



Children's Hospital Boston



Sleep in Tuberous Sclerosis Complex

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What is sleep?



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- State of reduced consciousness

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- Homeostatic = the less you sleep, the more you need to

What is sleep?

- State of reduced consciousness
- Reversible
- Homeostatic
- Species-specific



All animals sleep, but why?

- Restorative
- Safety
- Learning

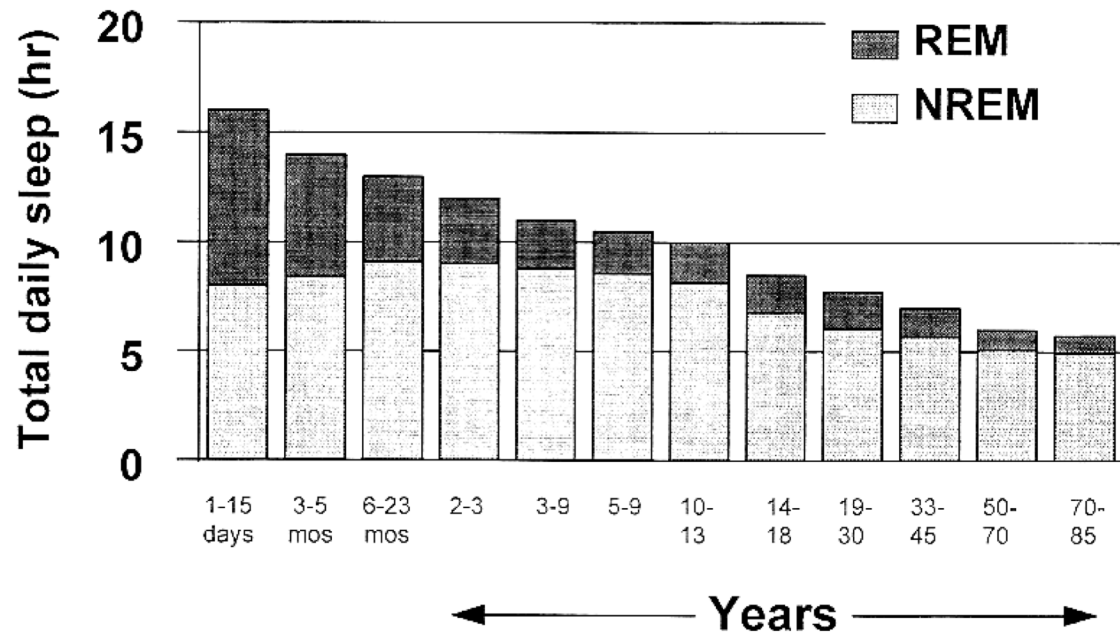
If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process ever made

Allan Rechtschaffen, 1971

Sleep and Health

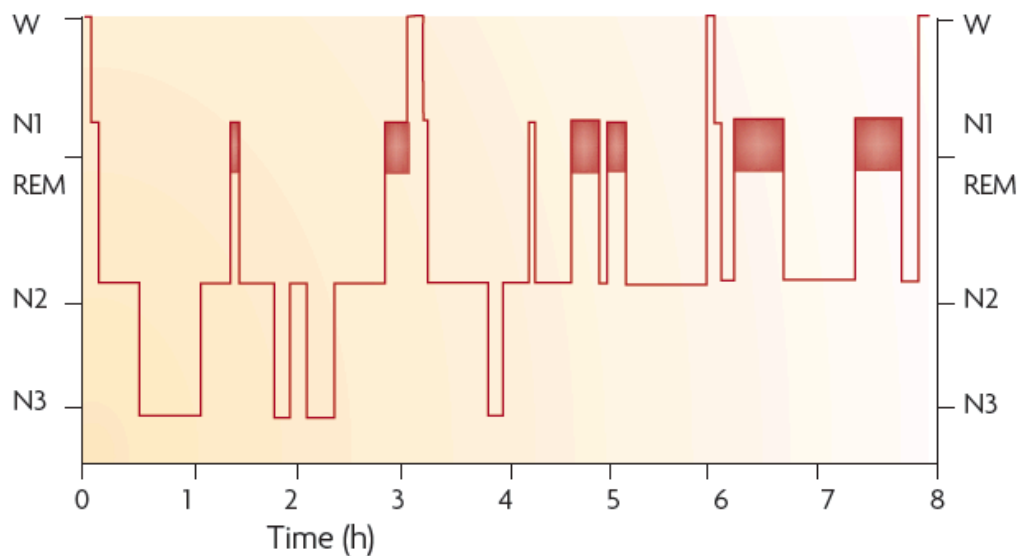
- About 30-45% of adults have insomnia in a given year
- About 70% of all children have a significant sleep disorder at some point during childhood
- Sleep dysfunction contributes to problems with:
 - Attention
 - Behavior
 - Metabolism
 - psychiatric health
- Sleep disorders are *very* common in children with neurological diseases such as autism and epilepsy

Sleep is Developmentally Regulated



Roffwarg *et al.*, *Science*, 1966

Sleep is Dynamic

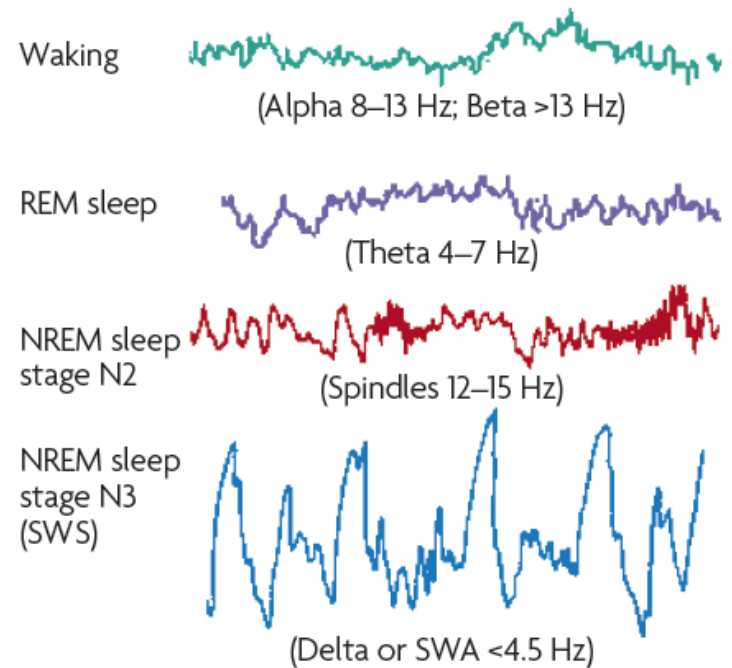


Measures of sleep quantity

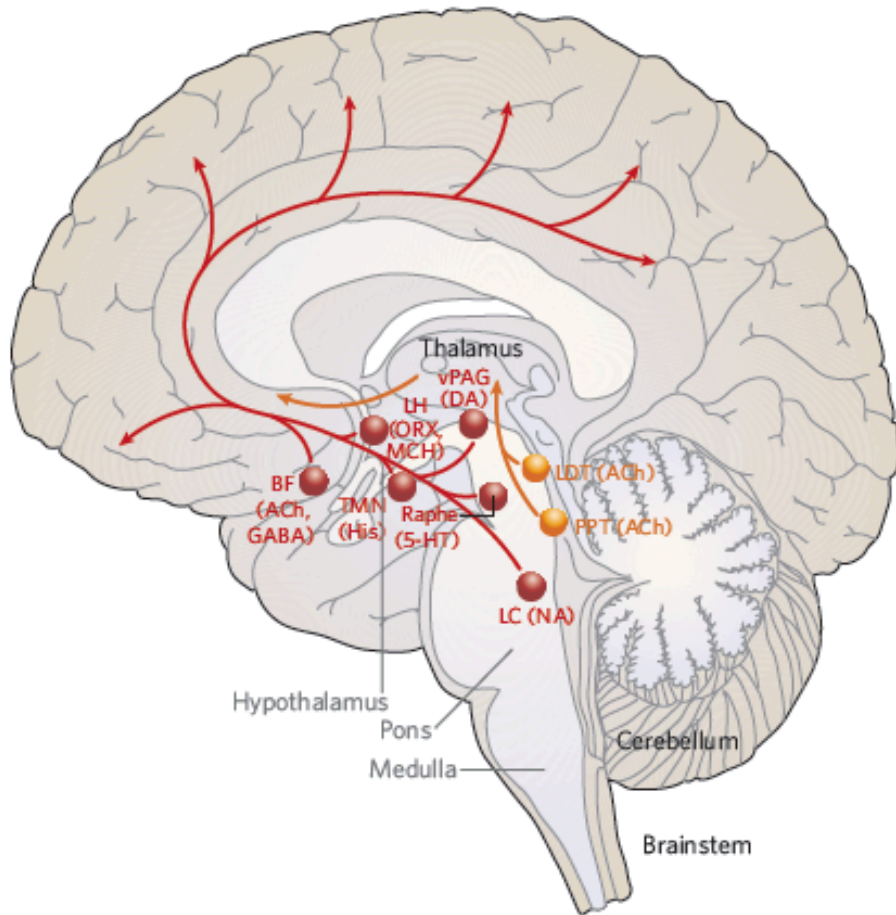
- Sleep duration (h per day)
- % NREM and REM sleep
- % NREM stages (N1–3)

Measures of sleep quality

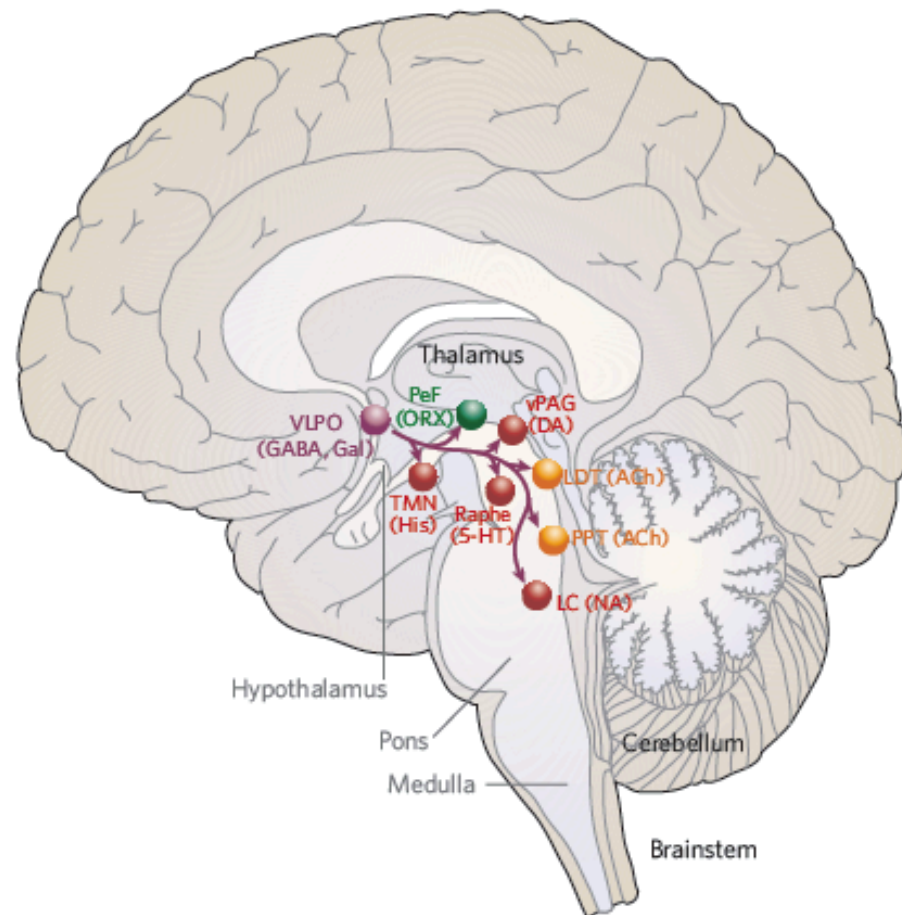
- Latency to sleep onset
- Latency to REM sleep onset
- Brief awakenings after sleep onset
- SWA in NREM sleep



Sleep anatomy



Ascending Arousal System

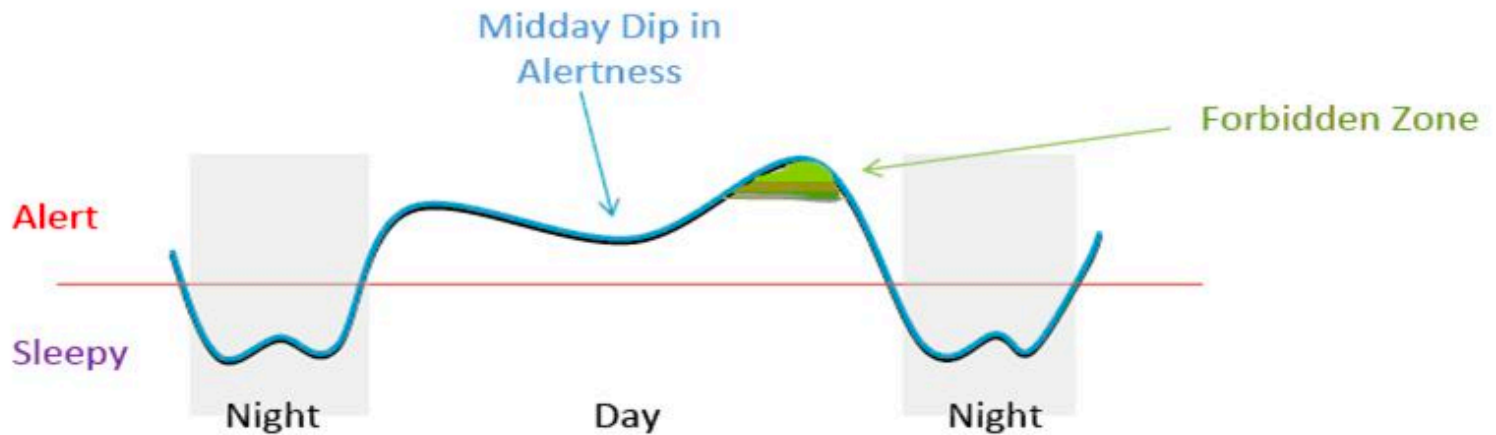


Descending Sleep System

The Dual Regulators of Sleep

- Sleep Drive – the longer the brain is awake, the more sleep it needs.
- Body Clock – the circadian timekeeping mechanism is a system that tells the body what “time it is”. This system is *synchronized* with the environment – for example, the light-dark cycle.

Ferber's forbidden zone



Adapted from: *Solve Your Child's Sleep Problems*, Richard Ferber, Simon & Schuster, 2006

Sleep Disorders

- Insomnias
 - sleep onset, sleep-maintenance
- Hypersomnia
 - idiopathic hypersomnia, narcolepsy
- Sleep-related breathing disorders
 - Sleep apnea
- Circadian rhythm sleep disorders
 - delayed, advanced, irregular
- Parasomnias
 - sleep walking, talking, eating
- Sleep-related movement disorders
 - periodic limb movements, restless legs syndrome

Sleep and TSC

But how big is the problem?

Studies vary A LOT

15-70% of affected individuals have significant sleep disorders

Major complaints: INSOMNIA

Sleep disorders and the TAND umbrella (TSC-associated neuropsychiatric disorders)

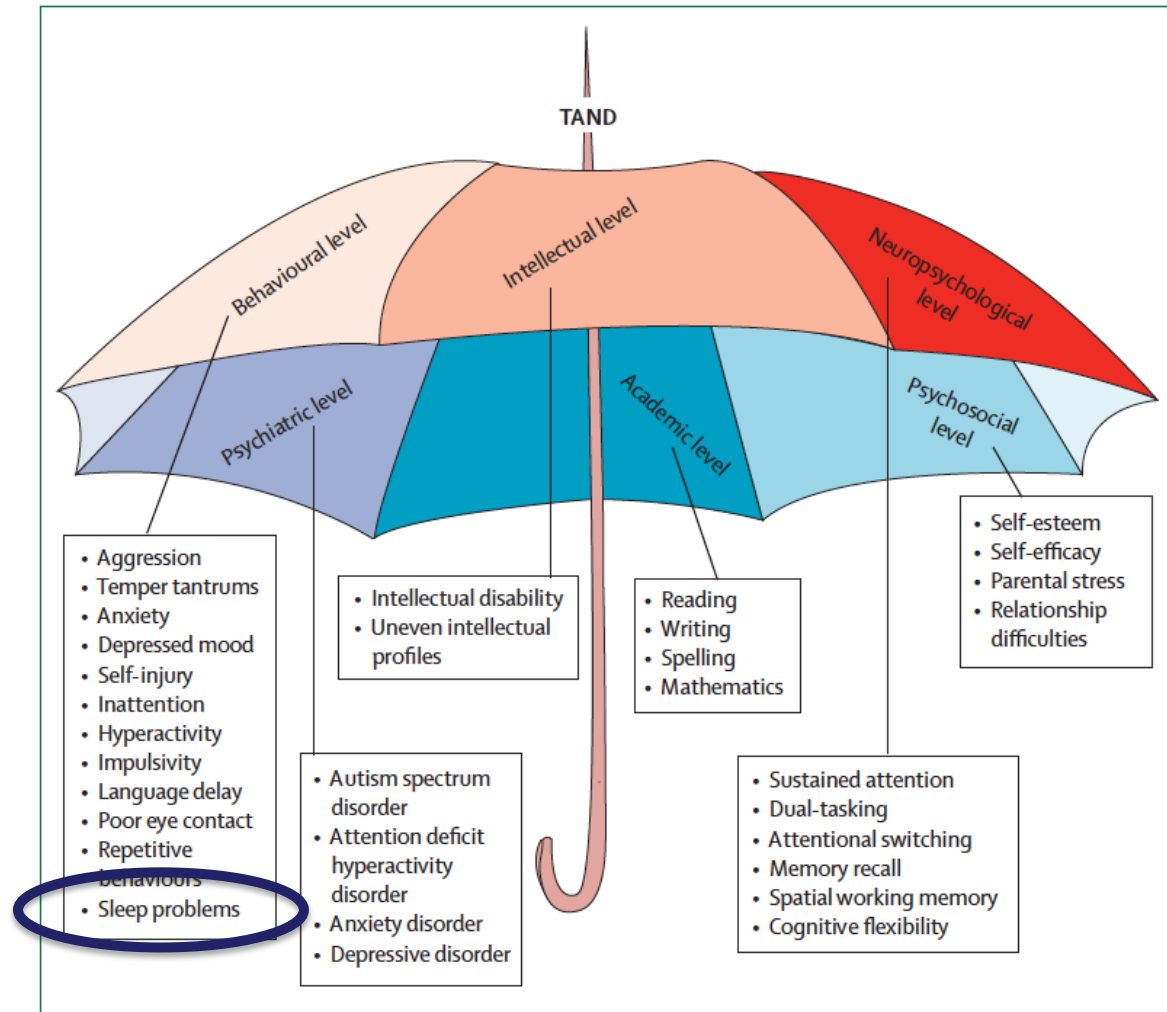


Figure 4: TAND

TAND is used as an umbrella term to capture the range of neuropsychiatric disorders associated with tuberous sclerosis across different levels of investigation. TAND=tuberous-sclerosis-associated neuropsychiatric disorders.

Do I Have A Sleep Disorder?

- Symptoms:
 - daytime sleepiness
 - insomnia
 - snoring, gasping for air at night
 - trouble with attention or memory
 - depressed mood
 - morning or evening headache
 - excessive or “unexplained” movements at night

Factors affecting patients with TSC that likely impact sleep

- *Seizures* – in general, more complex seizure disorders are associated with more sleep dysfunction
- *Intellectual disability* – associated with difficulty around behavioral strategies, understanding goals
- *Autism-spectrum disorder* – strong overlap between ASDs (related to TSC or not) and insomnia.
- *Medications* – anti-seizure medications can make you sleep and some can do the opposite.
 - Everolimus?
- In *adults*: sleep disordered breathing, restless legs syndrome

Promoting *Effective* Sleep

- Maintain a regular wake time
- Maintain a regular schedule – includes sleep routines and waking routines, meals
- Limit exposure to bright light in the evening
- Quality and safety of sleep environment
- When do I need a sleep study?
 - Snoring
 - Mouth breathing or very dry mouth in the morning
 - Morning headaches
 - Nocturnal seizures or unexplained events

Work on matching sleep need to the
time in bed

Medication is *never* the first option

Commonly used sleep meds

(most are off-label)

- Clonidine, guanfacine
- Clonazepam and other “-azepams”
- Melatonin receptor: melatonin, ramelteon, tasimelteon
- Antihistamines: Benadryl, doxylamine etc.
- “Seizure meds”: gabapentin, pregabalin
- Zolpidem, eszopiclone
- Antidepressants – amitriptyline, doxepin, trazodone, mirtazapine
- Antipsychotics: quetiapine, risperidone
- Orexin antagonists - suvorexant