SLEEP, AGING AND DEMENTIA

Lina Fine, MD, MPhil

October 27, 2023

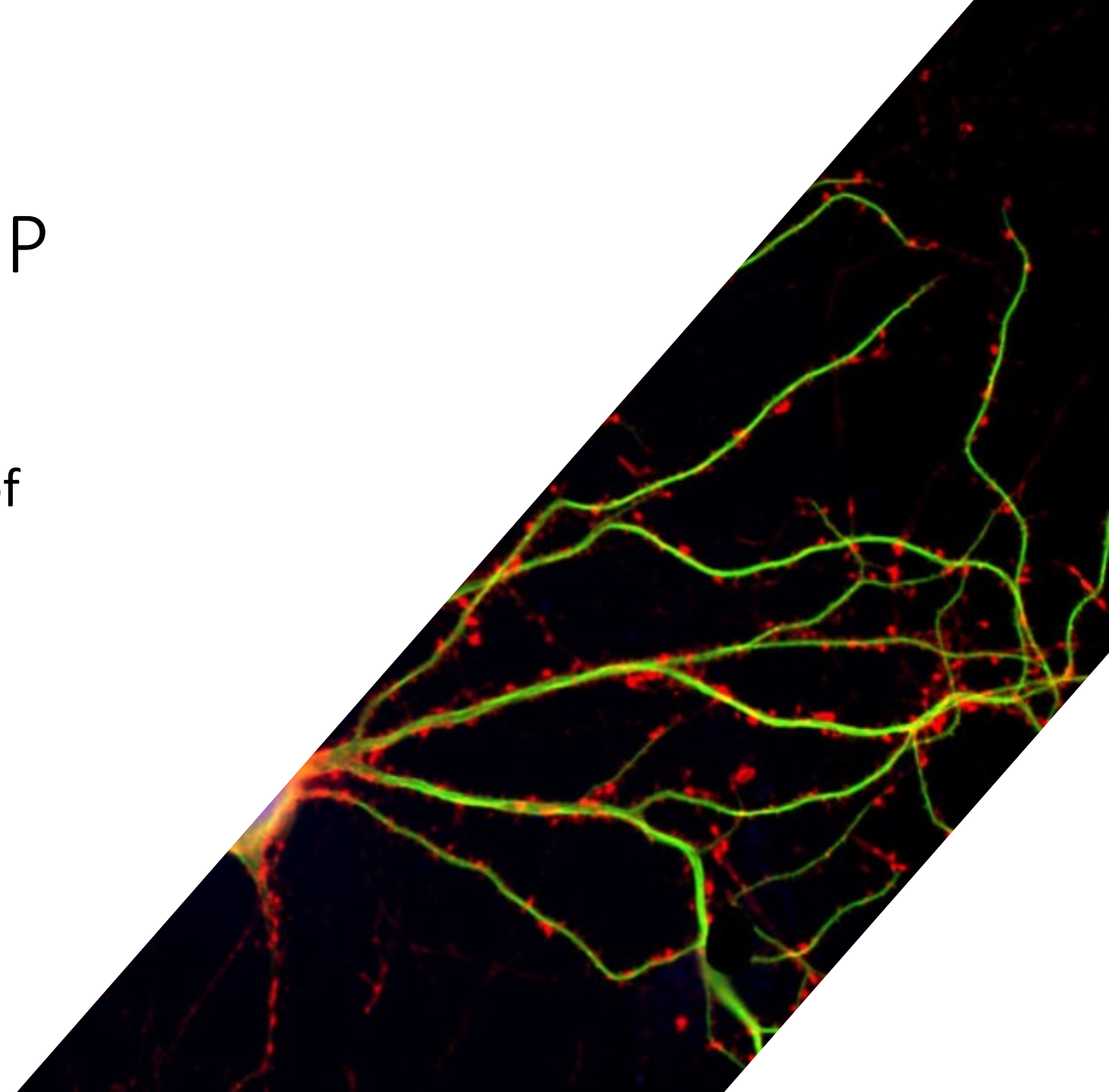
PURPOSE OF SLEEP

Memory consolidation

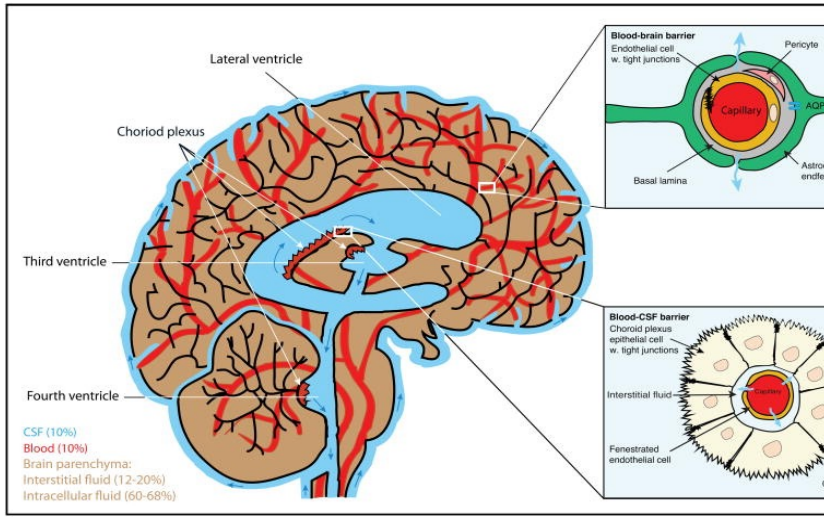
Pruning and development of dendritic spines

(REM sleep)

Possible role in psychosis

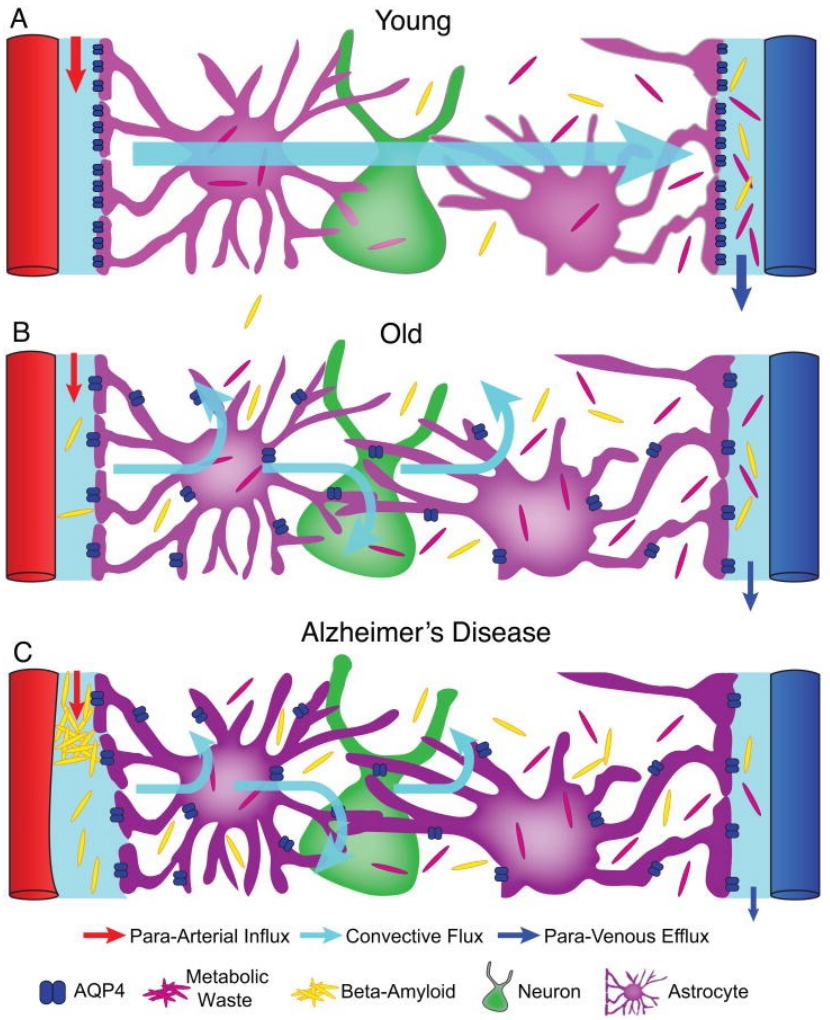


PURPOSE OF SLEEP
Glymphatic system



-Recovery and repair
-During sleep only
-Clearance and transport

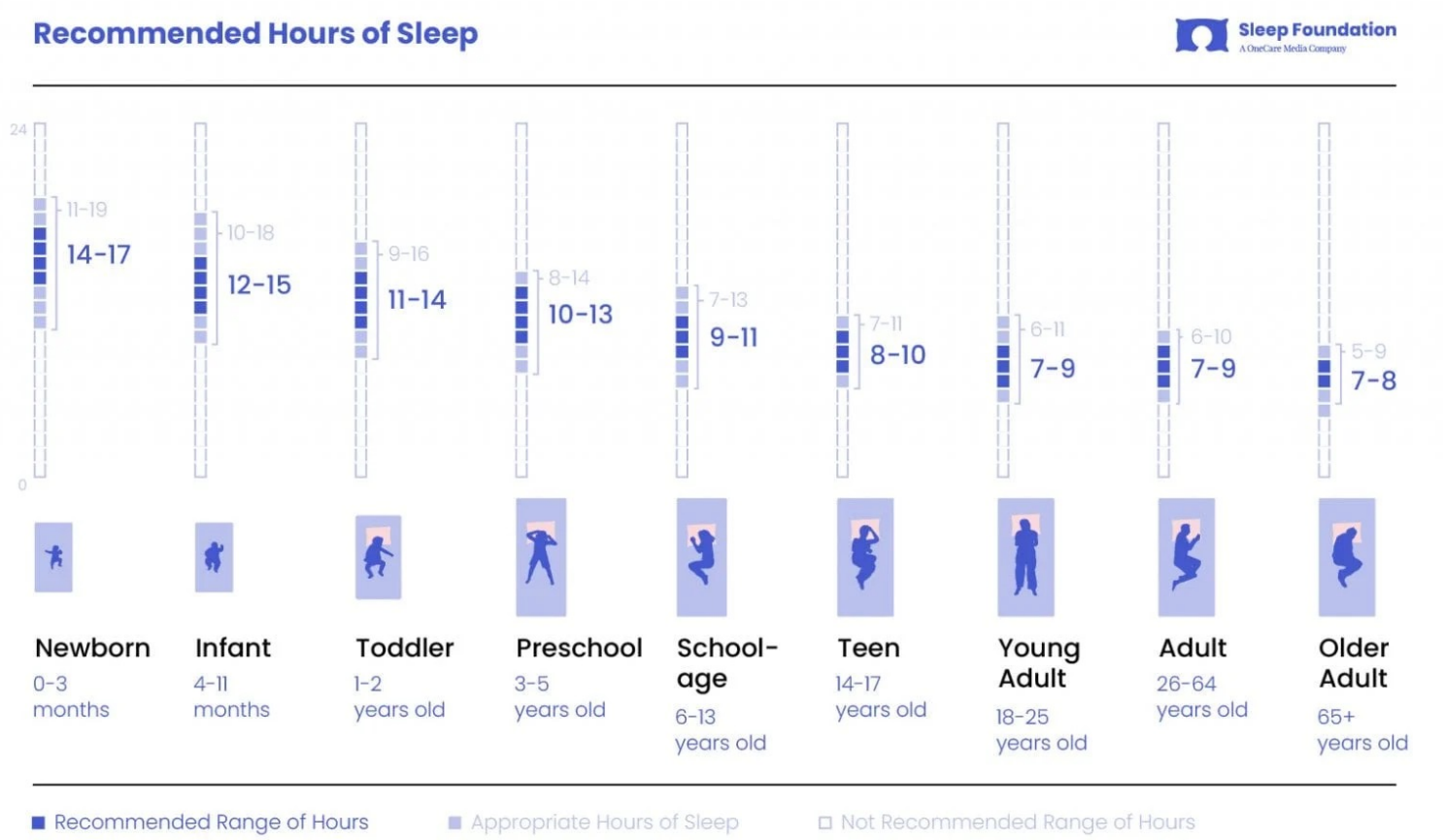
(Energy conservation – 25%)



Jenssen NA, 2015

EVALUATION OF SLEEP IN OLDER ADULT

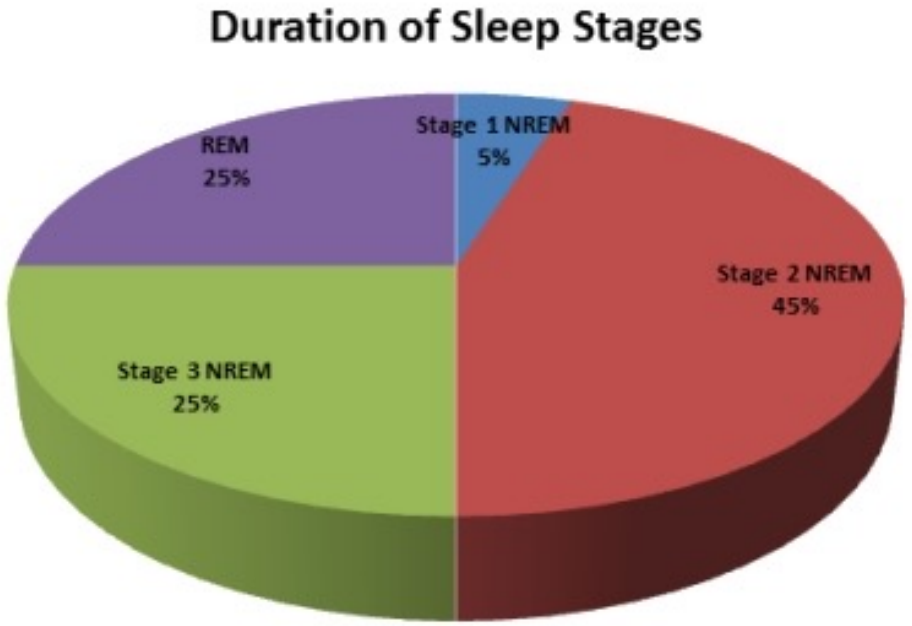
Airway
Movements (RLS, PLMs, neuropathy)
Mood/anxiety (symptoms as well as treatments themselves)
Metabolic
Circadian patterns
Lifestyle (diet, exercise, timing of activities)
Medications
Nocturia
Sleep beliefs

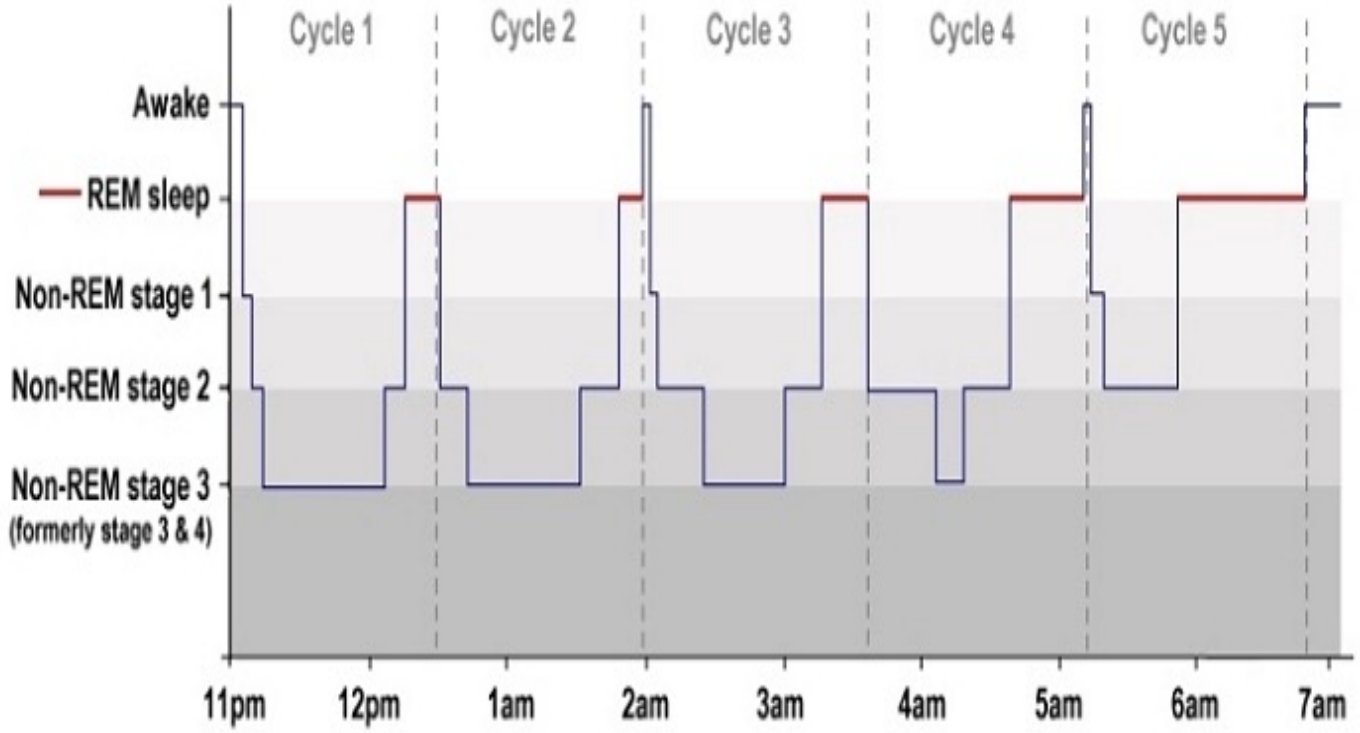


How much sleep

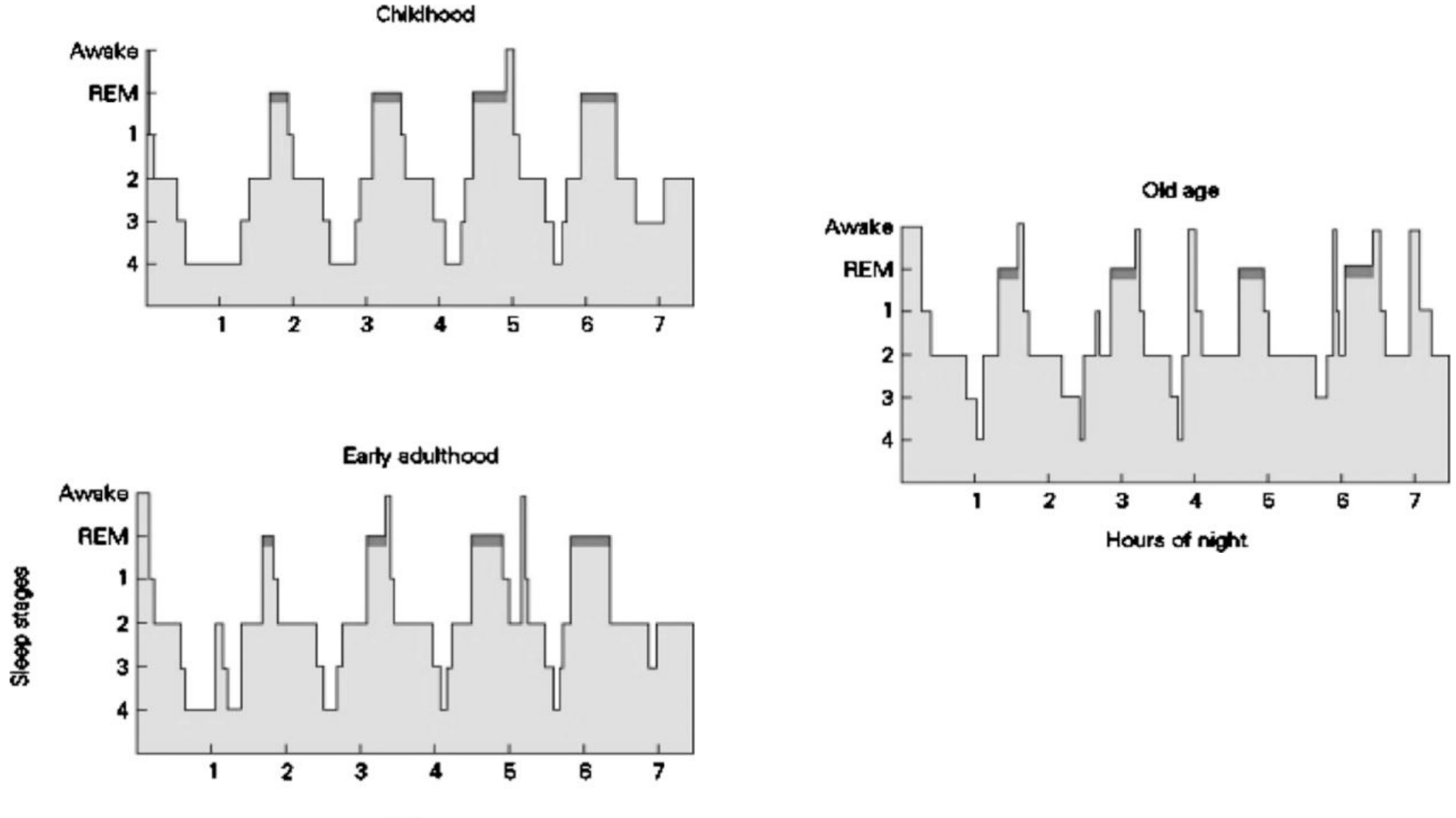
Sleep Foundation, 2022

STAGES OF SLEEP





SLEEP STAGES THROUGH AGES



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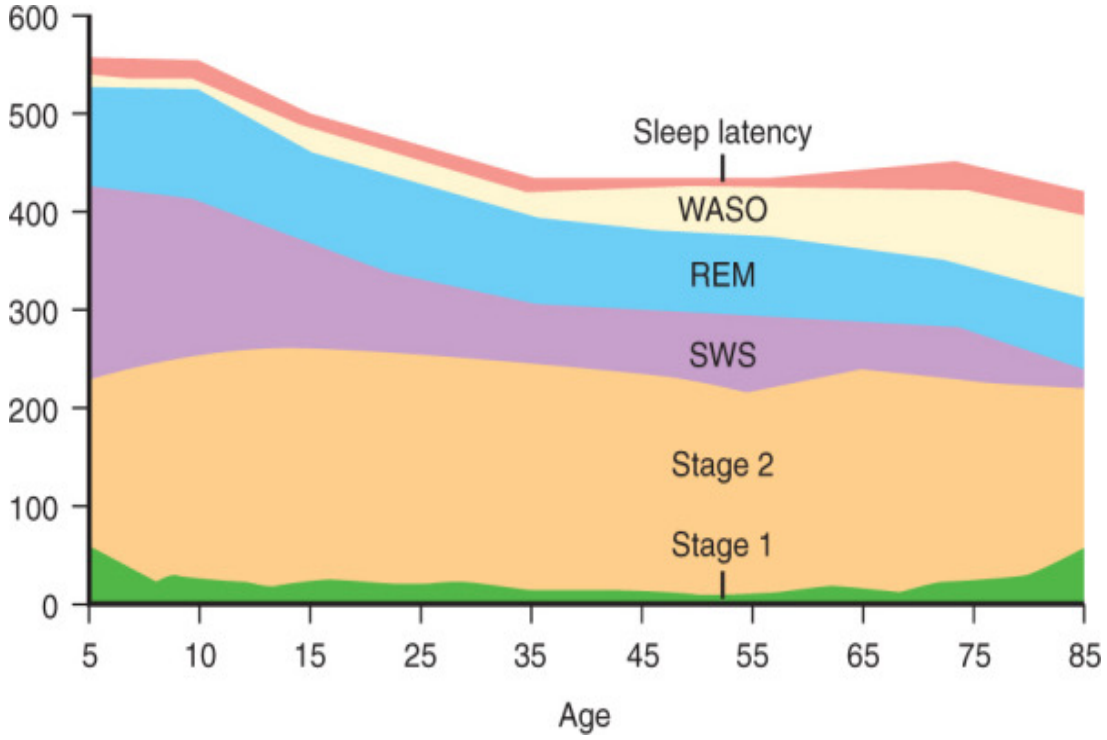
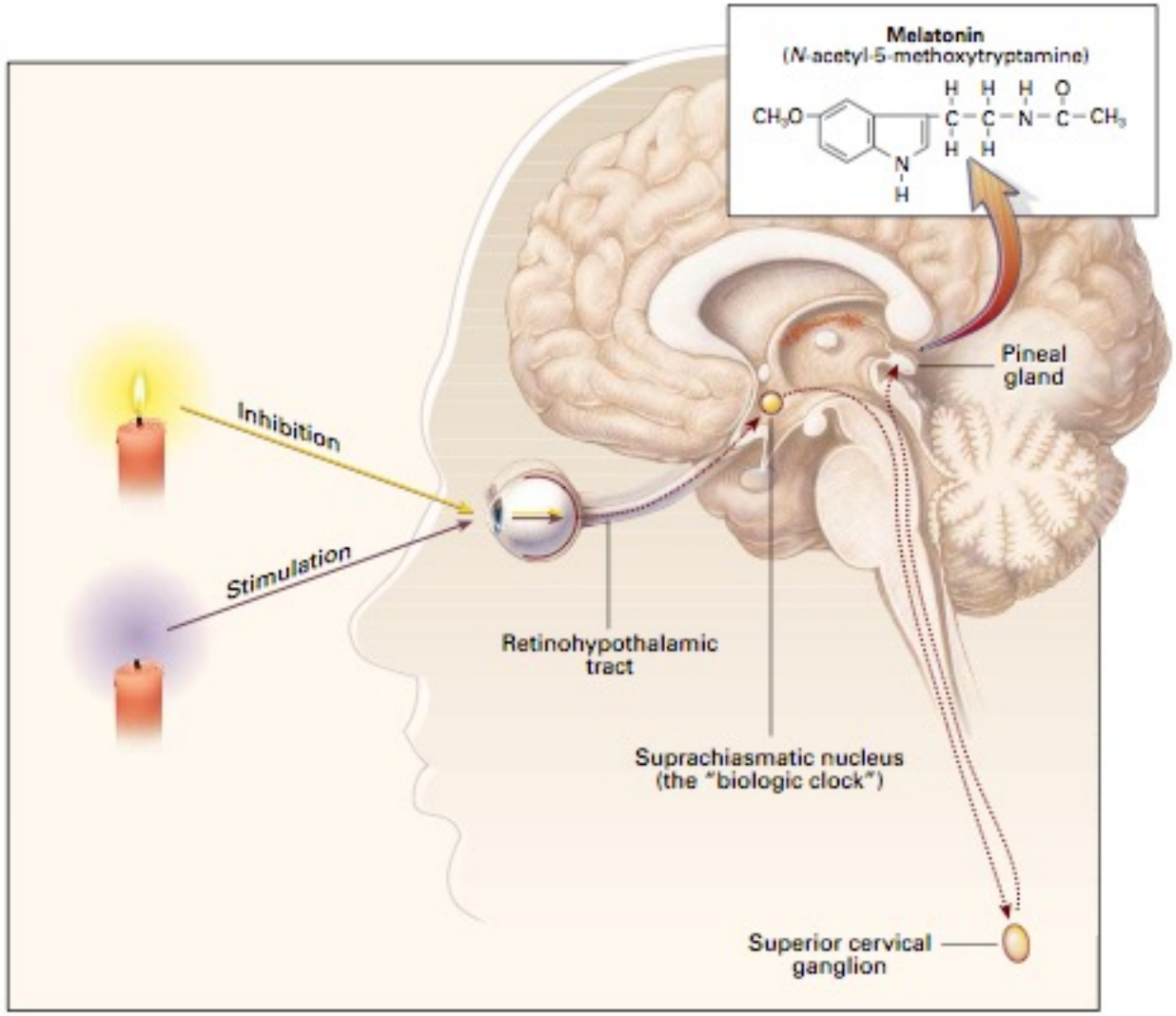


-SWS (Slow Wave Sleep, Stage 3) goes down and may disappear with age
-REM sleep duration slightly goes down
-WASO (wake after sleep onset) goes up – multiple awakenings

Circadian Sleep-Wake Cycle

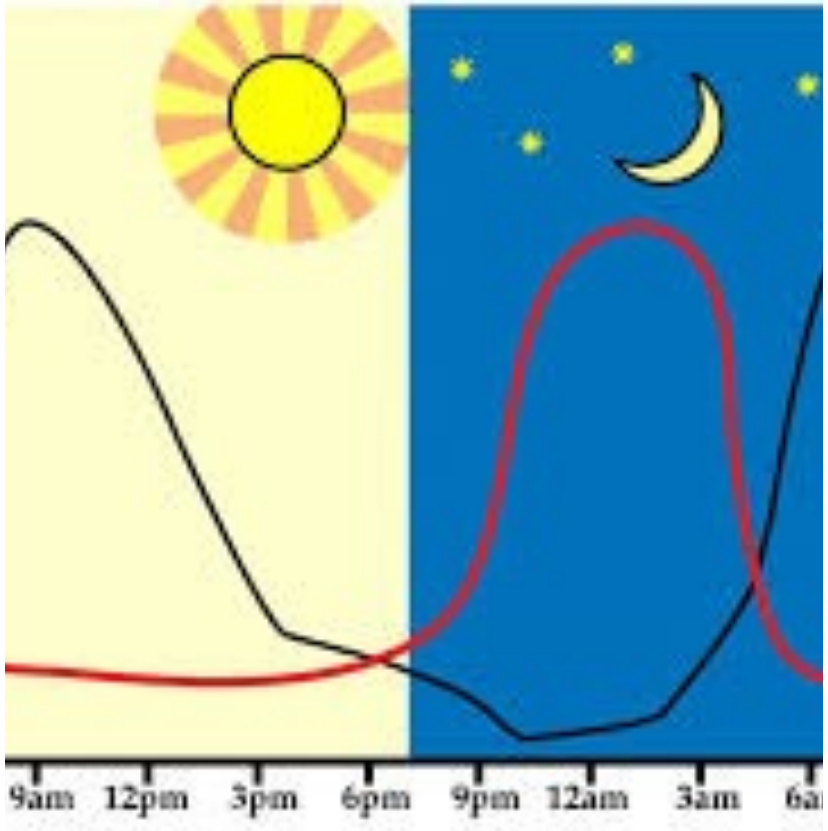


SCN becomes less sensitive to entrainment stimuli:

- Opacity of the lens
- Impairment in expression of *Per* genes in SCN (sensitivity of the system to light)
- Reduced activity of NMDA, histamine (act similar to light) in suprachiasmatic n.
- Advancing of sleep phase (super early to bed, super early to rise)

MELATONIN

- Melatonin is not influenced by sleep *per se* (NOT a sleeping pill) but by the circadian cycle
- Robust circadian rhythmicity in BIOLOGICAL night and day (as opposed to social)
- Neurodegeneration= loss of SCN neurons = melatonin drop
- SCN innervates PVN of the hypothalamus and so regulates CRH (GABA interneurons) and energy homeostasis via pre-autonomic sympathetic/parasympathetic systems.



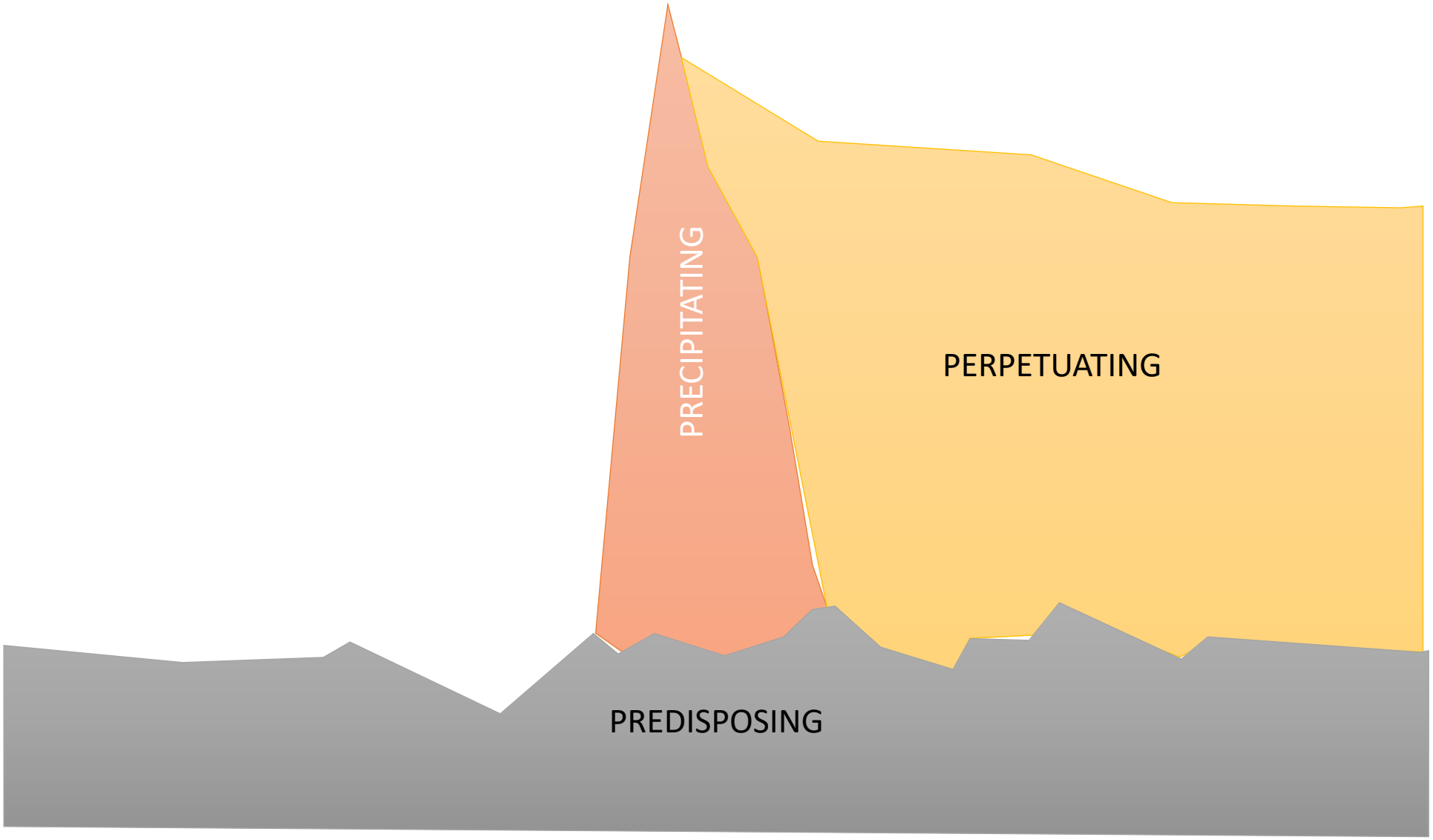
Circadian rhythm and neurodegeneration

- Disruption of circadian clock led to disrupted synapses, ability to form new dendrites (Karatsoreos, 2011)
- Parkinson’s disease: 60 percent have sleep problem vs healthy control 16% have excessive daytime sleepiness (Tandber et al, 1998)
  - Damage to SCN
  - Irregular napping

HOMEOSTATIC SLEEP DRIVE ADENOSINE

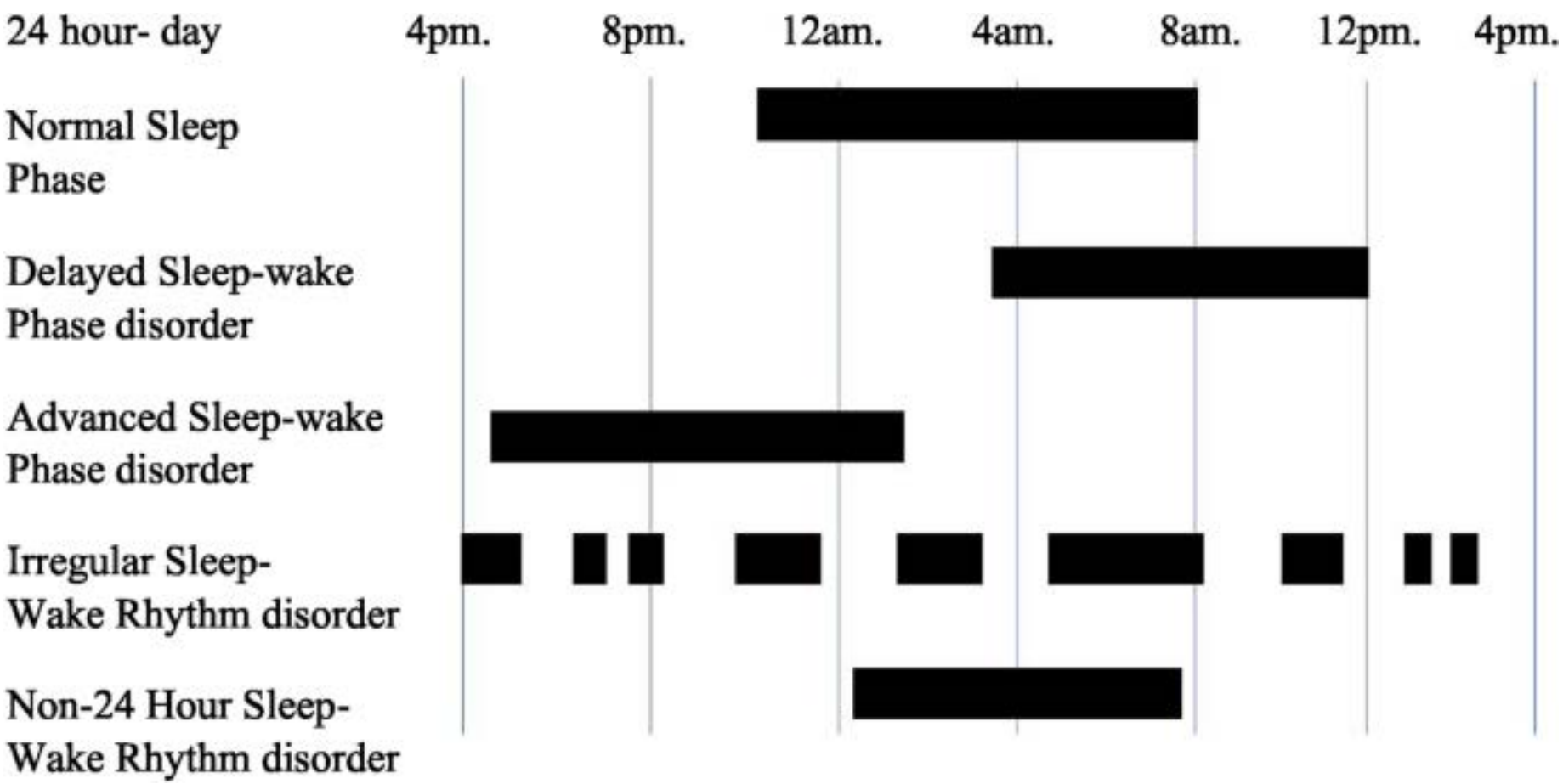
- Adenosine is a natural by-product of using up our internal energy stores (it forms the core of **adenosine triphosphate (ATP)**
- It IS influenced by sleep per se (and caffeine)
- As glycogen stores are used up, extracellular Adenosine is built up and removed at night
- Build-up of adenosine leads to pressure to enter NON-REM SLEEP
- Adenosine level increase with age?
- Nap = dissipation of sleep drive
- Napping in nursing home and low light

INSOMNIA



Spielman, 1987

ADVANCING OF SLEEP PHASE WITH AGE (Early to bed, early to rise)



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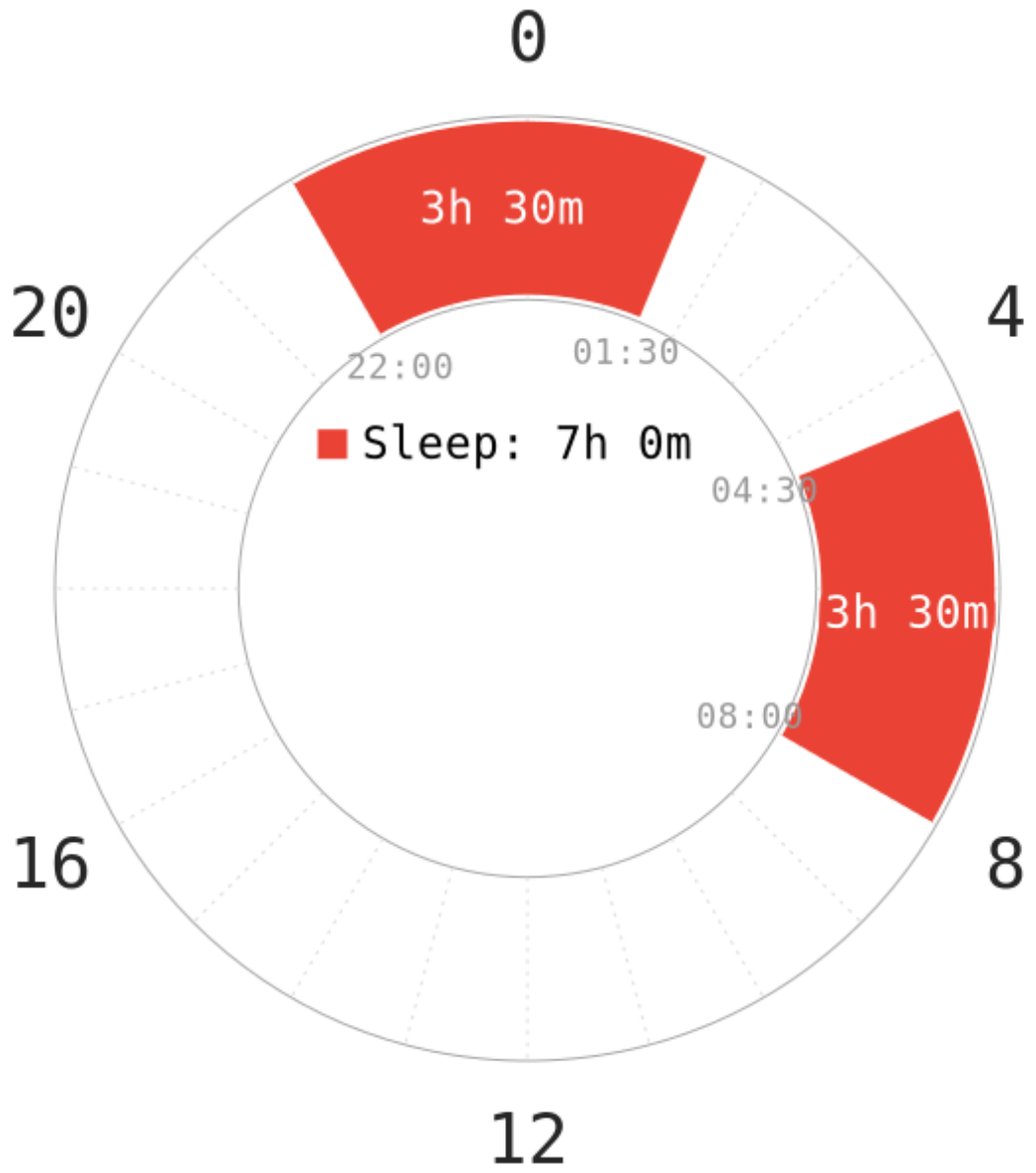
BIPHASIC SLEEP PATTERN



Polyphasic.net

“The forgotten medieval habit of two sleeps”, Zaria Gorvett, BBC, 2022

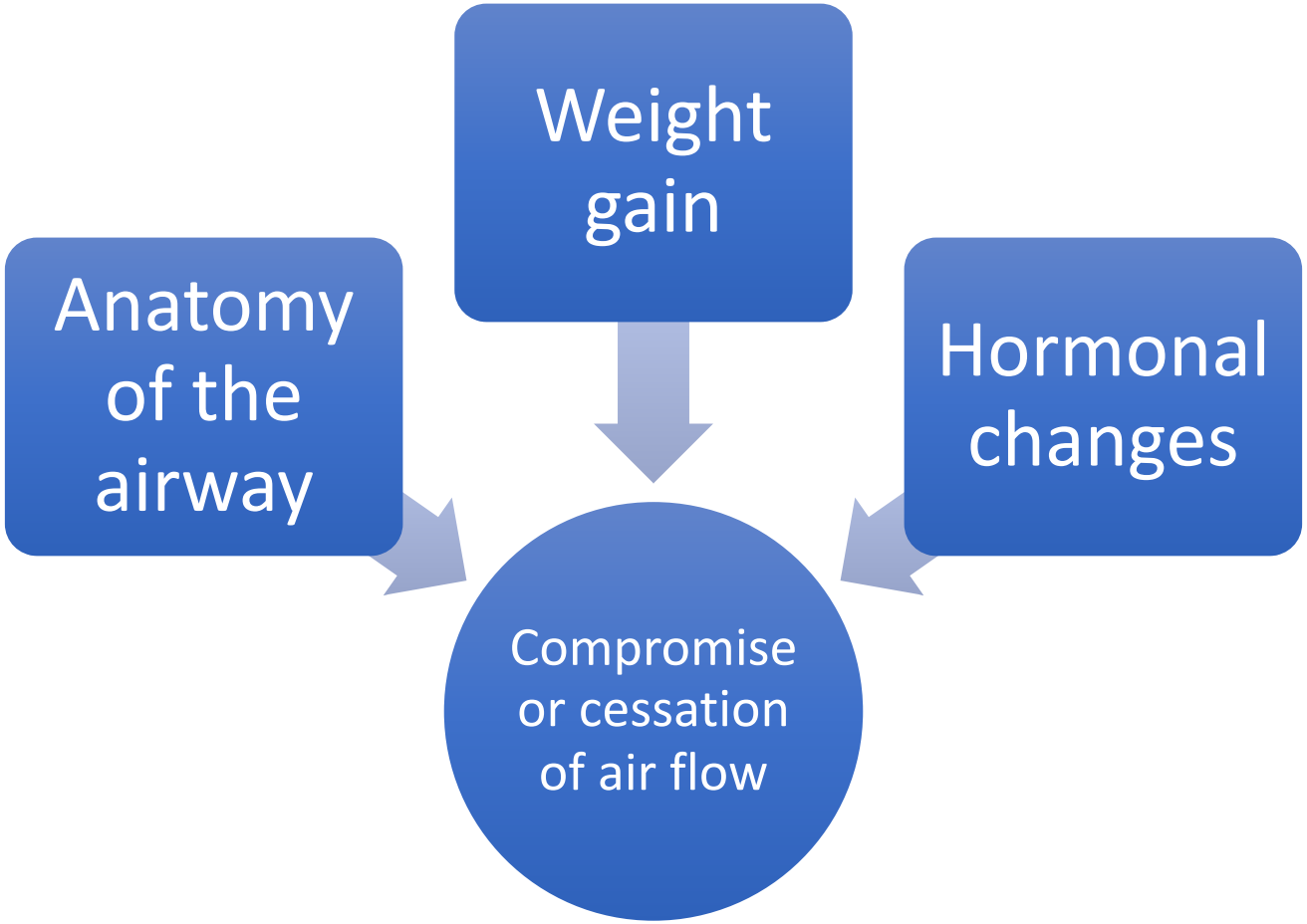
SLEEP COMPRESSION/RESTRICTION and PARADOXYCAL INTENT

INSOMNIA AS SLEEP EFFORT

Schematic by Michael Smith, PhD

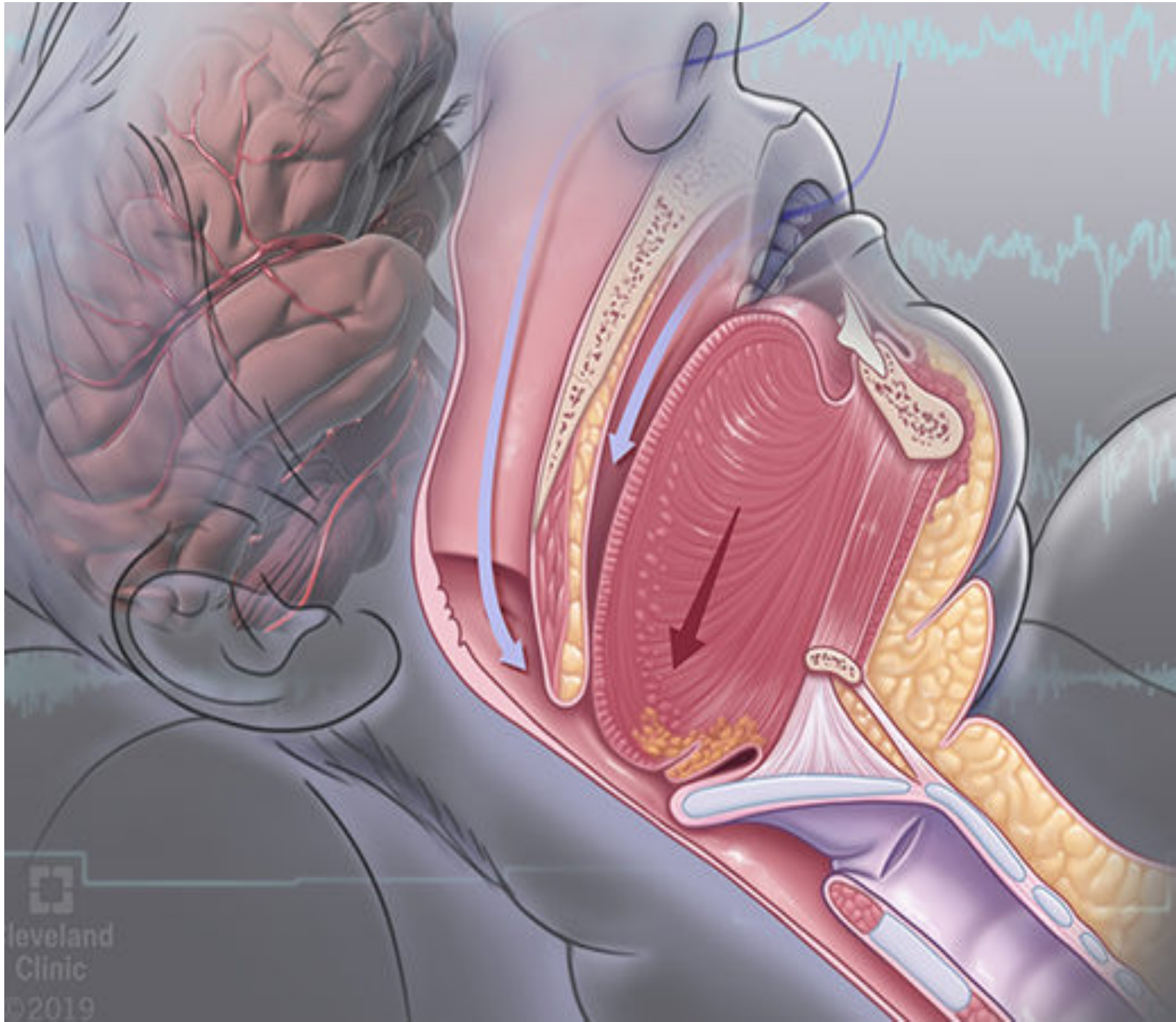
IMPORTANT SLEEP TENETS (CBT)

OBSTRUCTIVE SLEEP APNEA



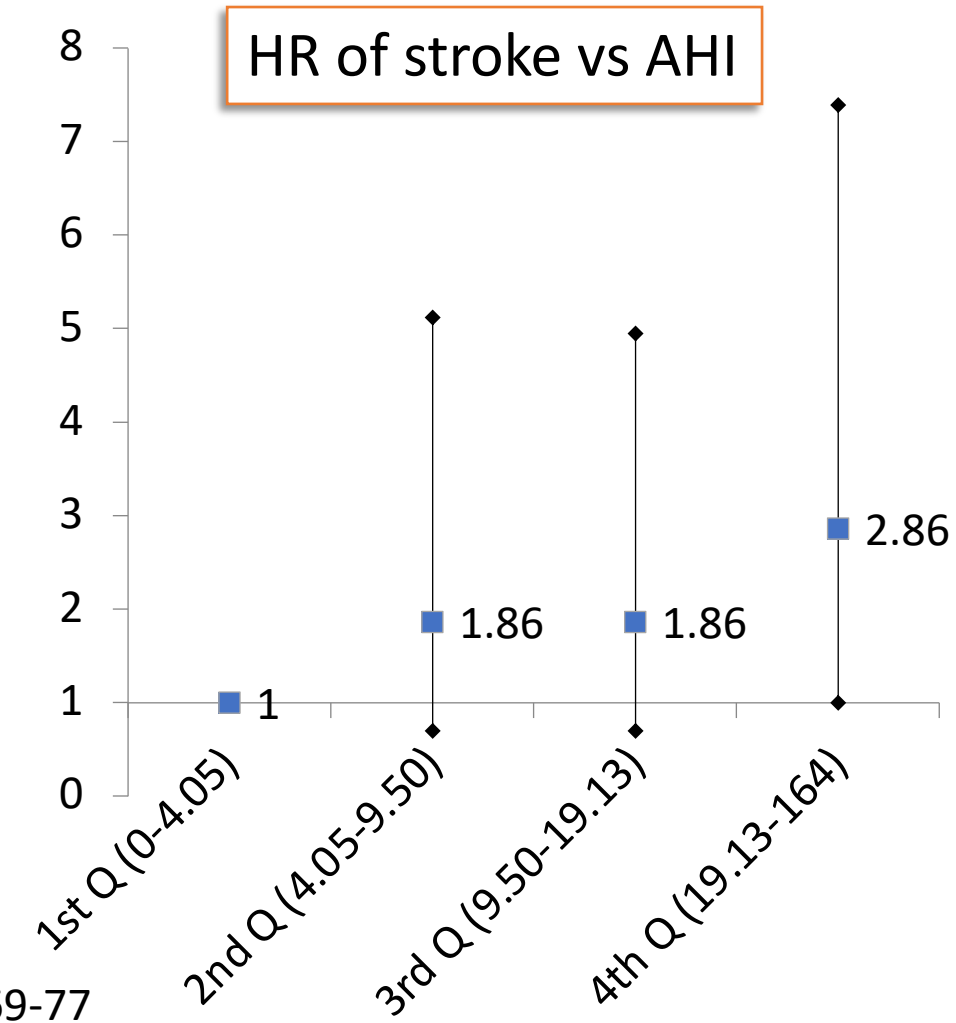
OBSTRUCTIVE SLEEP APNEA

- *ApoE4* - amyloid burden increase
- Elevated T-tau and P-tau – plasma but also CSF
- Hypoxia or sleep fragmentation
- Severity of apnea



Sleep Heart Health Study - 2010

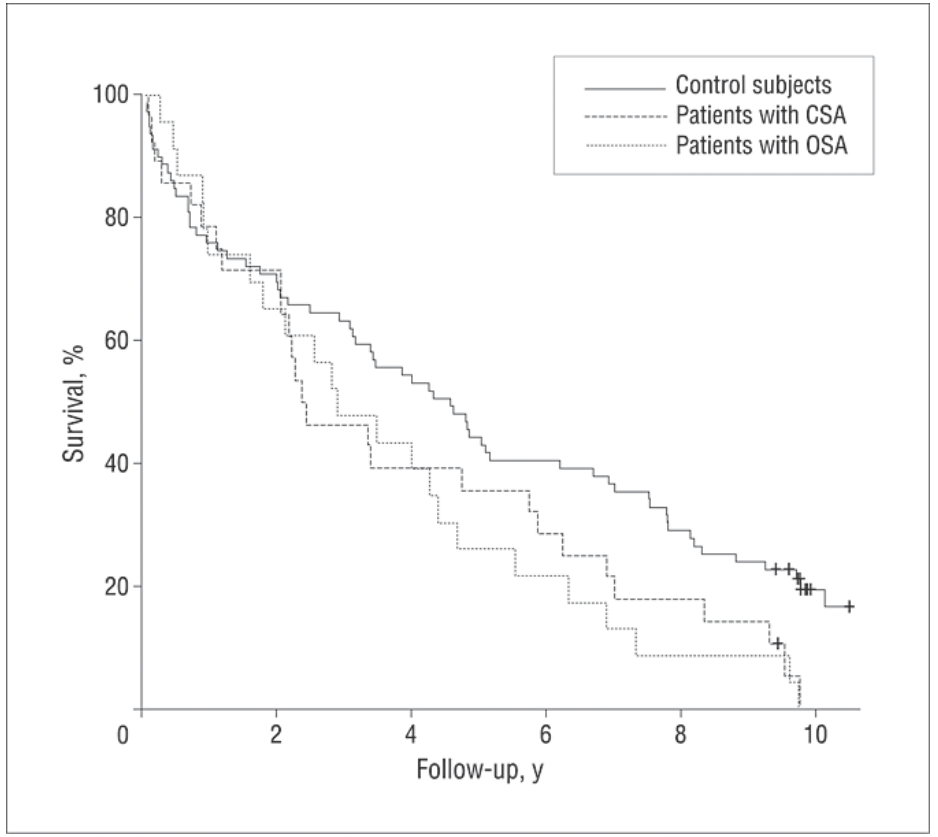
- n=5,422
  - 7.8 yrs follow-up after initial PSG
- Significantly higher risk of stroke in men with most severe OSA (AHI>19)



Redline et al. Am J Respir Crit Care 2010:182: 269-77

Obstructive Sleep Apnea and Stroke

- OSA=risk factor for death
- 151 pts with stroke, 132 had PSG within 1 month of stroke
- 23 found to have OSA (AHI>15)
- 10 year follow up, 116/132 died
- **Mortality increased in patients with severe apnea**



Sahlin 2008

Sleep apnea in stroke recovery

- Patients recovering from stroke have high incidence of OSA
- OSA on Inpatient unit
  - N=45, 86 % Ischemic/14% hemorrhagic
  - 9 patients without SA (AHI<9)

Table 2: Sleep Architecture of Participants (N=45)

Variable	Mean ± SD
Sleep efficiency	72.5±6.5
Awake (%)	23±15
Stage 1 (%)	21±12
Stage 2 (%)	33±13
Stage 3 and 4 (%)	12±8
REM (%)	11±6
Epworth Sleepiness Scale	7.5±4.2
AHI	32±19
Arousal (per hour)	38±18
Central hypopneas (per hour)	3±13
Obstructive hypopneas (per hour)	94±72
Mixed hypopneas (per hour)	33±64
Mean SaO_2	96±2
Minimum SaO_2 (%)	81±10
Mean PCO_2 (mm Hg)	47±4
Max PCO_2 (mm Hg)	51±5

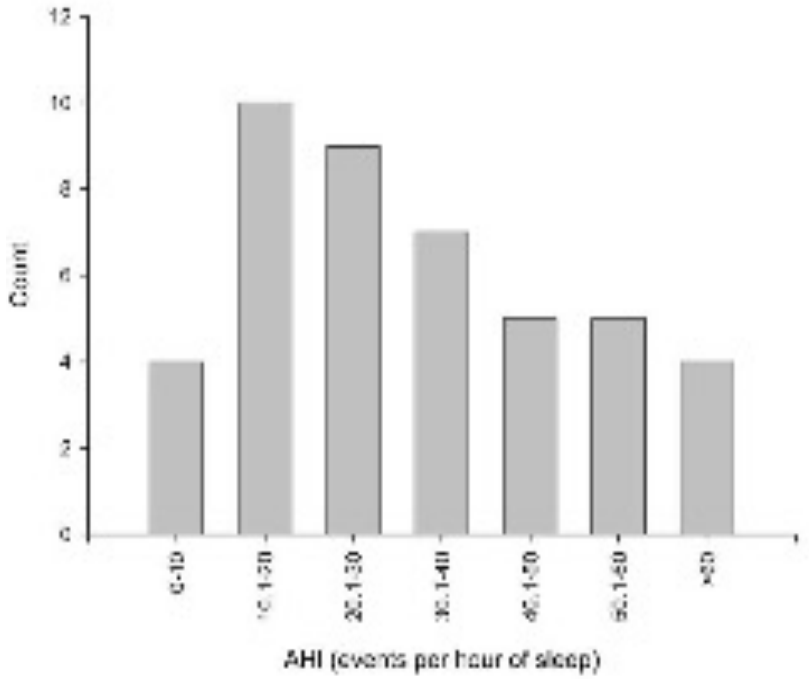
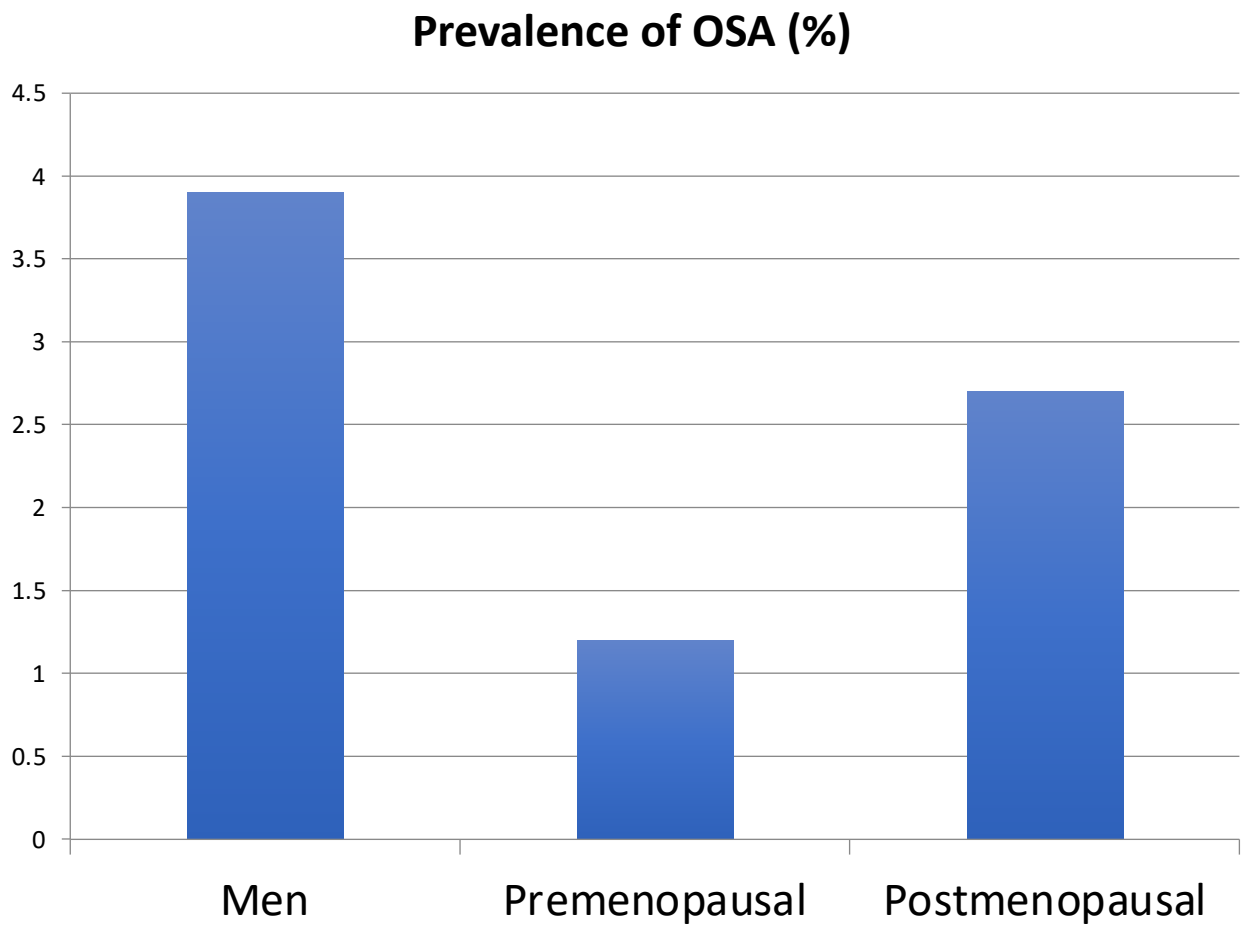


Fig 1. The distribution of AHI among the 45 subjects. Note that 4 had no evidence of SDB with an AHI <10 events per hour of sleep, and 21 had severe SDB with an AHI >30 events per hour of sleep.

Brooks D et al Arch Phys Med Rehabil 2010; 9;659

PREVALENCE

Obstructive Sleep Apnea (OSA)



Sleep 2002; 25:412

PRESENTING SYMPTOMS/SIGNS OSA

	Men	Women
Snoring/Apneas	***	*
Sleepiness	***	**
AM Headaches	*	***
Depressive Features	*	**
Apnea Freq.	**	*
Hypopnea Freq.	*	**

"Laugh and the world laughs with you, snore and you sleep alone" – Anthony Burgess

Arch Intern Med 1996; 156:2445
Sleep 2002; 25:412

STOP BANG

STOP

SNORE (loudly)

TIRED (daytime)

OBSERVED (stop breathing)

PRESSURE (Blood pressure)

BANG

BMI (greater than 35)

AGE (over 50)

Neck (circumference 40 cm+)

GENDER (male)

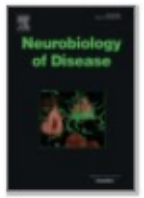
YES ***THREE*** OR MORE TIMES = HIGH RISK OF OSA

Home Sleep Testing

- Screening versus Diagnostic testing
- Three channels
- Limited validity
  - sensitivity 91%, specificity 95% for significant sleep apnea
  - 85% and 50% respectively for any sleep apnea

ELSEVIER

Neurobiology of Disease
Volume 145, November 2020, 105054



Review

Obstructive Sleep Apnea and Its Treatment in Aging: Effects on Alzheimer's disease Biomarkers, Cognition, Brain Structure and Neurophysiology

Anna E. Mullins [a], Korey Kam [a], Ankit Parekh [a], Omonigho M. Bubu [b], Ricardo S. Osorio [b, 1], Andrew W. Varga [a] [1] ✉

STOP BANG SCREENING

S	Snoring	
T	Tiredness	
O	Observed apnea	
P	High blood pressure	
B	Body mass index >35 kg/m²	
A	Age >50 years	
N	Neck circumference >40 cm	
G	Male gender	
Scoring:	0-3	Low risk
	4+	High risk

CPAP and COGNITION

- Cognition – mild improvement in severe OSA
- Possible reduction in AD biomarkers (Beta amyloid and tau)
- Compliance remains a confounder
- Delay of MCI onset
    - AD Neuroimaging Initiative:
        - OSA = MCI onset at 72
        - No OSA = MCI onset at 83
        - CPAP RX = MCI onset 82

AD Neuroimaging Initiative

REM BEHAVIORAL DISORDER

- Idiopathic (no neuro disease or relevant motor or cognitive complaints)
- Secondary (neurodegenerative disorder, antidepressants, BB, alcohol w/d)
- Dysfunction in subceruleus n or magnocellularis n)
- Prevalence 0.3-1.5% (when PSG confirmed, age 60+), 4.6-7.7% (population query)
- Behaviors start abruptly, last a few seconds to minutes, eyes closed, confined to bed, easily oriented when awakened
- Wax and wane course and range from jerking to full violent movements

THANK YOU!

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