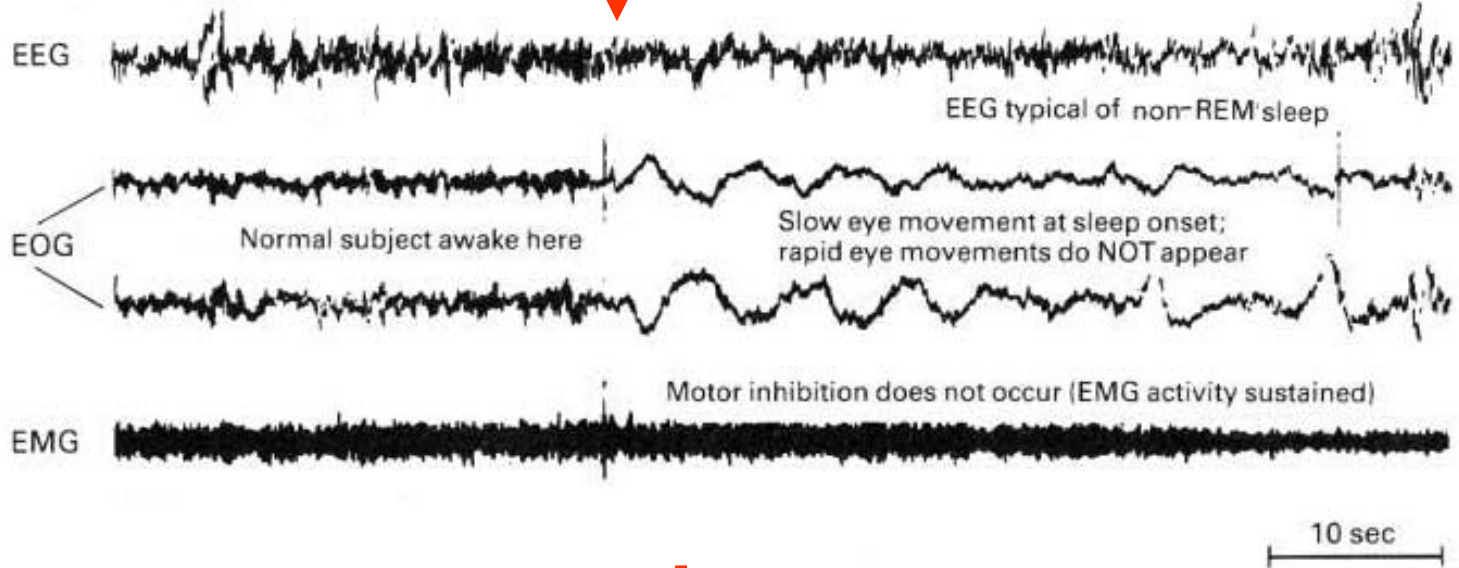
all'inizio o alla fine del sonno (durata: circa 10 min)
pz sveglio e terrorizzato
del tutto incapace di muoversi parlare aprire gli occhi o respirare profondamente

4. Allucinazioni ipnagogiche

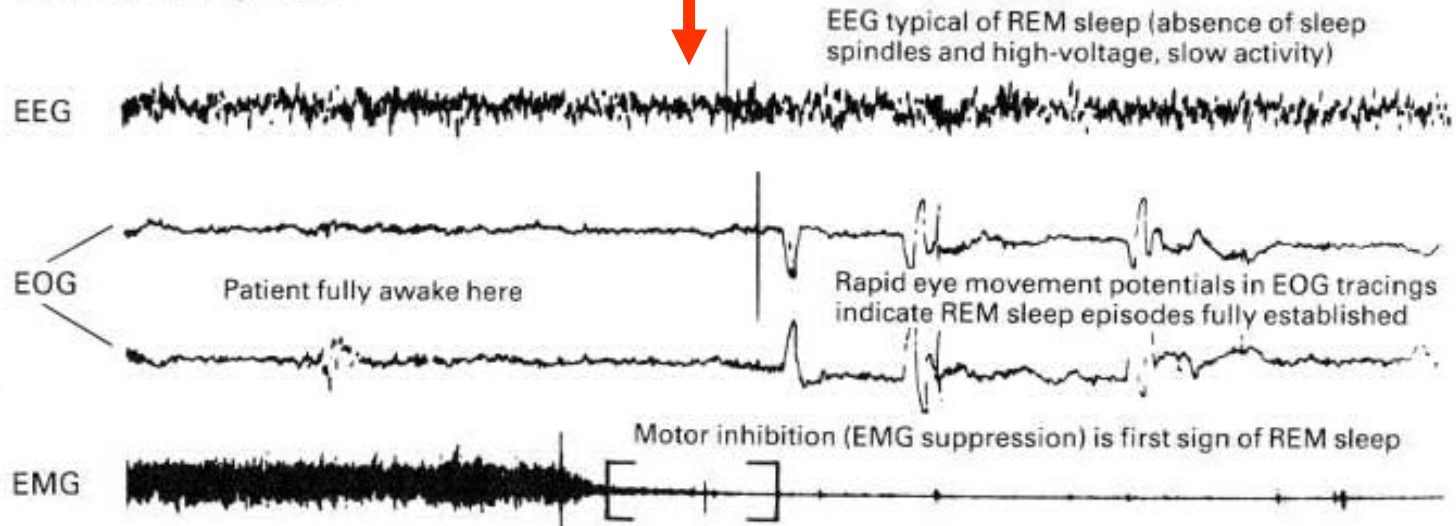
allucinazioni uditive o visive molto intense
all'inizio del sonno
spesso associate con la paralisi del sonno



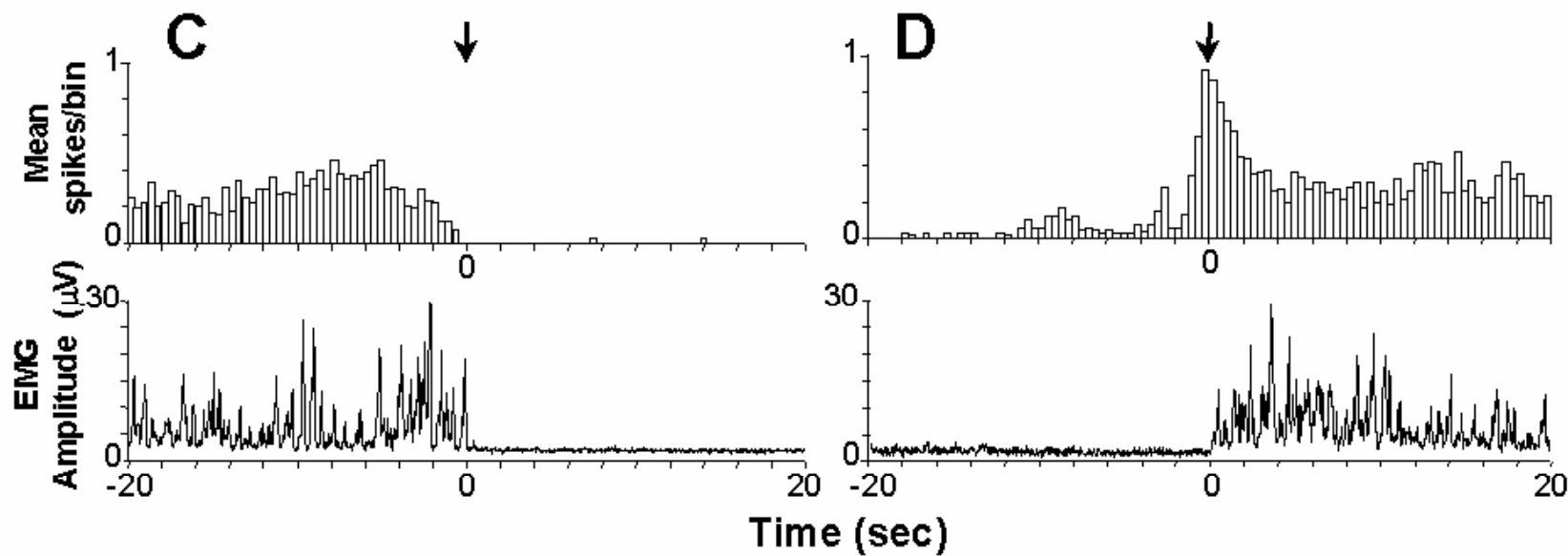
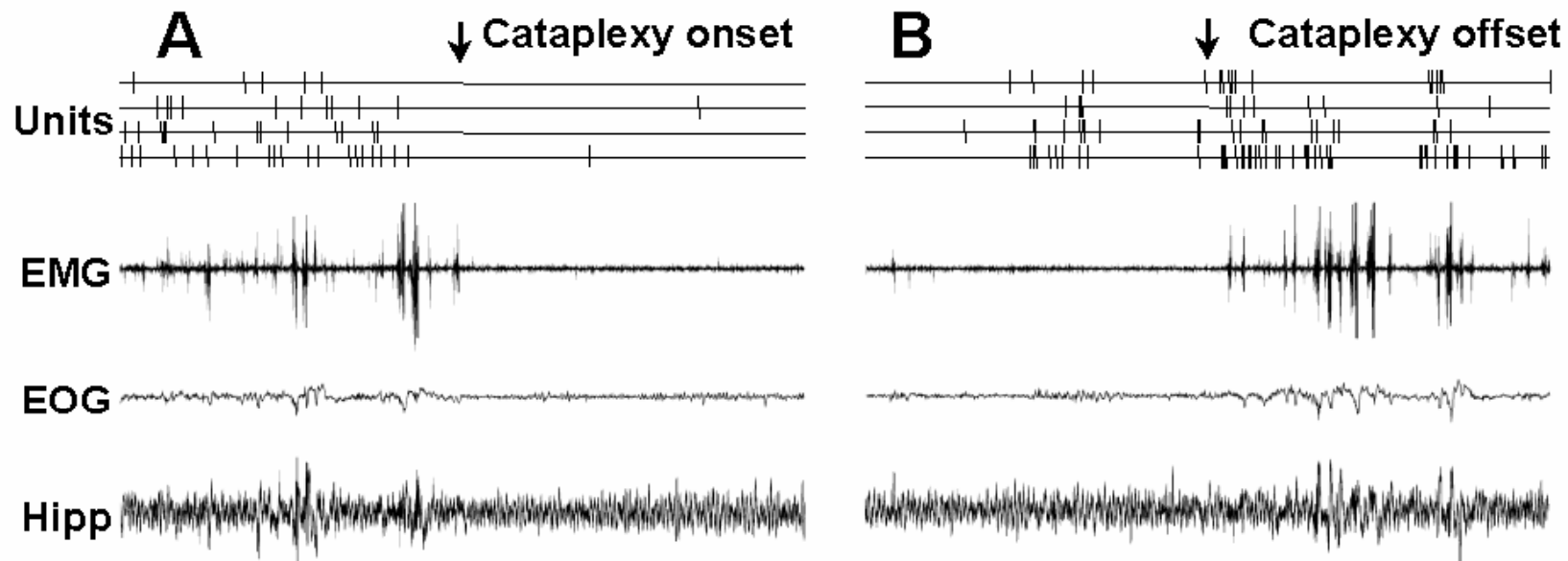
A Normal sleep onset



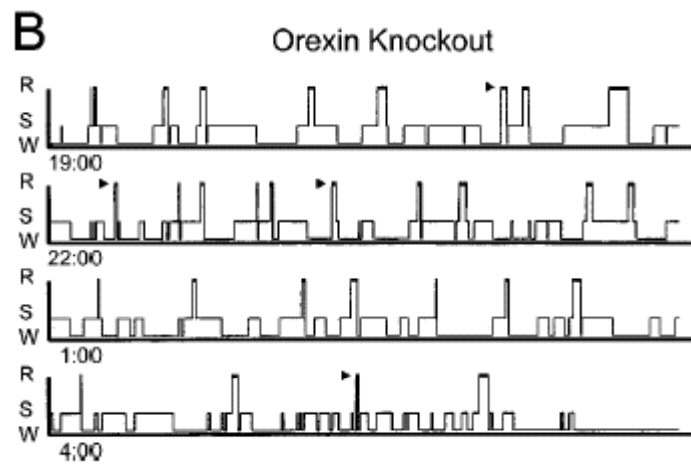
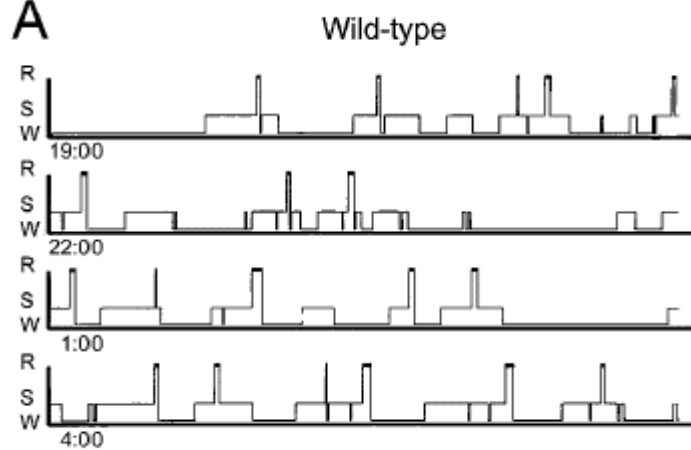
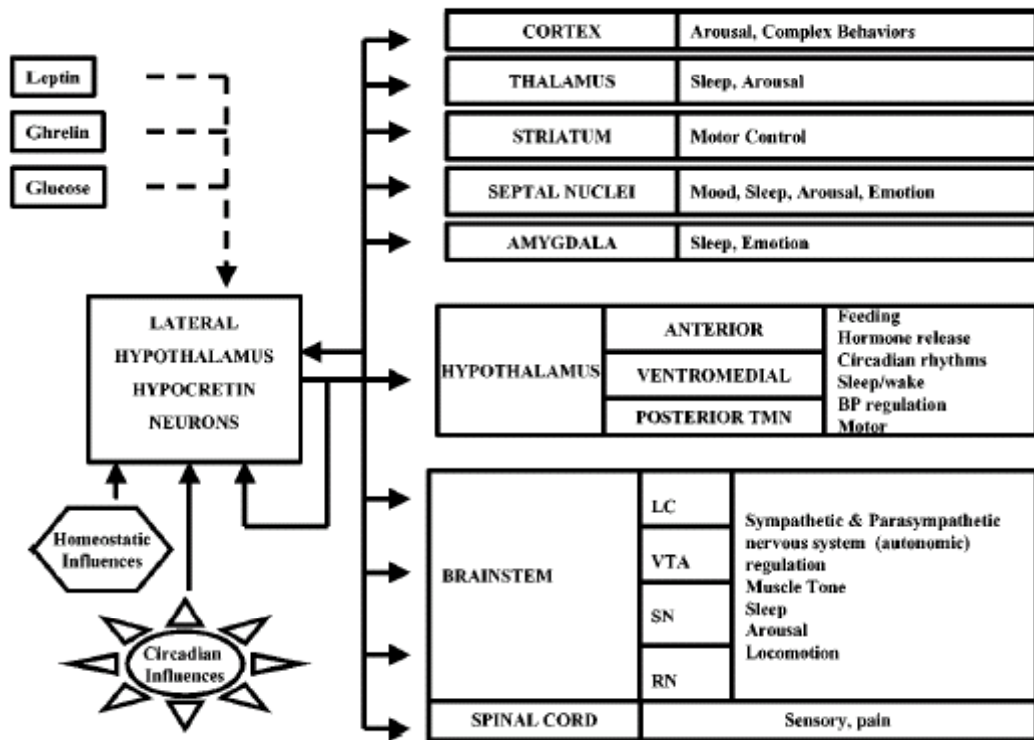
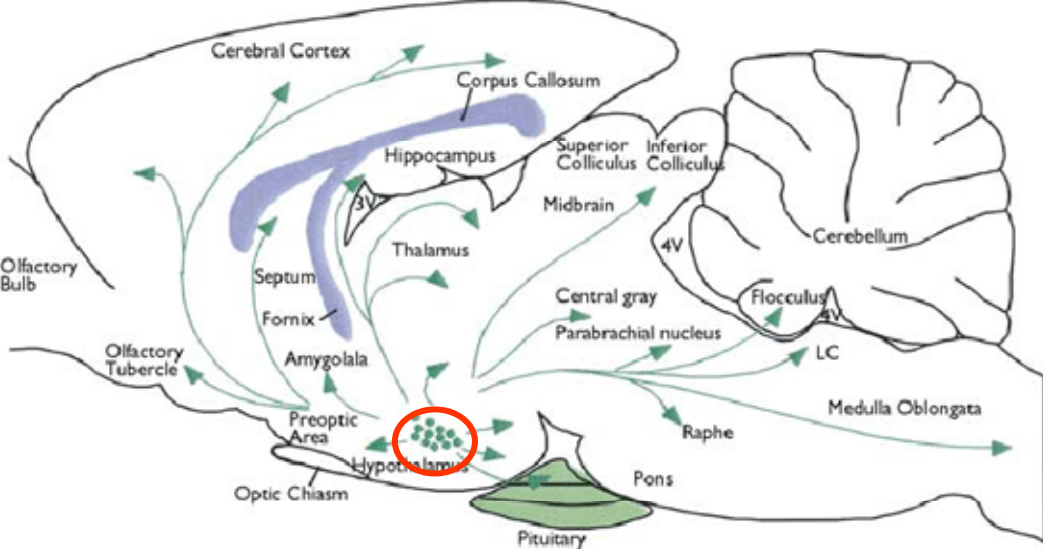
B Narcoleptic sleep onset



neuroni del locus coeruleus







Orexina/ipocretina: aumenta l'attività motoria, l'assunzione di cibo, riduce il sonno

Uomo: narcolessia da malattia autoimmune che distrugge selettivamente i neuroni ipotalamici che producono orexina

OSAS

Più frequente in maschi obesi di mezza età

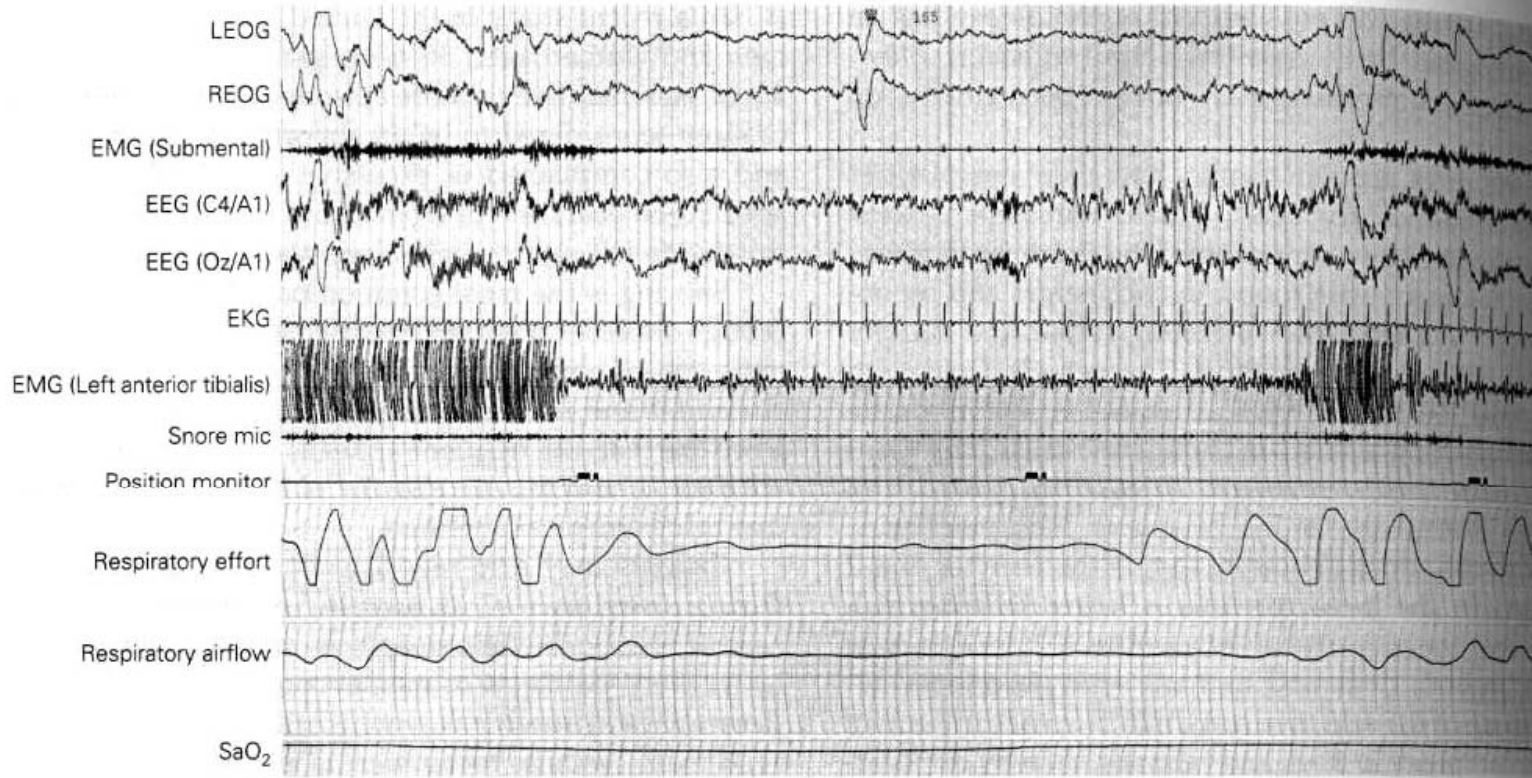
Lamentano sonnolenza diurna, cefalea mattutina, russano

Frequenti episodi di apnea nel sonno (4-5 per ora) di durata variabile (20-30 sec --- 2-3 minuti)

La sindrome è dovuta ad eccessivo rilassamento del tono muscolare nel sonno, associato ad anomalie anatomiche della faringe (es accumulo di grasso).



OSAS



Sindrome da insufficienza cronica di sonno

Comune fra maschi di 30-60 anni, studenti, persone con particolari orari di lavoro

Riportano frequente sonnolenza diurna ed affaticamento

La sindrome è dovuta ad una cronica restrizione del tempo di sonno giornaliero al di sotto delle necessità individuali (in media 7-8 ore).

Insonnia

Intrusione dello stato di veglia nel periodo delle ciclo circadiano di sonno-veglia usualmente dedicato al sonno

Transitoria

Cronica (spesso secondaria ad altra patologia, es. depressione)

Meccanismi

Ridotto stimolo omeostatico al sonno

Attivazione anormale dei sistemi di veglia:

stimolazione sensoriale alterata (nel tempo)

alterazione dei ritmi circadiani (jet-lag)

iperattivazione dei sistemi di veglia

Insonnia primaria cause non definite

Insonnia secondaria

- **Malattie psichiatriche (ansia, depressione)**
- **Stress emotivo**
- **Malattie organiche (dolore cronico, asma, cardiopatie, asma, ulcera peptica...)**
- **Malattie neurologiche (ictus, malattie neurodegenerative, tumori cerebrali, traumi cerebrali)**
- **Alterazioni del normale ciclo circadiano (lavoro notturno, jetlag)**
- **Abuso di caffeina, droghe o alcol**

History of Sleep Disorder Treatment

Historical — Opium and alcohol

1860s — Chloral hydrate

1870s — Bromides

1880s — Paraldehyde

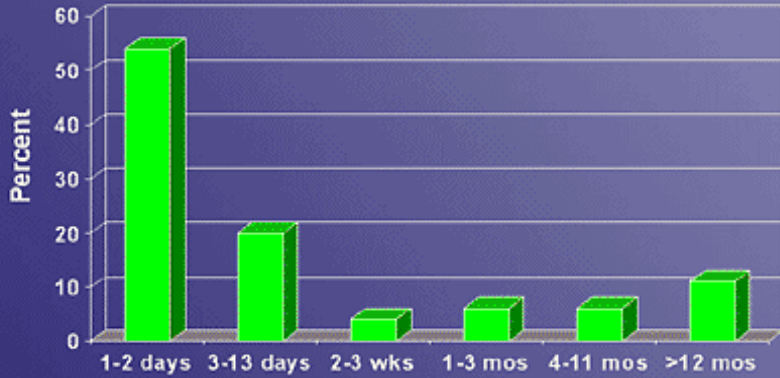
1900s — Barbiturates

1960s — Benzodiazepines

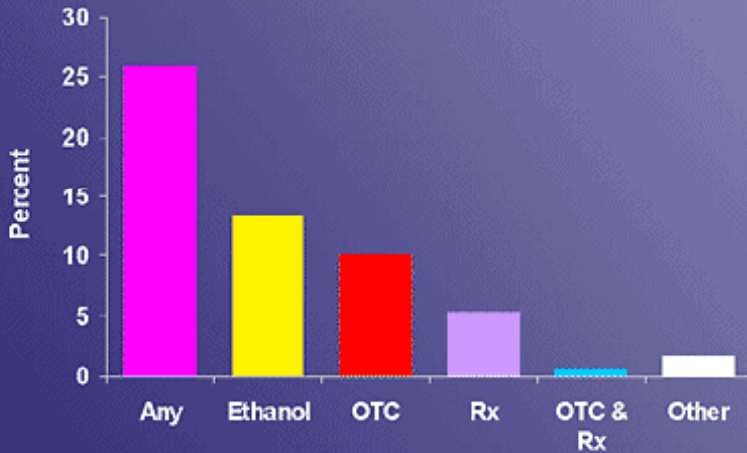
1980s — Non-benzodiazepine BzRAs

2000s — ???

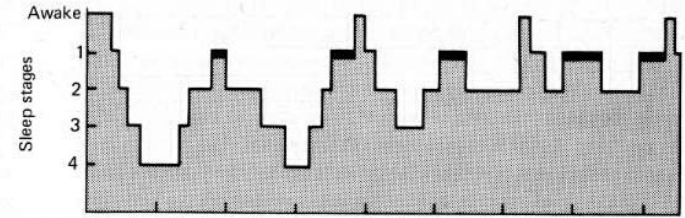
Longest Period of Regular Hypnotic Use



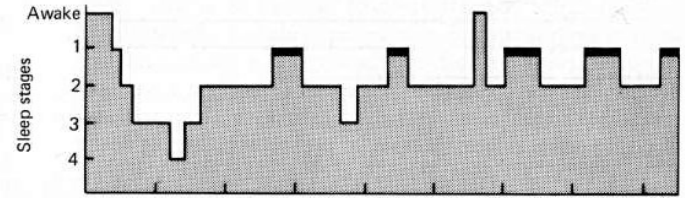
Percent of 18- to 45-Year-Olds Using Substances to Aid Sleep in Past Year



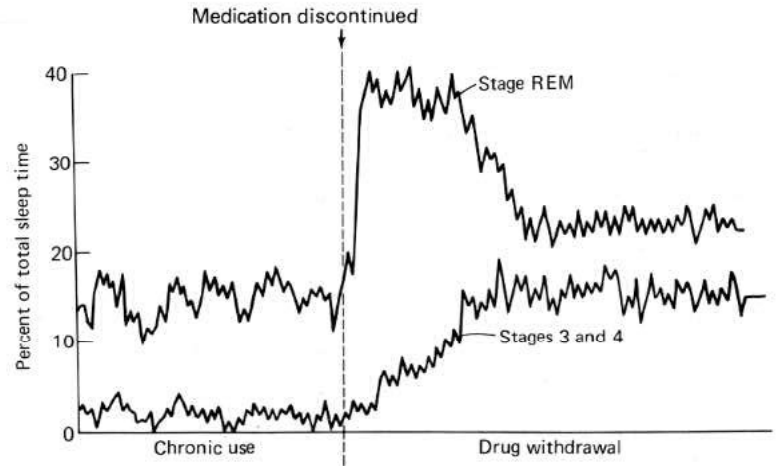
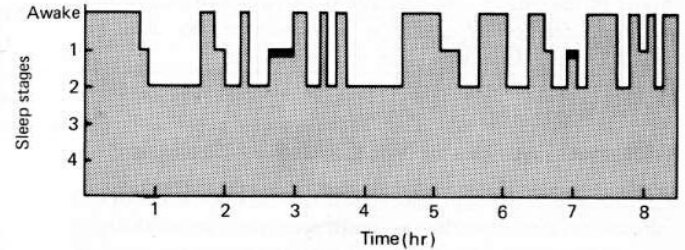
A. Untreated



B. Short-term drug administration (100 mg)



C. Chronic drug use



Parasonnie

Alterazioni dello stato di sonno con intrusione di caratteristiche dello stato di veglia

Possono avvenire

durante la transizione veglia-sonno

durante il sonno non-REM

durante il sonno REM

Parasomnia del sonno REM

EM behavior disorder

Episodi con movimenti violenti
d'agitazione durante il sonno
REM

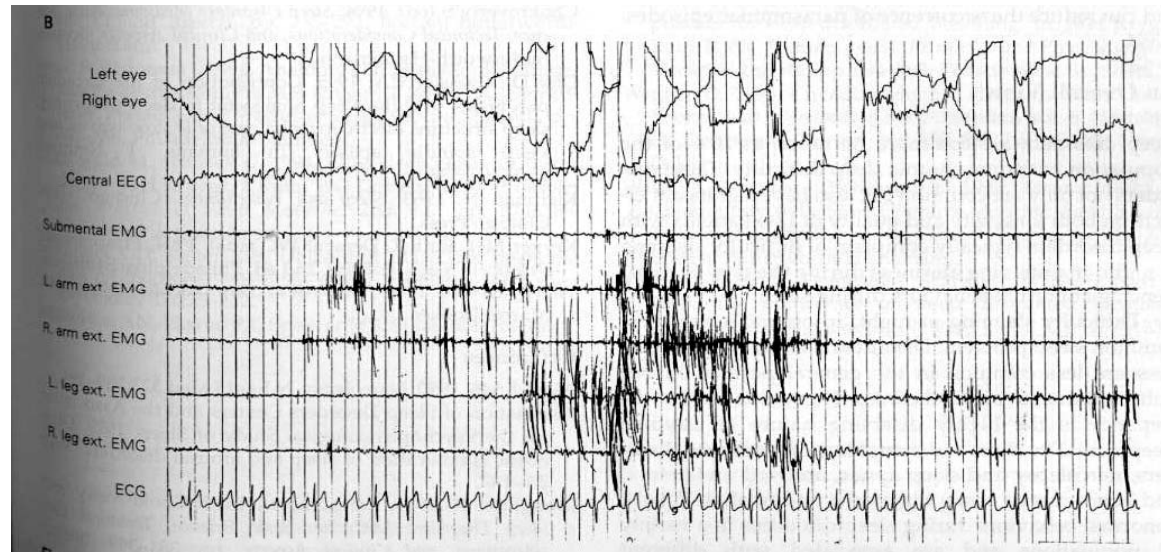
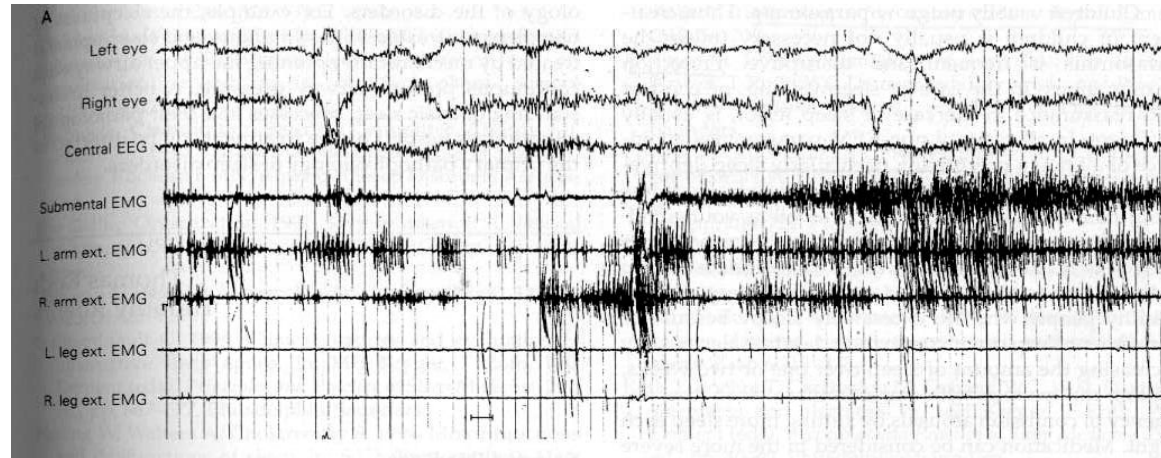
Associato a vivida attività
onirica

Simile alle lesioni del Locus
coeruleus nei gatti (dream
enactment)

Descritta riduzione dei neuroni
5-HT nel uomo

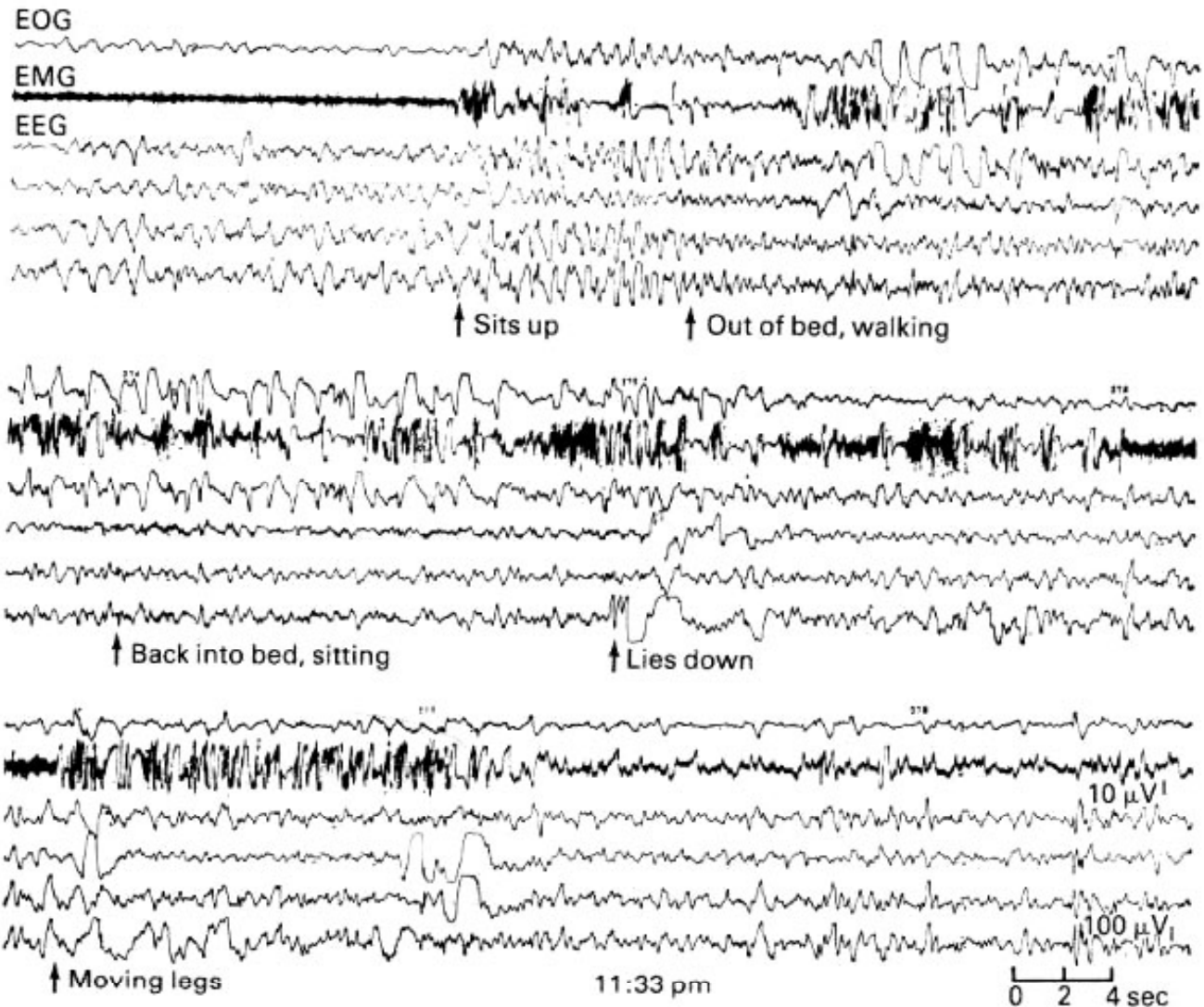
Soprattutto nei maschi

Associato ad alcolismo

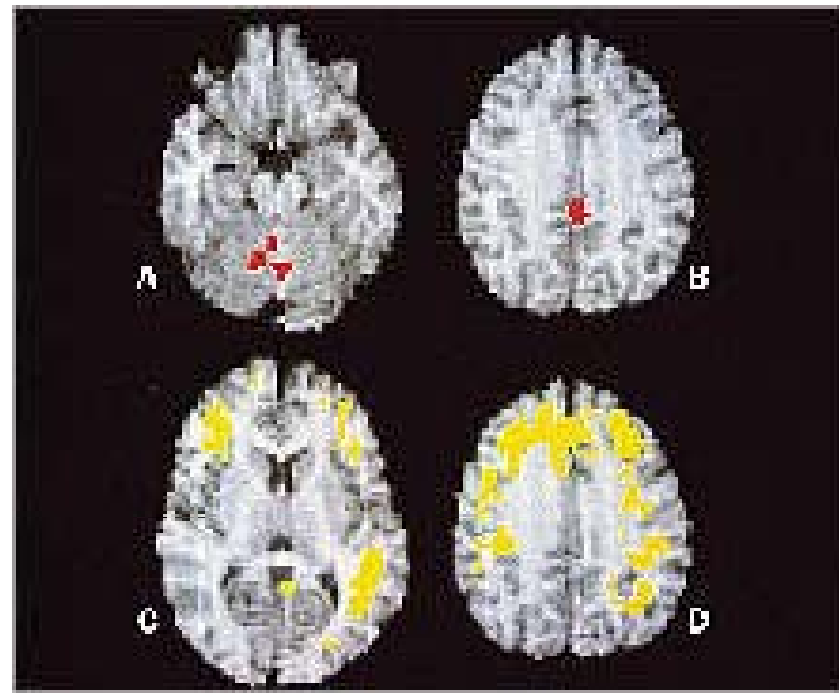


Parasonnie del sonno non-REM

Sonnambulismo



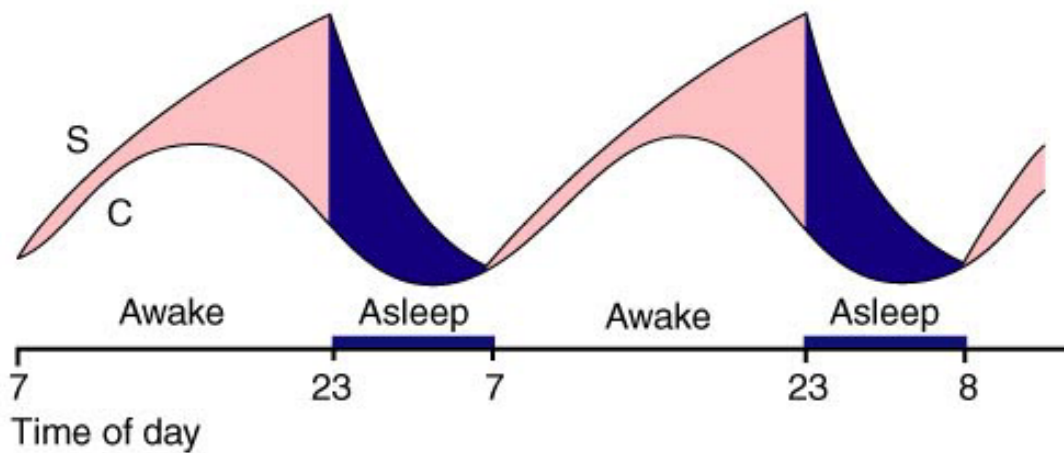
Onde delta nel sonnambulismo



altre parasonnie del sonno non-REM

Pavor nocturnus
Enuresi notturna
Sonniloquio

A Sleep/wake cycle



B Sleep deprivation

