Physiology of Normal Sleep: From Young to Old

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What is sleep?

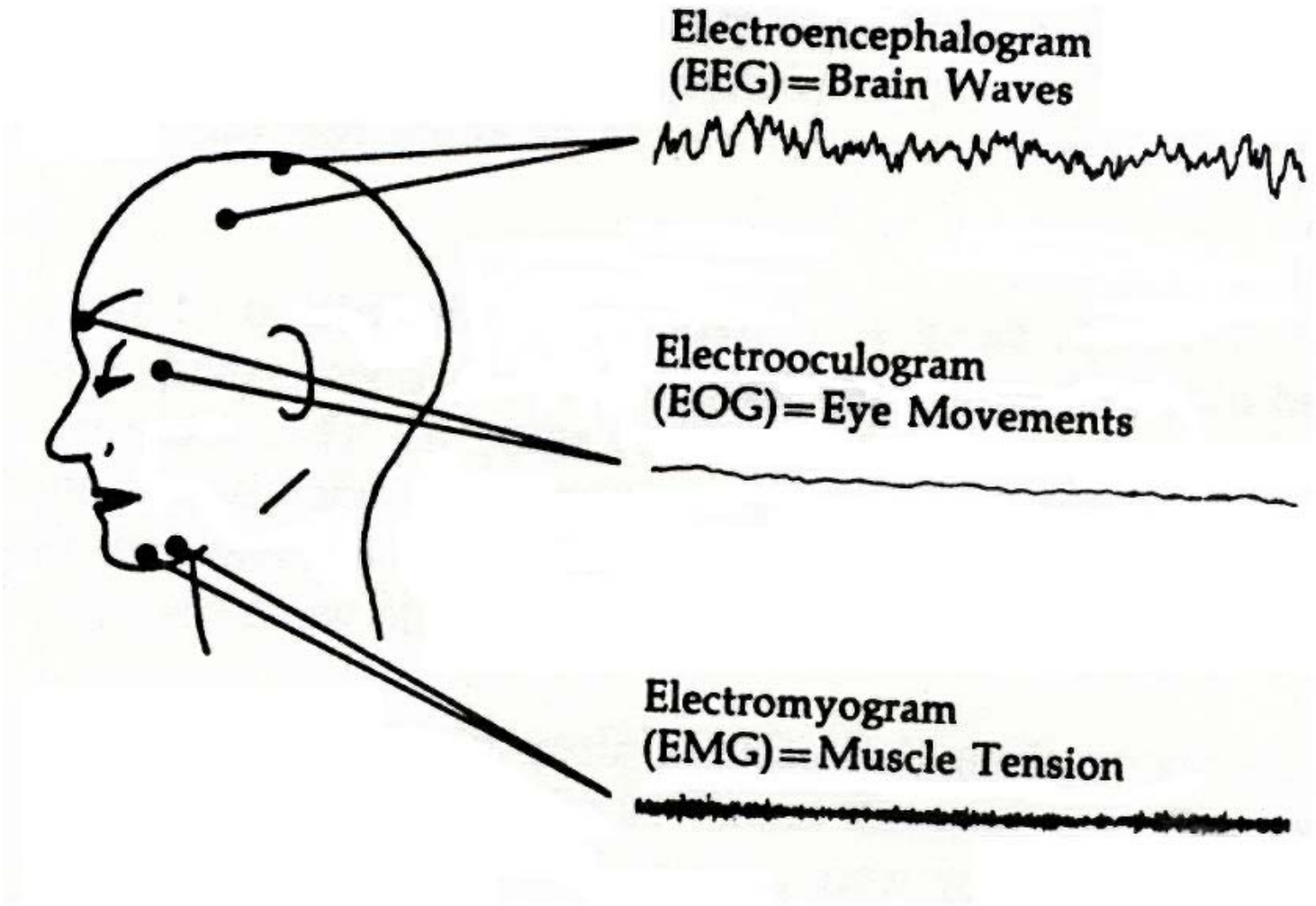
As per behavioral criteria:

- **Reduced motor activity.**
- **Decreased response to stimulation.**
- **Stereotyped posture.**
- **Easy reversibility (unlike coma, hibernation, torpor & estivation).**

Defined electrophysiologically:

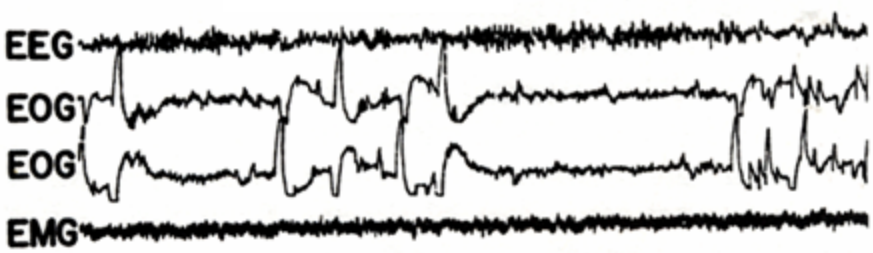
- **Definite changes in EEG, EMG & EOG.**
- **Modern definition & classification**
  - **Nathaniel Kleitman (1939) Book Sleep and Wakefulness.**
  - **Rechtschaffen & Kales (1966) A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages of Human Subjects.**
- **American Academy of Sleep Medicine (AASM) modified the staging rules in 2007.**

Sleep-wakefulness defined electrophysiologically

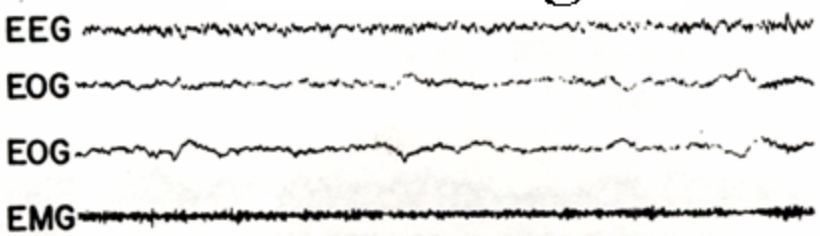


Stages of sleep & wakefulness

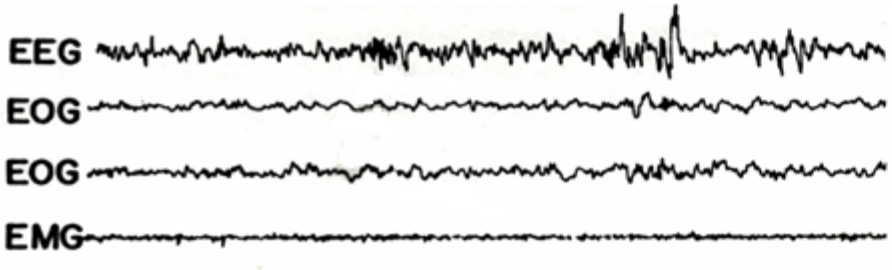
Awake



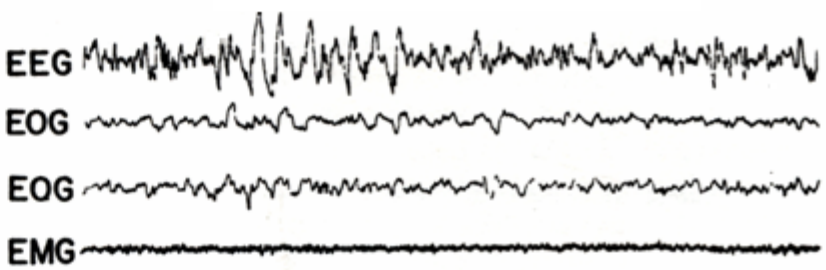
SWS stage 1



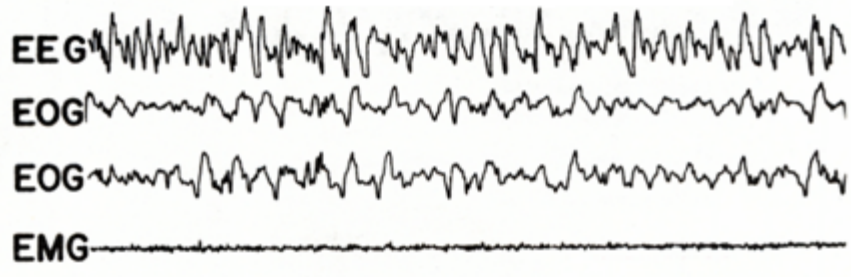
SWS stage 2



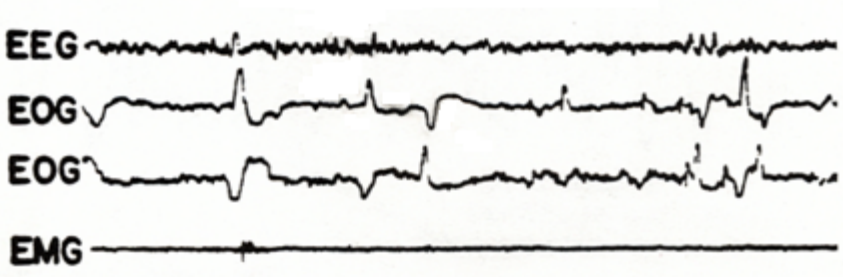
SWS stage 3



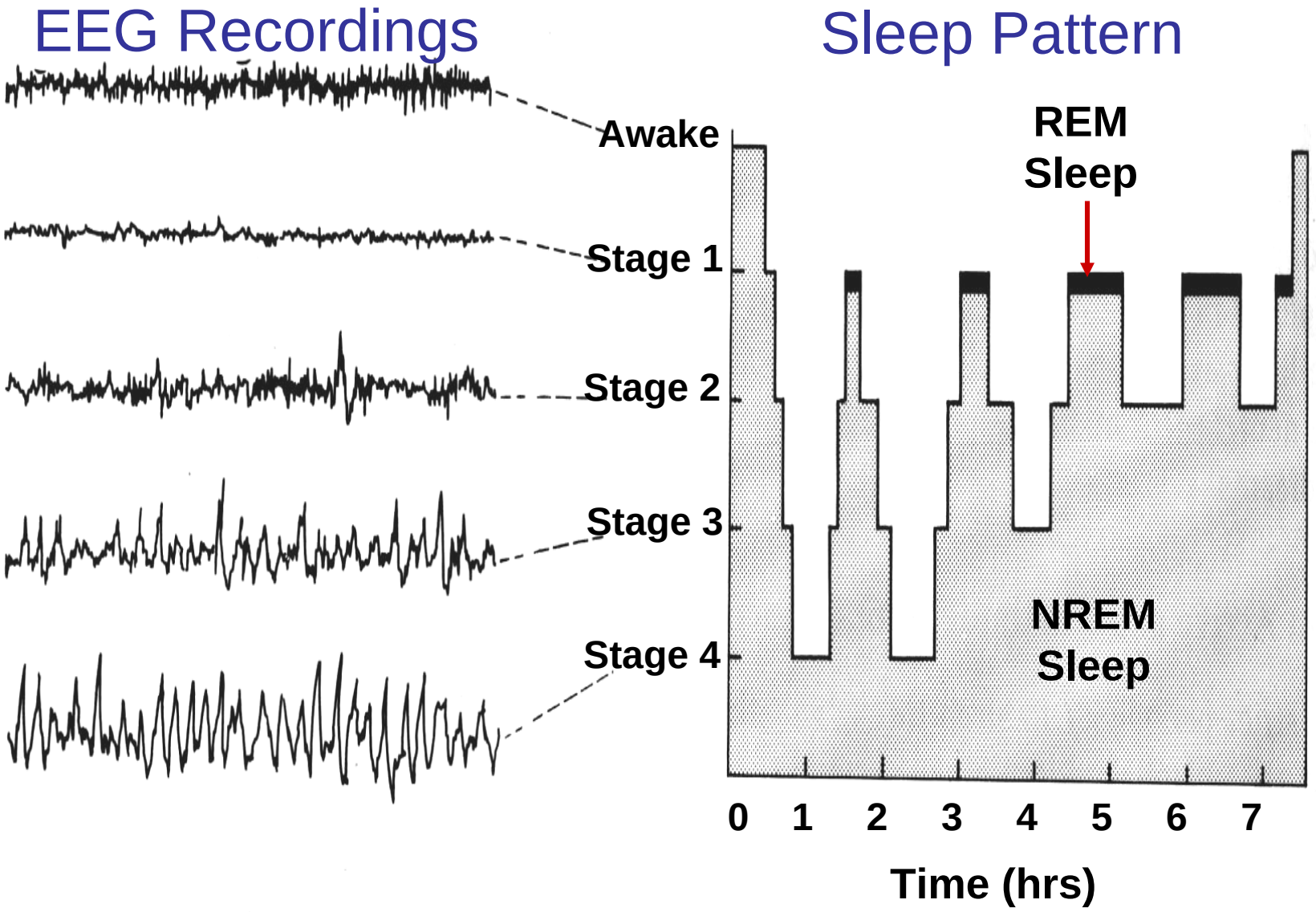
SWS stage 4



REM sleep



Sleep-wake changes every night: electrophysiologically assessed



NREM sleep

- Human NREM sleep was traditionally classified into 4 stages.
- American Academy of Sleep Medicine (AASM) in 2007 combined Stages 3 & 4 .
- NREM sleep stages1 to 4 represent successively deeper stages of sleep.
- EEG of deeper NREM sleep shows increasing voltage & decreasing frequency.
- Muscles, including upper-airway muscles, are progressively relaxed during deeper NREM sleep.
- Muscle relaxation is produced by progressive hyperpolarisation of lower motor neurons.

NREM sleep (continued)

- Body temperature is slightly reduced. It is actively maintained at this lower level.
- Heart rate & BP decline, but gastrointestinal motility increases.
- Parasympathetic activity predominates.
- Sleeper makes postural adjustments (at around 20 minutes intervals).
- Those awakened from NREM sleep have poor sensory-motor function (as compared with those awakened from REM sleep).
- NREM sleep alternates with REM sleep. REM sleep appears after 30-90 minutes of NREM.

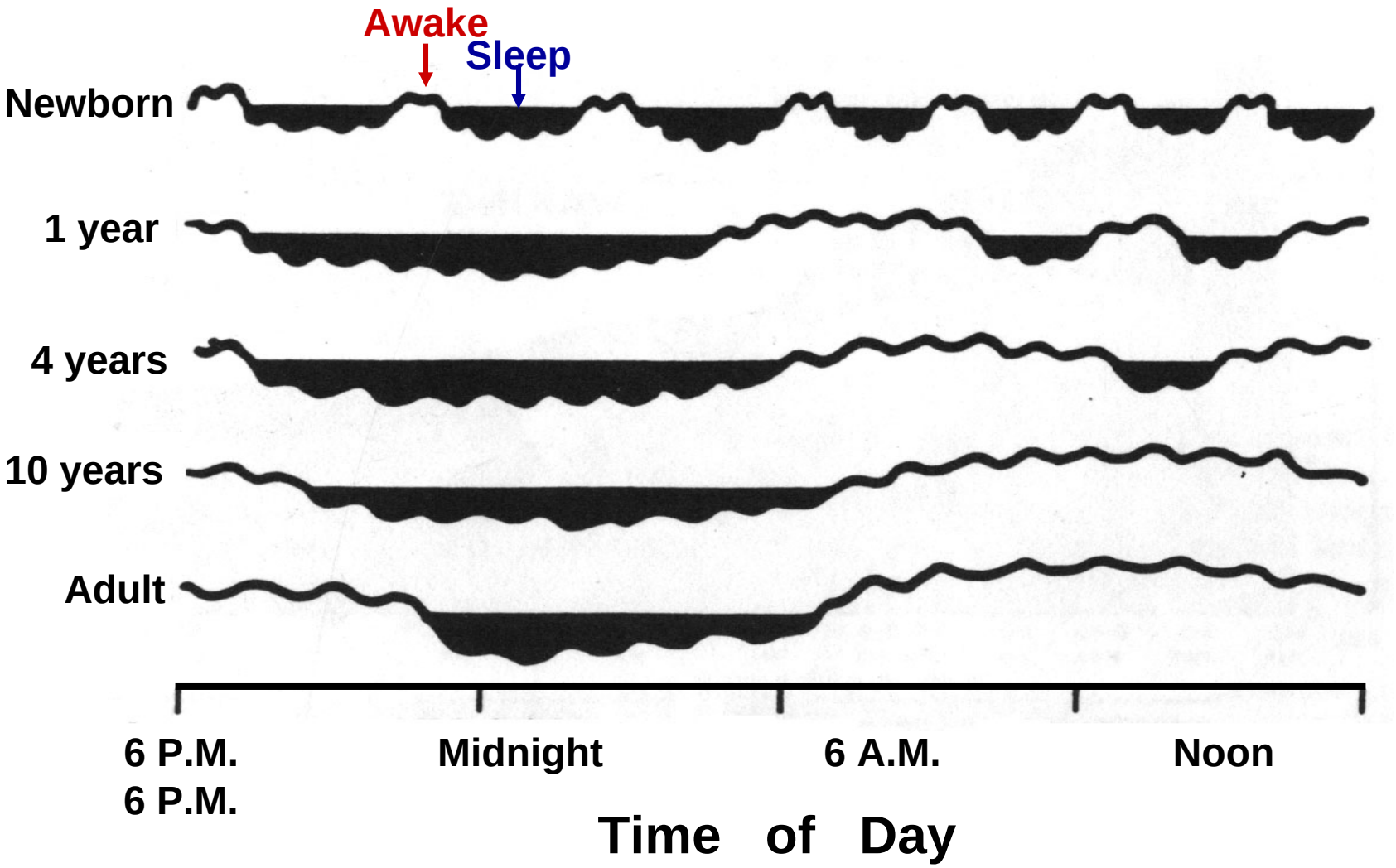
REM Sleep

- Shows bursts of Rapid Eye Movements (REM).
- Correlated with REM, there are PGO waves (best recorded with depth electrodes in animals).
- EEG resembles wake stage EEG in animals (low voltage fast activity). So it’s called paradoxical sleep.
- In humans, EEG resembles that of stage 1 of NREM sleep (low voltage mixed waves).
- There is decreased thermoregulatory ability. Body temperature drifts towards ambient temperature.
- Brain temperature and brain metabolism are increased.
- There is a high parasympathetic tone. Pupils become highly constricted.

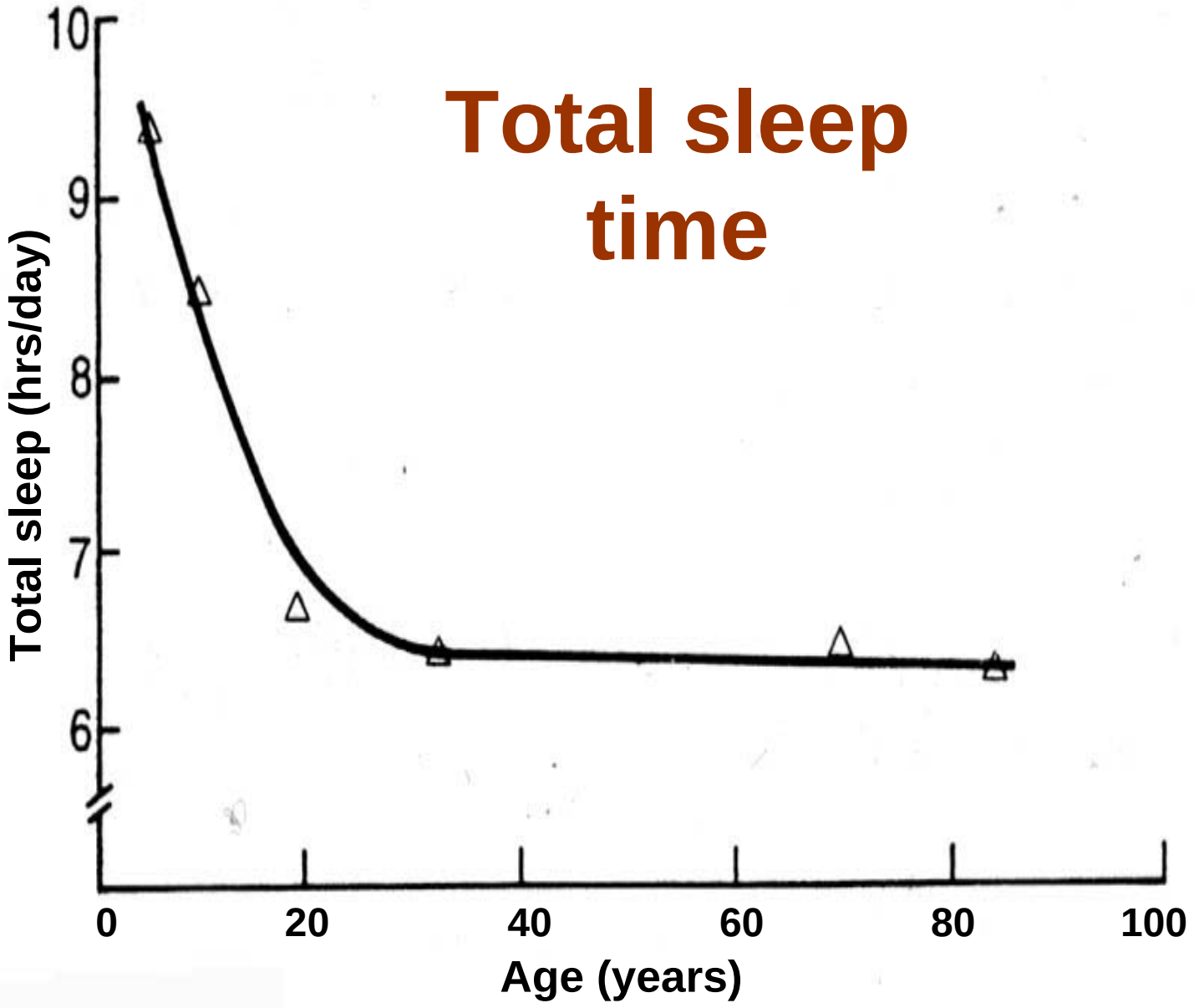
REM Sleep (continued)

- Profound loss of muscle tone (including muscles of upper respiratory passage), produced by hyperpolarisation of lower motor neurons.
- But respiratory muscles, and those of eyeballs & middle ear remain active.
- Muscles show sudden twitches in between.
- There are also sudden respiratory changes, increased heart rate & coronary blood flow.
- Respiratory response to hypoxia is blunted & response to CO_2 is grossly reduced.
- Reduced waking threshold in humans. (Increased waking threshold in animals).

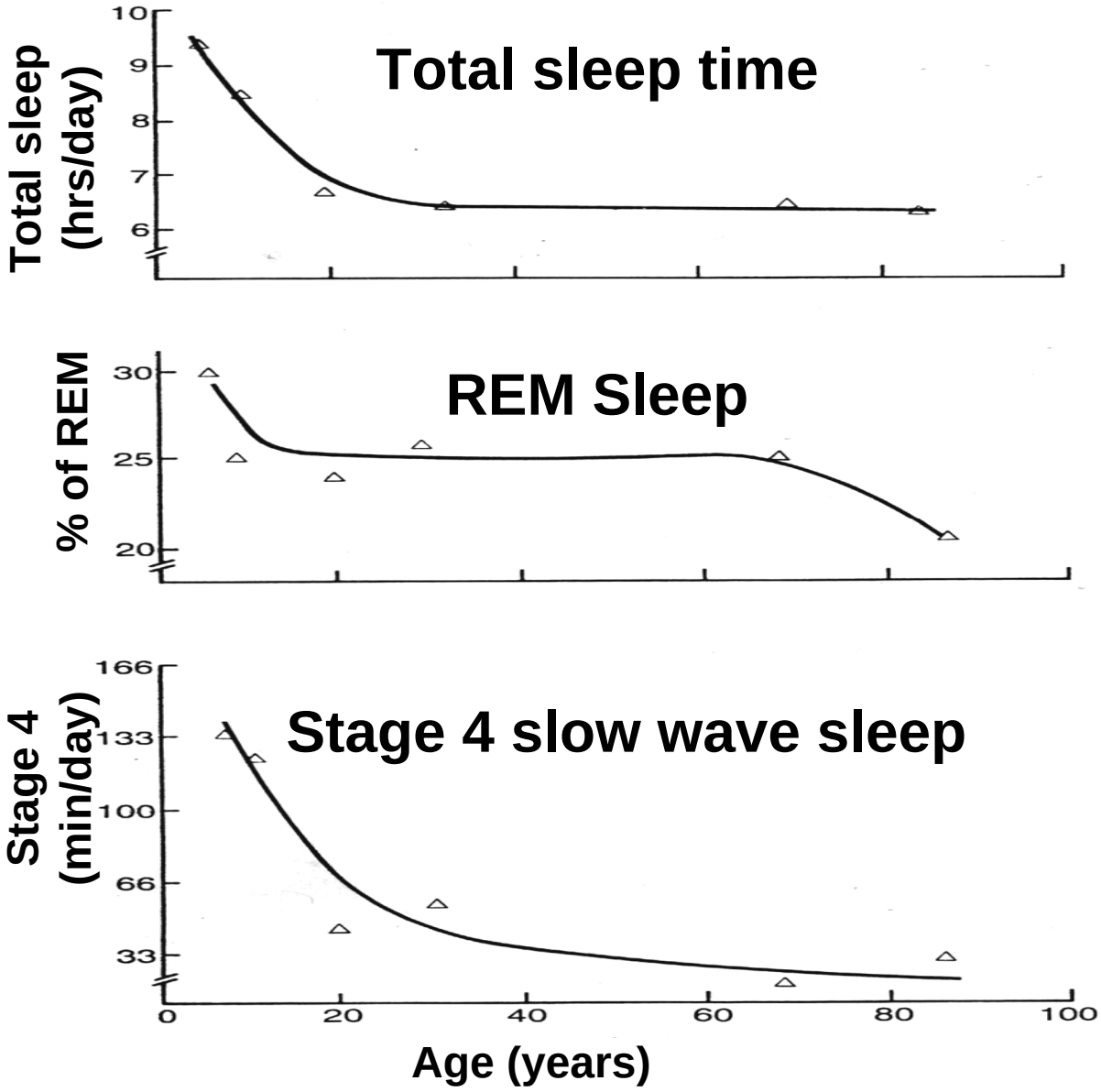
Sleep pattern as the child grows



Total sleep time



Human sleep pattern with age



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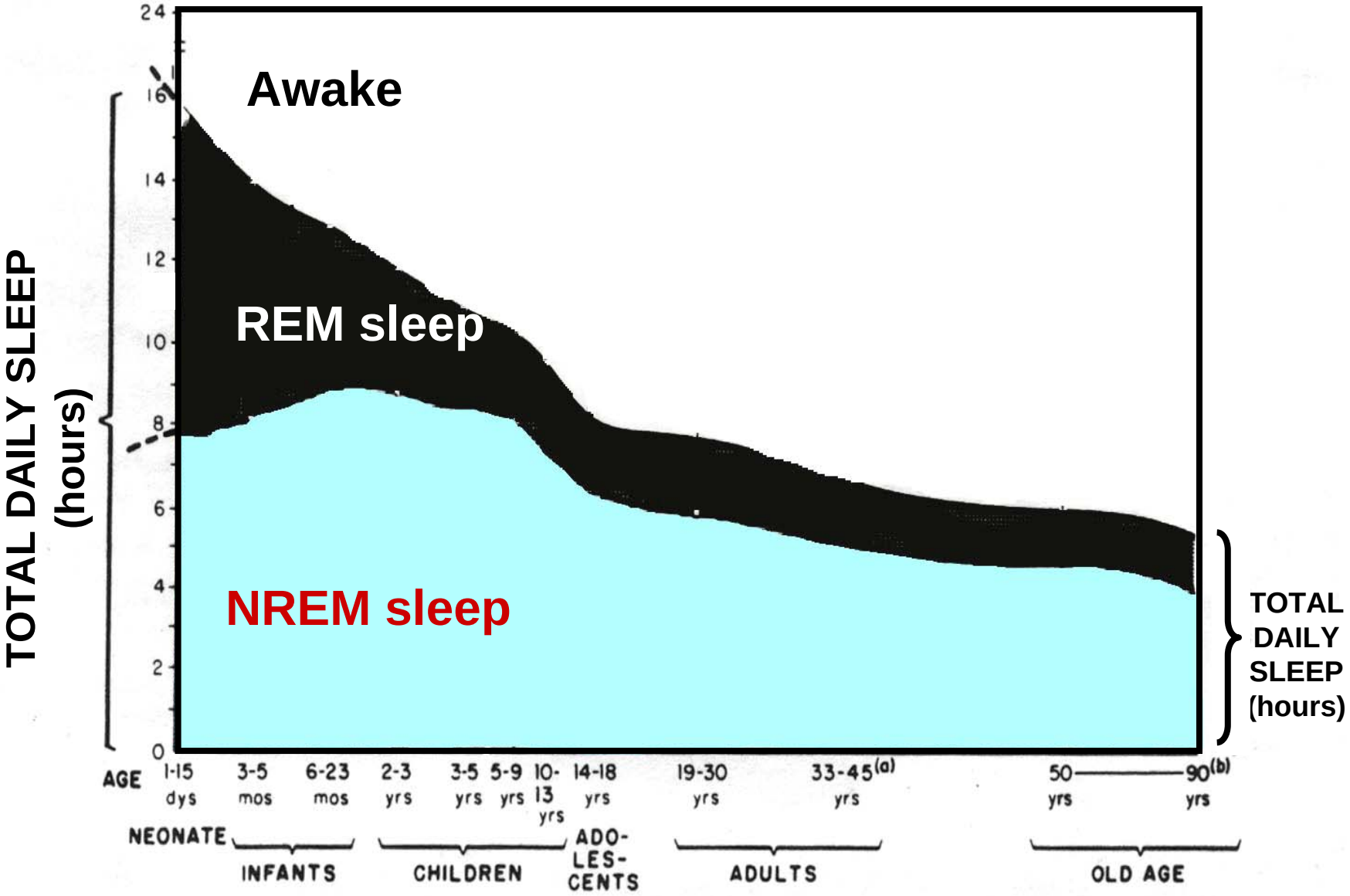
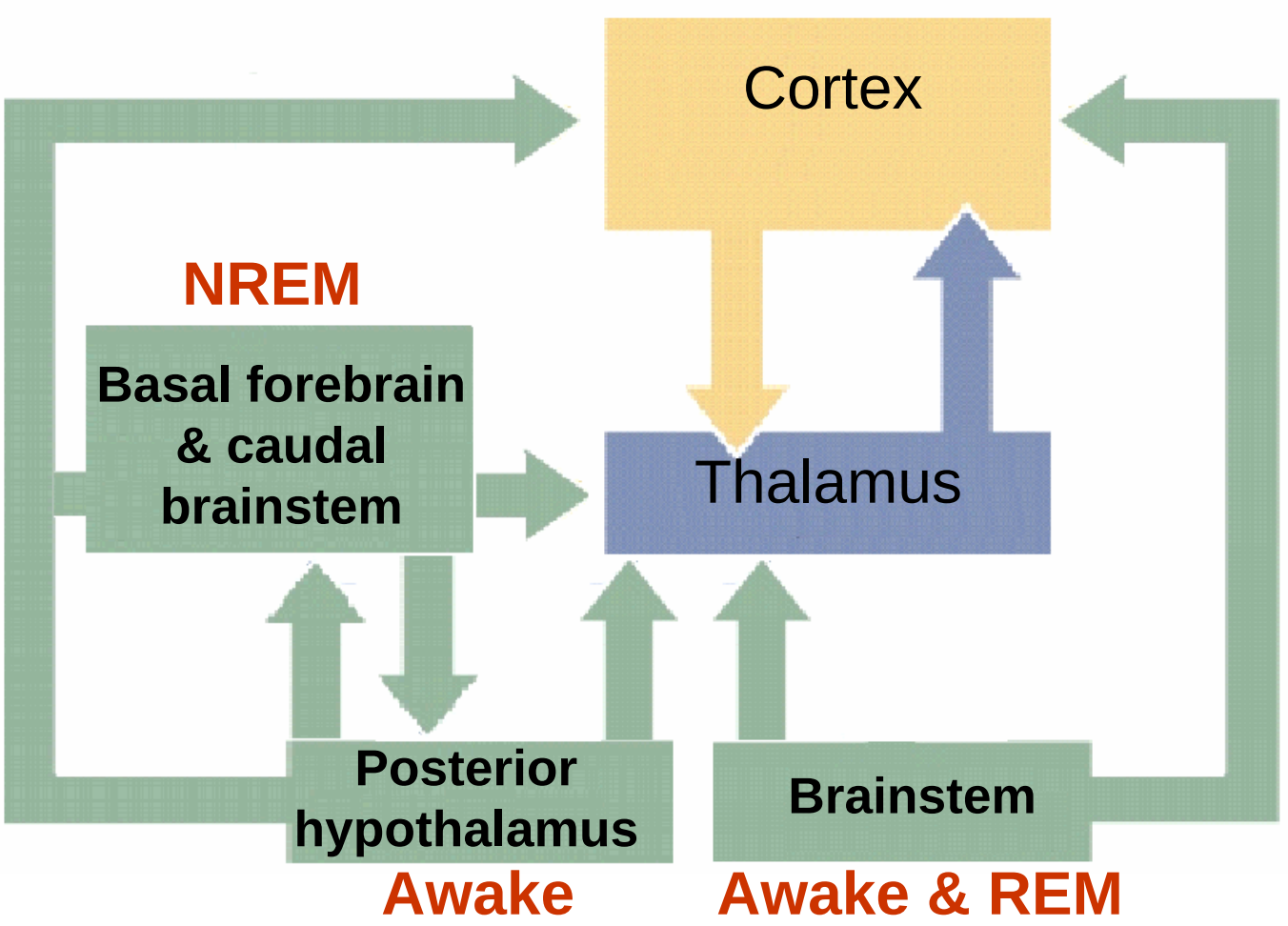


Theories sleep regulation

- Traditional belief: Prolonged activity of the brain during the day is followed by rest, at night, in the form of sleep (Charles Sherrington & Ivan Pavlov)
- Sleep was considered as a passive process till the 1950’s
- Passive theory of sleep replaced by the active sleep genesis concept.
- Employing various modern experimental techniques discrete areas regulating wakefulness, NREM and REM sleep were identified .

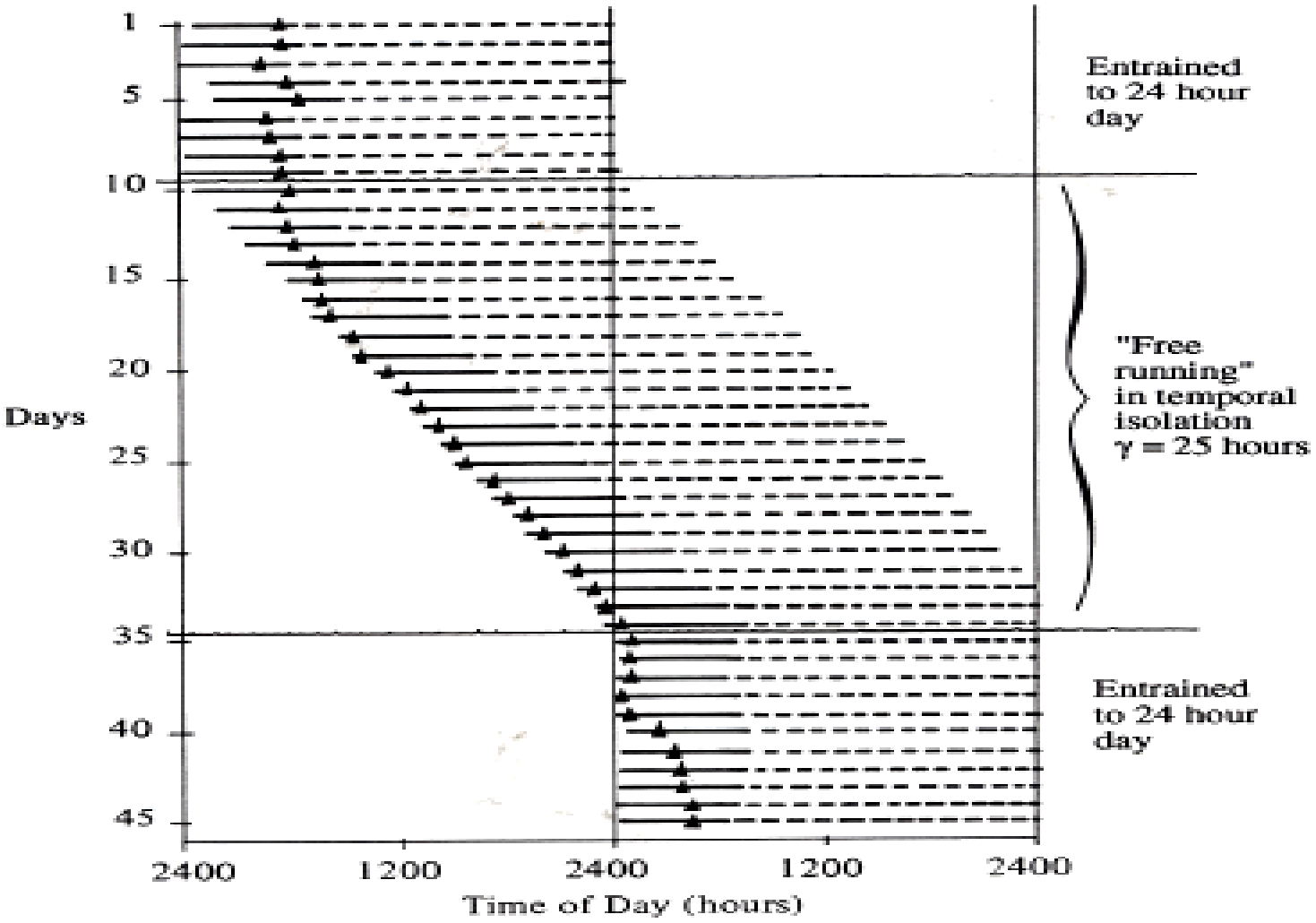
Simplified diagram of sleep-wakefulness modulating circuit



Sleep is auto-regulatory global phenomenon

- Sleep is neither active nor passive
- All brain segments: inherent sleep-wake oscillation
- Dynamic interaction of neuronal network throughout the brain result in sleep-wake oscillation
- Different sleep signs appear during non-REM & REM sleep
- Sleep signs add state specific qualities to sleep & wakefulness
- Basal forebrain-hypothalamic regions integrate sleep with somatic & visceral responses

Sleep-wake cycle with & without external clues



Is sleep essential for life?

- Sleep-deprived rats die in 2-3 weeks, though food-deprived animals can live up to 4 weeks.
- Sleep is preserved through evolution (lower forms of animals show rest-activity cycles).
- All mammals show NREM–REM cyclic alternation.
- REM and NREM sleep show rebound after deprivation.
- Man shows disturbed behavior after sleep deprivation.

Functions of sleep

- Protected from metabolic injury: Sleep facilitates the synthesis of molecules that protect brain cells from oxidative stress.
- Restorative: Sleep may be having a restorative and recovery function, especially for the brain.
- Energy conservation: Energy consumption during sleep is less by 15%. Sleep is more in infants and small mammals where energy cost of thermoregulation is high.
- Thermoregulation: Many sleep-active neurons are thermosensitive. Brain temperature increases during REM sleep, even though thermoregulation is suppressed. REM sleep is maximum during early morning, when the body temperature is at the lowest level.

Functions of sleep

- Brain growth: Premature babies have higher REM sleep. REM sleep amount correlated with brain maturity at birth, in animal kingdom.
- Facilitate neurogenesis: Protein synthesis in brain increased during NREM sleep. Sleep deprivation, blocks proliferation of cells in the dentate gyrus.
- Memory consolidation: Sleep deprivation reduce concentration and learning. Non-declarative memory (motor skill) is enhanced during sleep. Several genes, believed to contribute to memory consolidation, are up-regulated during sleep.
- Discharge of emotions through dreaming is an age-old function ascribed to sleep.

Sleep is essential for life

- Many physiological changes, which are essential for life, occur during sleep.
- Though we know of some functions of sleep, there are many that we still do not know.
- Electrophysiologically and behaviorally defined sleep do not explain all the aspects of sleep.
- **Importance of sleep for health and survival is best demonstrated by the disastrous consequences resulting from its repeated interruption.**


THANK
YOU