NORMAL SLEEP AND SLEEP DISORDERS WITH AGING

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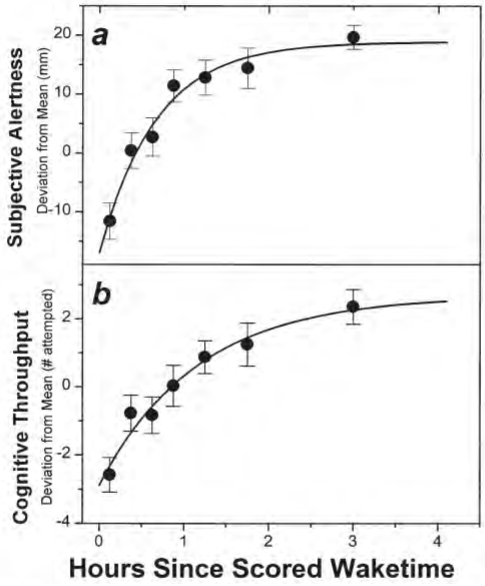
1

David Wyatt, my father, my first research subject (in 1985, 2 years before I knew about sleep research)

2

SLEEP INERTIA



Surprising: NOT related to sleep stage upon awakening

Jewett et al., *JBR*, 1999

3

WHY SLEEP MATTERS FOR HEALTH

DURING SLEEP:

- Development and restoration (growth hormone)
- Nervous system restoration
- Memory (re)processing
- Digestion
- Immune system boost
- Preparation for the day (cortisol)

DURING WAKEFULNESS:

- Optimal alertness and performance
- Avoidance of accidents, dangers

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EPWORTH SLEEPINESS SCALE

How likely are you to doze off or fall asleep in the following situations, in contrast to just feeling tired? This refers to your usual way of life. Even if you have not done some of these things recently, try to work out how they would have affected you. Use the following scale to choose the *most appropriate number* for each situation:

0 = would *never* doze
1 = *slight* chance of dozing
2 = *moderate* chance of dozing
3 = *high* chance of dozing

Situation	**Chance of Dozing**
Sitting and reading	
Watching TV	
Sitting inactive in a public place (e.g., theater or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when the circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a minute in traffic	

Johns MW. Sleep, 1991; 14: 50-55.; Johns MW. Sleep, 1992; 15: 376-381.

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EPWORTH SLEEPINESS SCALE (ESS) SCORING

- 4.6 = WNL mean
- 0-10 = WNL range (remember this number, **10**)
- 13-15 = moderate excessive daytime sleepiness
- 16+ SEVERE excessive daytime sleepiness

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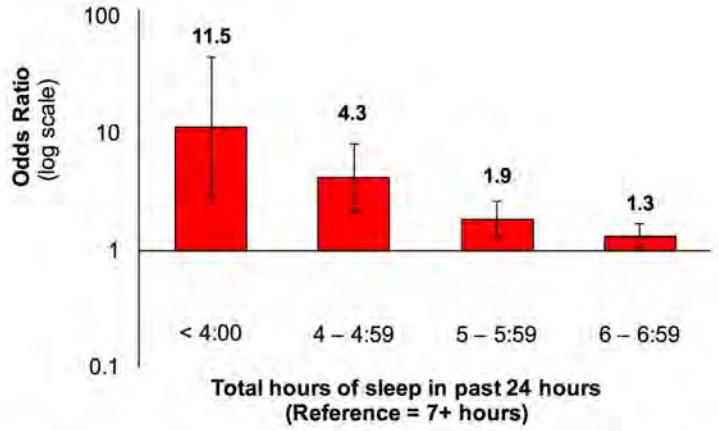
Figure 1. Adjusted odds ratios for contribution to crash in relation to total hours of sleep in the past 24 hours, sample of 7,234 drivers involved in crashes in which EMS was dispatched and at least one vehicle was towed, United States, 2005 – 2007.



Data: National Motor Vehicle Crash Causation Survey (National Highway Traffic Safety Administration, 2008). Odds ratios are from a case-control study in which cases were drivers who on-scene investigators found to have contributed to the crash by means of an unsafe or illegal action, inaction, or error; controls were drivers not found to have contributed in such a way. Odds ratios were adjusted for driver age, time of day of crash, intersection vs. non-intersection location, and recent changes in sleep schedule.

http://publicaffairsresources.aaa.biz/wp-content/uploads/2016/11/Acute-Sleep-Deprivation-and-Risk-of-Motor-Vehicle-Crash-Involvement.pdf

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SOME OF THE CONSEQUENCES OF SLEEPINESS

- Reaction time
- Judgment
- Risk taking
- Coordination
- Balance
- Mood
- Relationships
- Attention
- Memory
- Accidents
- Errors
- Immune system
- BMI
- HTN
- Glucose regulation
- Insulin sensitivity
- Life expectancy
- 10% of MVAs / 83K

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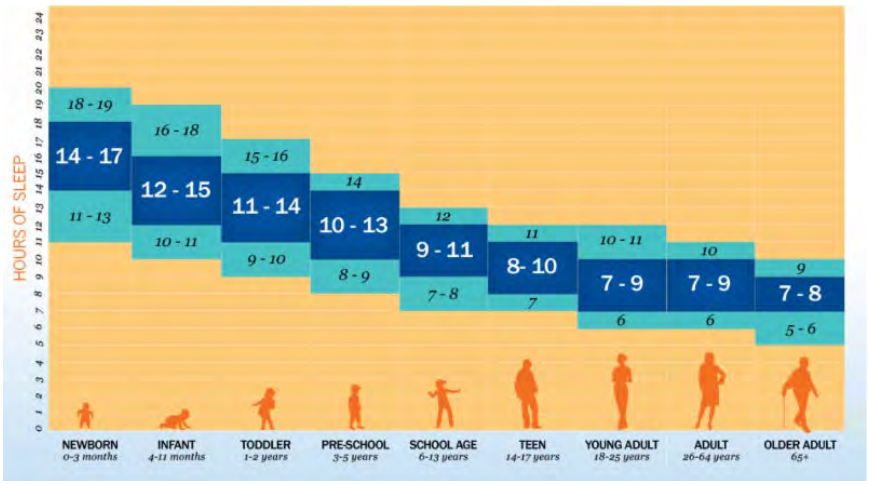
SLEEP NEED (2015): National Sleep Foundation



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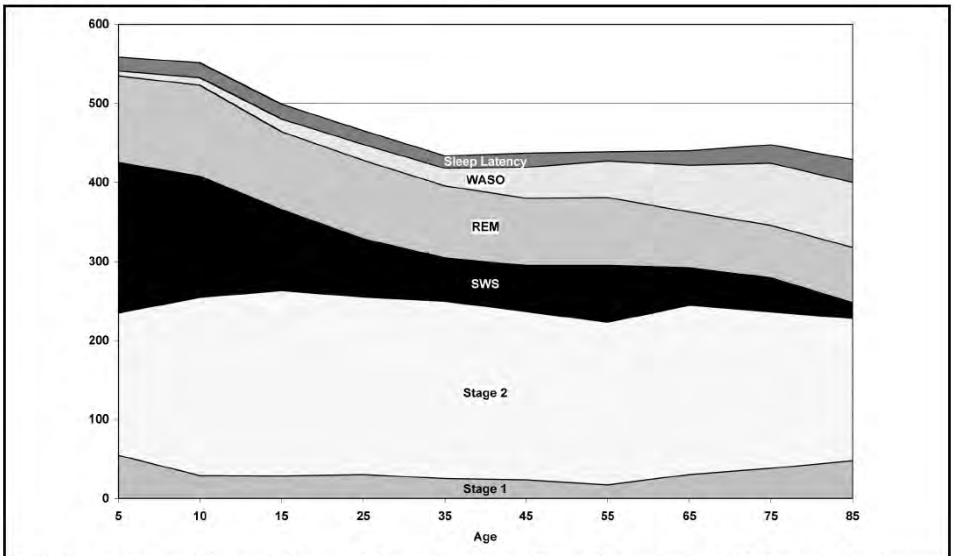

Figure 2—Age-related trends for stage 1 sleep, stage 2 sleep, slow wave sleep (SWS), rapid eye movement (REM) sleep, wake after sleep onset (WASO) and sleep latency (in minutes).

Ohayon et al., *Sleep*, 2004

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POSITIONING (VALIDITY)

SUBJECTIVE
- Sleep Questionnaire
  - Retrospective, good for presenting complaint
- Observer Report
  - Parents of young children, nurses
- Self-Report
  - Epworth Sleepiness Scale (chronic)
  - Karolinska Sleepiness Scale (acute)
- Sleep Diary/Log
  - Prospective, refines presenting complaint
  - Requires clockwatching, adherence

OBJECTIVE
- Dead Man's Switch
- Wrist Actigraphy
- Ambulatory Polysomnography (EEG-based)
- Laboratory Polysomnography
  - The "Gold Standard"

WORST

BEST

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WRIST ACTIGRAPHY

- 16.5 grams
- 64kb memory
- 180 day battery
- Waterproof

- Movement sensor
- Event marker
- Light monitor

- Estimate sleep & wake based on rest & activity recording each minute

www.minimitter.com

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Dijk et al., *AJP*, 2001

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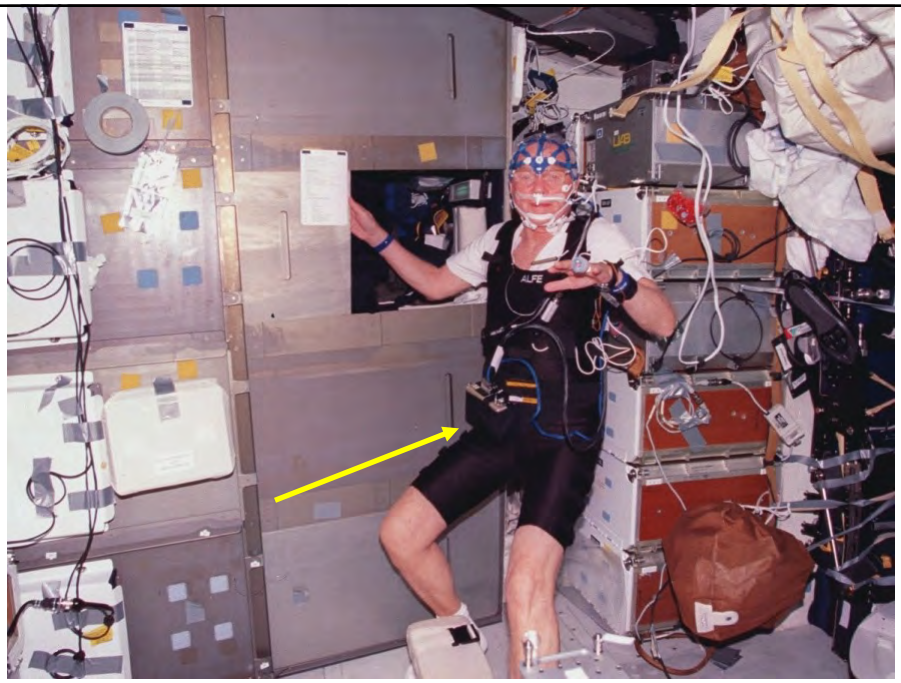

Image courtesy of NASA

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WARNING SIGNS

DAYTIME

- Daytime sleepiness (yawning, nodding, naps)
- Fatigue
- Memory or concentration problems
- Needing too much coffee or soda

NIGHTTIME

- Difficulty falling asleep or staying asleep
- Loud snoring or gasping during sleep

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1. OPTIMIZE SLEEP

- 7-9hr on normal nights
- Consistent sleep schedule
- Sleep quality (minimize disruptions)
- Optimal environment
  - Dark (or eye mask)
  - Quiet (or ear plugs/white noise)
  - Cool (65-68F)
  - Safe (internal/external threats)
  - Pets in another room
  - Cell phone on VIP only

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INTERNATIONAL CLASSIFICATION OF SLEEP DISORDERS – 3rd EDITION

1. Insomnia
2. Sleep Related Breathing Disorders
3. Central Disorders of Hypersomnolence
4. Circadian Rhythm Sleep-Wake Disorders
5. Parasomnias
6. Sleep Related Movement Disorders

ICSD-3, *AASM*, 2014

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SLEEP RELATED BREATHING DISORDERS

- Upper airway narrowing or obstruction
  - Obstructive Sleep Apnea (OSA) - adult
  - Obstructive Sleep Apnea (OSA), pediatric
- No respiratory effort
  - Central Sleep Apnea (CSA) - 8 subtypes
- Sleep Related Hypoventilation Disorders
  - 6 subtypes
- Sleep Related Hypoxemia Disorder
- Isolated Symptoms and Variants
  - Snoring
  - Catathrenia

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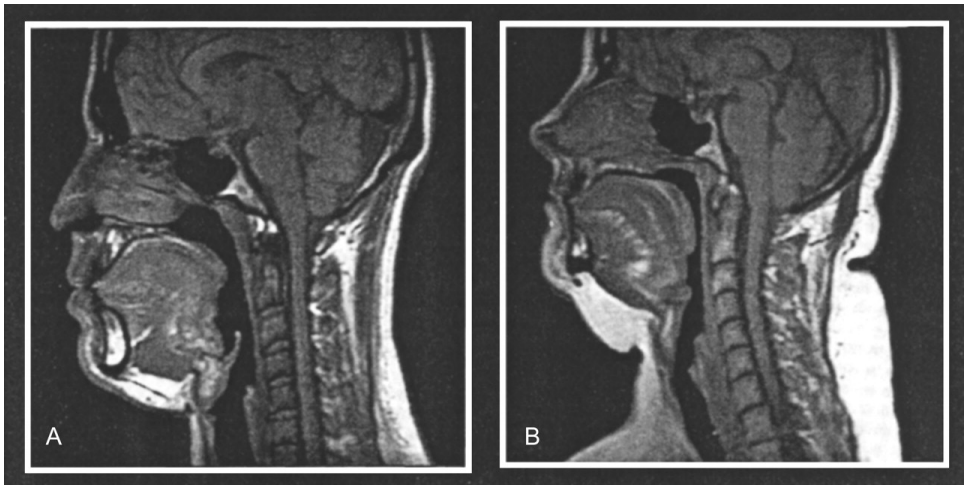

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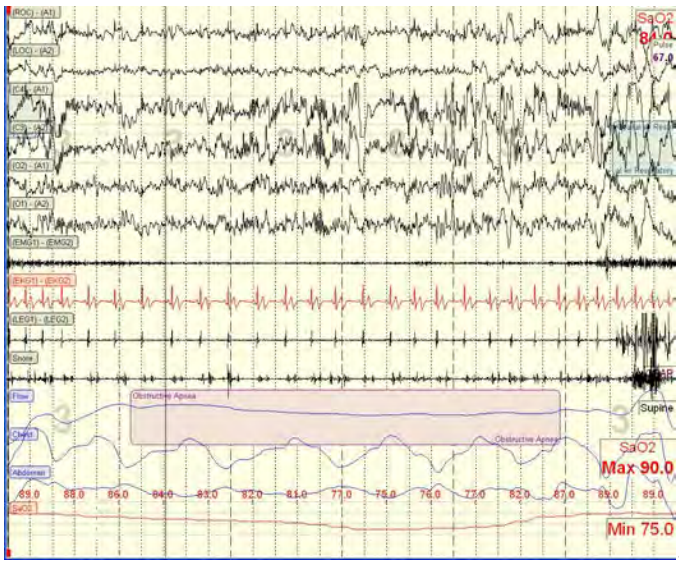
OBSTRUCTIVE APNEA



30 seconds

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OBSTRUCTIVE SLEEP APNEA

- Upper airway crowding
- Pharyngeal dilator fatigue
- Occasionally nasal obstruction
- Upper airway narrowing or collapse
- >10 second airflow reduction or cessation
- ↑ C02 detected -> CNS "alarm", arousal, hyperpnea, rapid return to sleep, repeat
- Increased risk of hypertension, heart attacks, heart rhythm problems, stroke, accidents

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RISK FACTORS

- Obesity
- Neck circumference: ≥17" M, ≥ 16" F
- Women partially "protected" until menopause
- 4% men, 2% of women have OSA syndrome (OSA + EDS)
- **23% men, 9% of women have AHI ≥5**
- Likely HIGHER NOW – obesity epidemic

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"STOP-BANG" screening

- Snoring (loud)
- Tired (EDS, fatigue)
- Observed (witnessed apnea/choke/gasp)
- Pressure (HTN)
- BMI (over 35)
- Age (over 50
- Neck (17"+ men, 16"+ women)
- Gender (male)

- 0-2 low, 3-4 moderate, 5-8 high risk

Chung F et al. Anesthesiology 2008; 108: 812-821

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CARDIOPULMONARY SEQUELAE

- Cardiac arrhythmias (n-sVT, a fib, PAC, PVC)
- Systemic HTN
- MI, CVA
- Changes in inflammatory markers (e.g., CRP)
- worsening LVEF
- (not to mention EDS, accidents, mood & cognitive problems)

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TREATMENT OPTIONS

- PAP (CPAP, bilevel, auto, servo, other)
- ORAL APPLIANCES
  - Mandibular repositioning devices
  - Tongue retaining devices
- WEIGHT LOSS (behav, Rx, surgical)
- ENT SURGERY
  - Tongue base reduction
  - Uvulopalatopharyngoplasty (UPPP/LA-UPPP)
  - Genioglossus advancement w/ hyoid suspension
  - Maxillary-mandibular advancement
  - Stimulator implantation
- POSITION TRAINING
- ELEVATION
- TRACHEOSTOMY
- MICROGRAVITY

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POSITIVE AIRWAY PRESSURE (CPAP, bilevel PAP, autoPAP, servo-vent)

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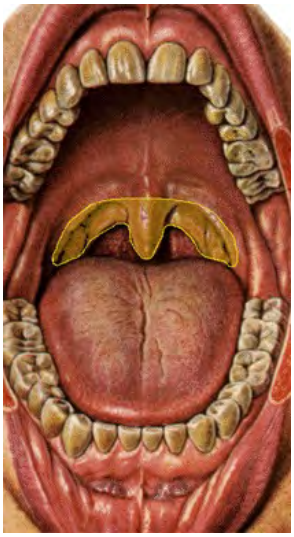
UPPER AIRWAY SURGERY:
UVULOPALATOPHARYNGOPLASTY (UPPP)



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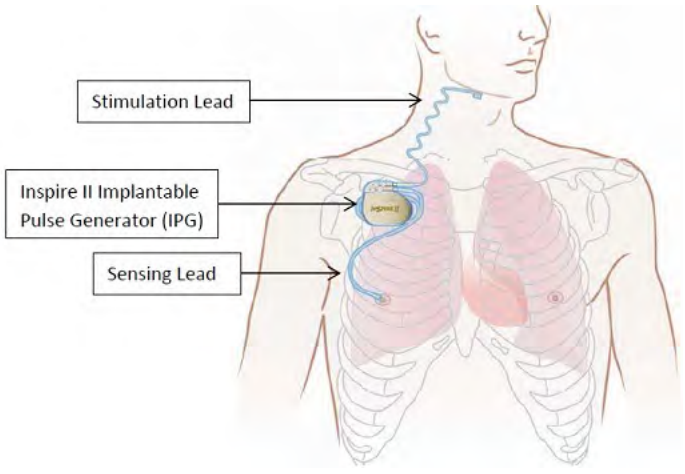
INSPIRE:
unilateral hypoglossal nerve stimulator



http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm398321.htm

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PERIMENOPAUSAL WOMEN…

- 59% have insomnia a few nights per week
- 43% report symptoms of a sleep disorder such as snoring, sleep apnea or RLS
- Noise (36%) and co-sleeping with pets (20%) are the most common nighttime disturbances
- 20% experience night sweats and hot flashes

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POSTMENOPAUSAL WOMEN…

- Have the highest incidence of:
  - Limited time in bed - less than 6 hours (14%)
  - Sleep disorders such as snoring or sleep apnea (42%)
  - RLS (22%)
  - Sleep aid use (41%)
  - Obesity (30%)

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RESTLESS LEGS SYNDROME

- "Ekbom's Disease" – 1944

Clinical diagnosis: must include:

1. Irresistible urge to move legs
2. Uncomfortable sensation ("creepy-crawly")
3. Movement or walking relieves Sxs
4. Onset in presleep/evening hours

- Idiopathic vs. secondary (anemia, pregnancy, ESRD, neuropathy)
- **5-10% prevalence**

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RLS TREATMENTS

STANDARD

- DA agonists: Requip (gone), Mirapex

GUIDELINE

- Carbidopa/Levodopa (Sinemet)
- Long acting gabapentin (Horizant)
- Opiods

OPTION

- Gabapentin (Horizant), pregabalin (Lyrica), carbamazepine (Tegretol)
- Clonidine
- Iron supplement: if ferritin < 75 µg/L
- Avoid most antidepressants

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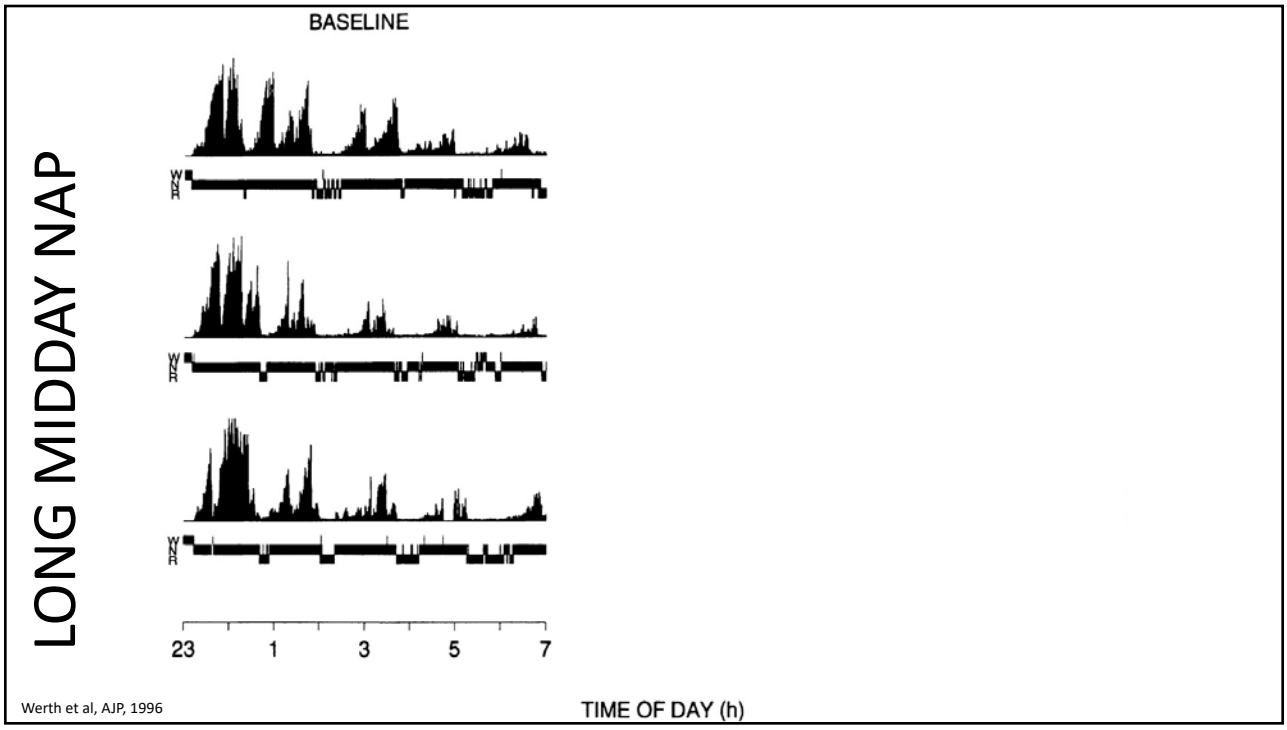

Werth et al, AJP, 1996

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SLEEP HOMEOSTASIS

- During each hour you are awake ("cost" of being awake):
  - Sleep-promoting substances build up in the brain (e.g. adenosine)
  - Wake-promoting substances are used up in the brain (e.g., NE, 5-HT)
- During sleep
  - Sleep-promoting substances are cleared
  - Wake-promoting substances are replenished

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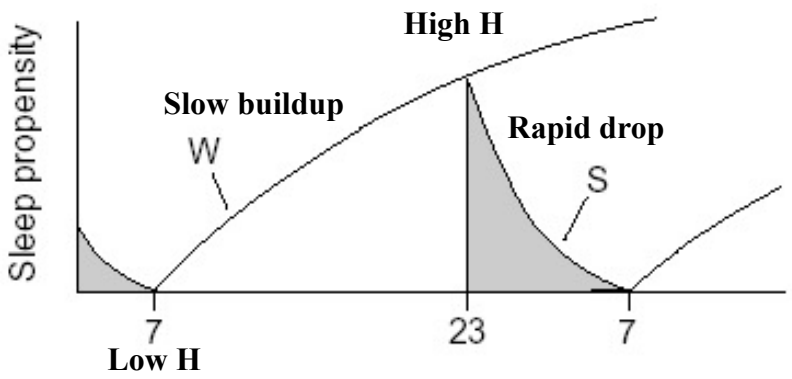
Borbély, Hum Neurobiol, 1982;
Borbély et al model, *HFSP*, 2000

SLEEP HOMEOSTASIS



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INTRINSIC CIRCADIAN TIMEKEEPING SYSTEM

- 24-hour clock in the brain
- Suprachiasmatic nucleus (the “SCN”)
- Regulates timing of (for example):
  - Core body temperature
  - Appetite
  - Amount of urine production
  - Alertness / sleepiness
- Coordinates clocks throughout the body

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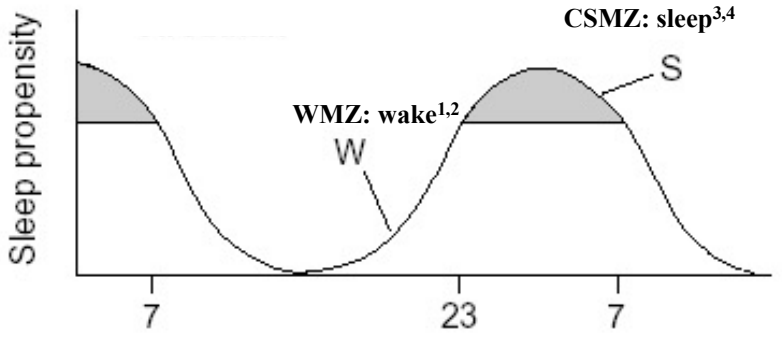
CIRCADIAN SYSTEM

1 Strogatz et al., *Am J Physiol* 253, 1987
2 Lavie, *Electroencephalogr. Clin. Neurophysiol* 63, 1986.
3 Stepanski & Wyatt, *Sleep Medicine Reviews* 7, 2003
4 Wyatt et al., *Sleep* 27, 2004



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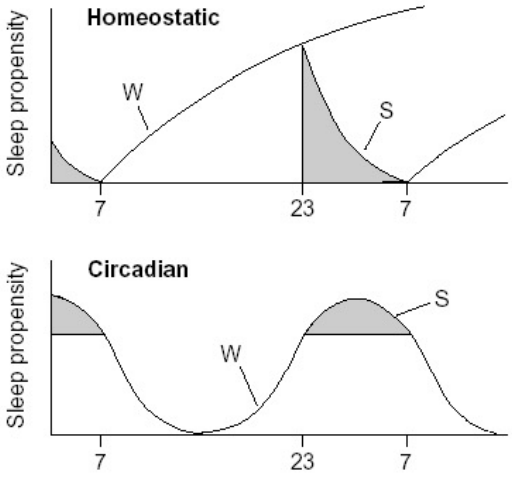
2-PROCESS MODEL OF SLEEP-WAKE CONTROL: 4-person relay race

Borbély, Hum Neurobiol, 1982;
Borbély et al model, *HFSP*, 2000



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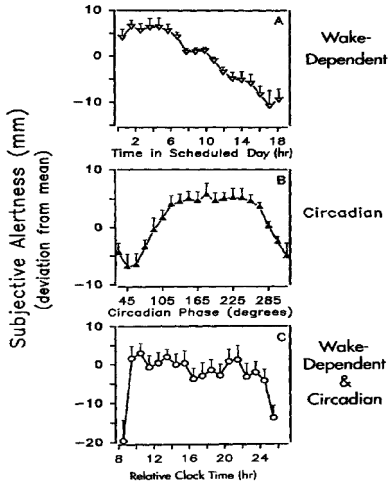
THE BRAIN IS PROGRAMMED FOR 14-17 HOURS OF STABLE WAKEFULNESS



In normal sleepers:

- Increased sleep drive with hours of wake

  + offset by

- Circadian drive for wake during daytime

  =

- ~16 hours of stable daytime alertness
- Midafternoon dip is part of biology

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CHRONIC INSOMNIA DISORDER

A. "The patient reports, or the patient's parent or caregiver observes, one or more of the following:[1]
   1. Difficulty initiating sleep.
   2. Difficulty maintaining sleep.
   3. Waking up earlier than desired.
   4. Resistance to going to bed on appropriate schedule.
   5. Difficulty sleeping without parent or caregiver

ICSD-3, *AASM*, 2014

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B. DAYTIME COMPLAINTS (1 or more)

1. Fatigue/malaise.
2. Attention, concentration, or memory impairment.
3. Impaired social, family, occupational, or academic performance.
4. Mood disturbance/irritability.
5. Daytime sleepiness.
6. Behavioral problems (e.g., hyperactivity, impulsivity, aggression).
7. Reduced motivation/energy/initiative.
8. Proneness for errors/accidents.
9. Concerns about or dissatisfaction with sleep.

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INSOMNIA TREATMENT

Short-term management

- OTCs (”PM”s, BBB-antihistamines)
- Hypnotics: 1-2 weeks, rarely longer

Curative

- Cognitive-behavioral treatment

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3-P model: AN expanded interpretation

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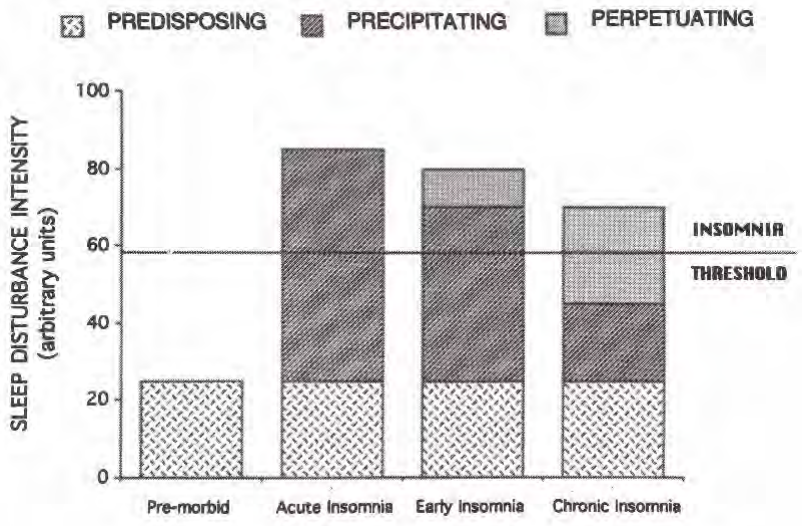
SPIELMAN MODEL OF INSOMNIA



Spielman & Glovinsky, in Hauri, 1991

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ART SPIELMAN'S "3-P MODEL"

- Predisposing factors
  - "Physiological hyperarousal"
  - Lower sleep homeostatic drive
- Precipitating events
  - Stressful life event (74% identify; Healy et al., 1981)
  - Good or bad stressors
- Perpetuating factors
  - Examples on next slides

Spielman, Clinical Psychology Review, 1986
Wyatt & Crisostomo, Sleep Medicine, 2008

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PERPETUATING FACTORS:
after insomnia onset, patient begins to…

- too much time in bed (C and H)
  - "catch sleep if it occurs"
- sleep later when possible (C and H)
- nap after poor night's sleep (H)

Behavioral

- caffeine & stimulants for EDS (H)
- alcohol self-medicating for sleep
- random use of hypnotics

Pharmacologic

- Conditioned arousal to bed/bedtime
- unreasonable concerns over next-day consequences

Cognitive

C = circadian implications, H = homeostatic implications

Spielman, Clinical Psychology Review, 1986
Wyatt & Crisostomo, Sleep Medicine, 2008

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MORE COGNITIVE FACTORS

- Catastrophic thinking
  - Lost control over my sleep
  - Going to lose my job because of performance
- All-or-nothing thinking
  - Bad nights vs. good nights
  - "I didn't sleep at all last night"
- Overgeneralization
  - Paying attention only to the bad nights
- Sleep math
  - If I fall asleep now, I can still get X hours of sleep

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STIMULUS CONTROL (Standard)

Richard Bootzin, Ph.D.

- Good and bad conditioning to the bed/bedroom
- Go to bed only when sleepy
- Bed for sleep (and sex) only
- If not asleep in 15-20 minutes, leave the bed and engage in calming activity elsewhere
  - Return to bed when sleepy
  - Repeat as needed
- Fixed wake time
- No napping

Bootzin RR, *Proceedings of the American Psychological Association*, 1972

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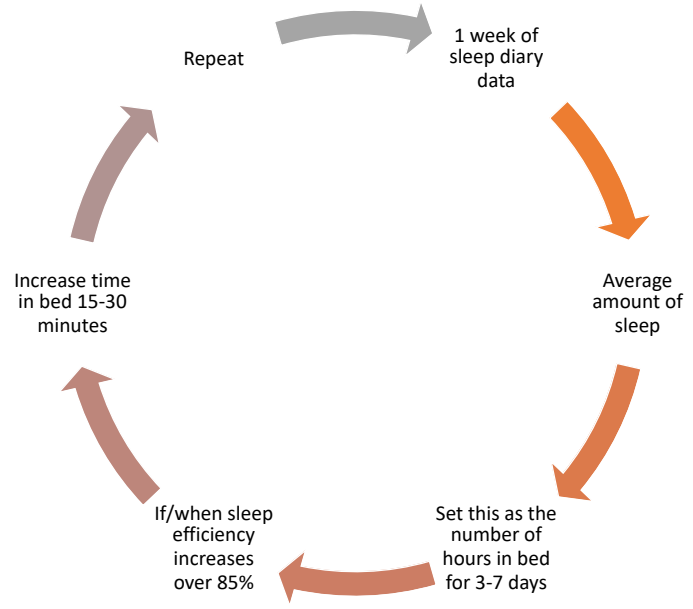
SLEEP RESTRICTION



Goal: build higher sleepiness pressure

Spielman et al., *SLEEP*, 1987

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SLEEP RESTRICTION (Guideline)

Art Spielman, Ph.D.

- Increase sleepiness, to ease the DIMS complaint
- Reduce TIB to match estimated mean TST
- Minimum of ~ 4.5-5 hr TIB
- Caution for EDS, no napping
- Hold 3-7 days until SE ≥ 85%
- Increase TIB 15-30 minutes
- Hold 3-7 days until SE ≥ 85%
- Decrease TIB if SE drops
- Contrast to "Sleep Compression"

Spielman, Saskin, & Thorpy, *Sleep*, 1987

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SLEEP COMPRESSION

- Gentler treatment
- May take longer
- Goal: build higher sleepiness pressure
- Example averages from a sleep diary
  - 8 hours in bed
  - 5 hours of sleep
- Start treatment with 7 hours in bed for a week
- Possibly decrease to 6.5 or 6 hours in bed the next week

Lichstein, *Behav. Ther.*, 1988

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MELATONIN

Endogenous

- Secreted by the pineal gland at night
- Suppressed by ocular light exposure
- 2 receptors on the SCN–phase shifting and suppressing the alerting system

Exogenous

- 45min half-life (unless SR)
- 0.1 - 0.5mg physiologic peak dose
- Can shift circadian phase
- Circadian-phase dependent hypnotic
  - suppresses circadian alerting

Side effects

- EDS, headache, vivid dreams
- Antigonadotropic data in seasonal breeding animals

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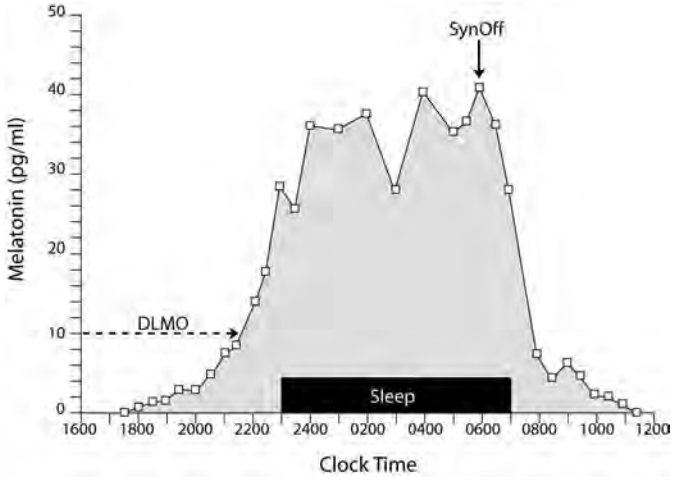
FIGURE FROM: Lewy & Sack, *Neuropsychopharmacology,* 2002

DLMO



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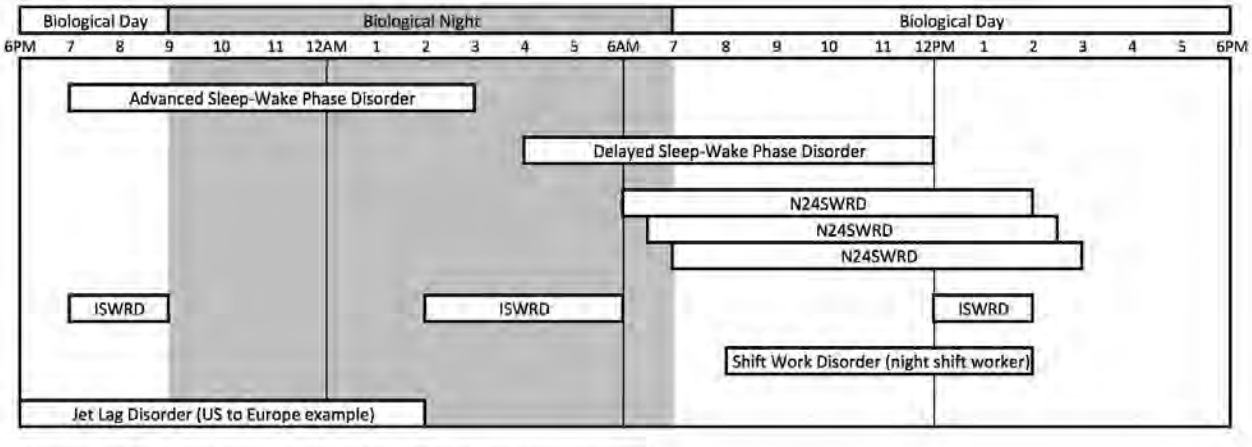

CIRCADIAN RHTYHM SLEEP-WAKE DISORDERS

Wyatt, UpToDate

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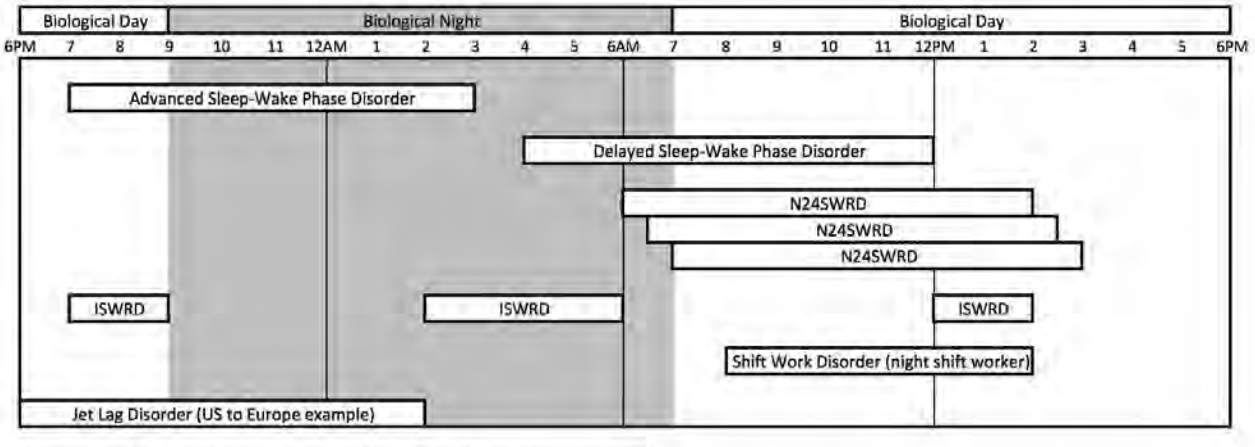

Wyatt, UpToDate

55

Advanced Sleep-Wake Phase Disorder

- Early phase of the major sleep episode vs. the desired or required sleep time and wake-up time,
- Chronic or recurrent complaint of inability to reach the desired bedtime and EMA.
- Symptoms for **at least three months**.
- When sleeping at this earlier phase, sleep quality and duration are **improved (may not be WNL)**
- Sleep log (and ideally actigraphy) for **at least 7 days** (ideally 14 days) show advance timing of the habitual sleep period. Look for both work/school days vs. free days
- The sleep disturbance is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder

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ASPD NOTES

- Standardized **chronotype questionnaires are useful** tools to assess the chronotype of "eveningness" and "morningness." Individuals with advanced sleep phase score as "morning types."
- **Demonstration of an advance** in the timing of other circadian rhythms such as the dim light melatonin onset or urinary 6-sulfatoxymelatonin is **desirable** to confirm the advanced circadian phase.

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ASWPD Developmental Issues

- ASWPD is most common in older adults
- ASWPD in children or young adults
  - Look for family history
  - Unrealistic parent/guardian expectation about normal wake-time for kids
  - "motivated" early wake time (e.g., Saturday morning cartoons)
  - Early bedtime may reflect insufficient sleep syndrome / sleep deprivation

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Irregular Sleep-Wake Rhythm Disorder

- The patient or caregiver reports a chronic or recurrent pattern of **irregular sleep and wake episodes throughout the 24-hour period**, characterized by symptoms of insomnia during the scheduled sleep period (usually at night), excessive sleepiness (napping) during the day, or both.
- Symptoms are present for **at least three months**.
- Sleep log and, whenever possible, actigraphy monitoring for at least seven days, preferably 14 days, demonstrate no major sleep period and **multiple irregular sleep bouts (at least three) during a 24-hour period**.
- The sleep disturbance is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.

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Melatonin and Bright-Light Treatment for Rest–Activity Disruption in Institutionalized Patients with Alzheimer's Disease

Glenna A. Dowling, PhD,† Robert L. Burr, PhD,‡ Eus J. W. Van Someren, PhD,§ Erin M. Hubbard, MA,*† Jay S. Luxenberg, MD,*‖ Judy Mastick, MN,*† and Bruce A. Cooper, PhD**

Journal of the American Geriatric Society, 56:239-246, 2008

- 1 baseline week
- 10-week intervention
- LM: bright light 0930-1030, M-F, >2,500 lux (6,204 median) + 1700-1800, 5mg melatonin
- LP: same light + 1700-1800 placebo
- Control: 150-200 routine indoor light

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Dowling et al., *JAGS*, 2008

RESULTS

- LM
  - **Decrease** in daytime TST = 66 mins.
- LP and Control
  - **Increased** daytime TST = 25, 50 mins.

- No reporting of statistical tests for changes in nighttime TST
- Data suggests all groups slightly increased nightly TST

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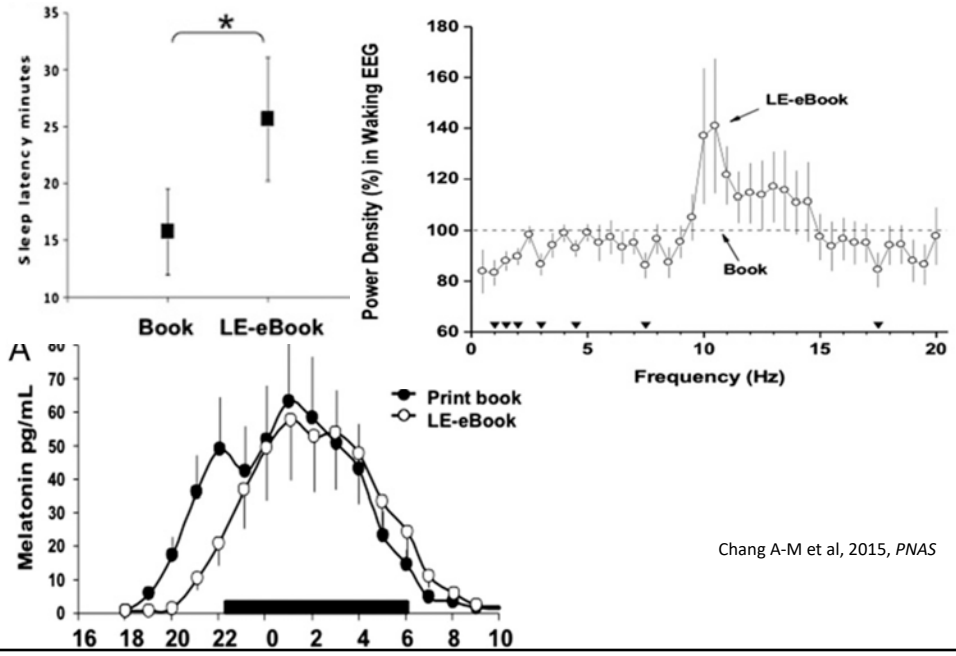
Evening reading: 4 hours of pre-bedtime iPad vs. book



Chang A-M et al, 2015, *PNAS*

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Negative consequences of evening device prohibition

- Rumination can escalate without distraction
- Sometimes doing physical chores instead
- Sleep doesn't improve, patient discounts advice of doctors

- Statistical significance ≠ clinical significance
- Flawed study design
  - very dim light in daytime
  - light "history" determines how meaningful the evening light may be

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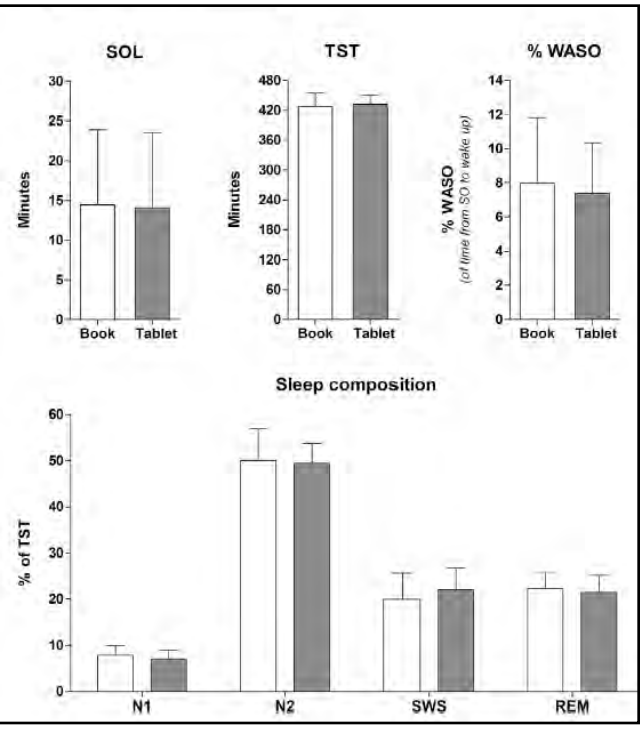
Rångtell et al,. SleepMed 2016

- N=14; crossover design
- >500 lux in daytime
- book or tablet 9-11PM

"Bright light exposure during daytime has previously been shown to abolish the inhibitory effects of evening light stimulus on melatonin secretion. Our results could therefore suggest that exposure to bright light during the day – as in the present study – may help combat sleep disturbances associated with the evening use of electronic devices emitting blue light.



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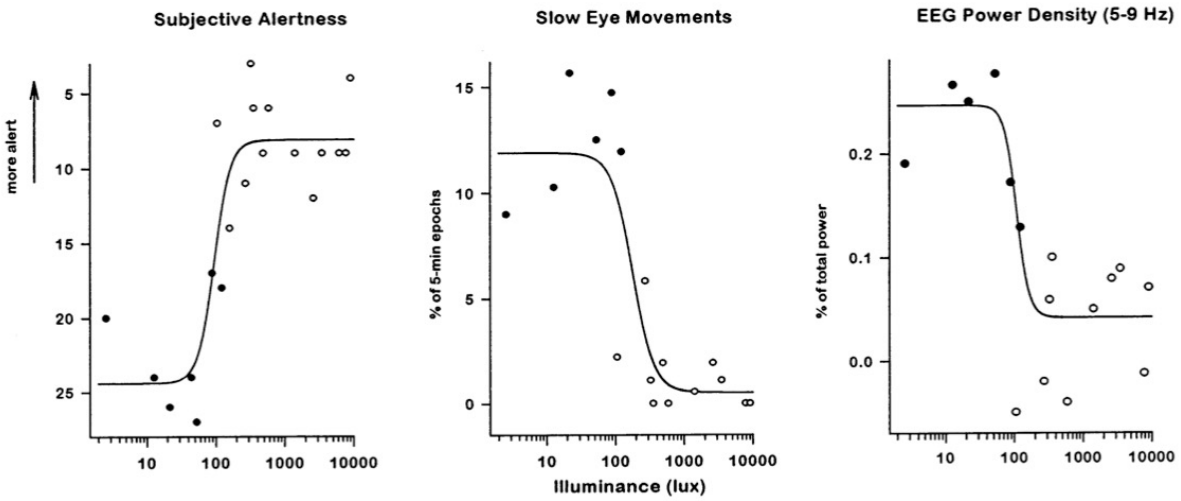
Nighttime light exposure – acute alerting effect (100+ lux)

C. Cajochen et al. / Behavioural Brain Research 115 (2000) 75–83



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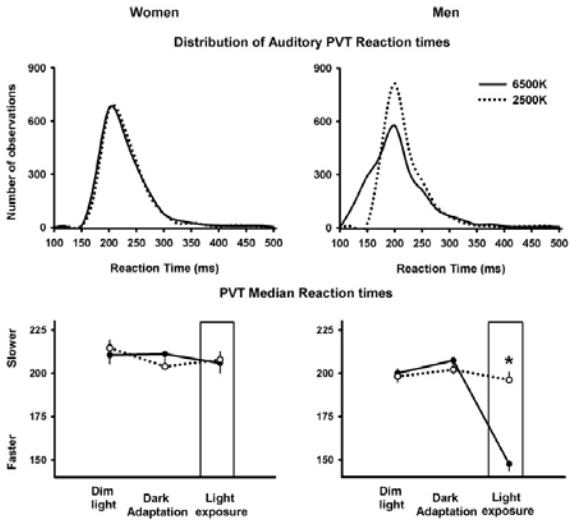
MEN: faster RT with blue light



Chellappa et al, Sci Rep., 2017

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LOGICAL PREDICTION

MEN showed faster reaction times to blue light

Men should have MORE sleep disruption

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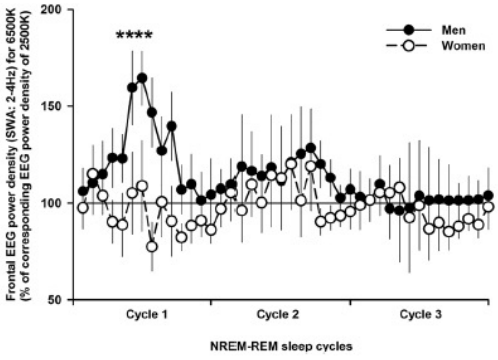
MEN: The brighter the perceived blue light, faster the RT, higher the SWA(? lower in women)



Chellappa et al, Sci Rep., 2017

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Review. J Clin Ophthalmol. 2019 Dec 6;13:2427-2438. doi: 10.2147/OPTH.S213280
eCollection 2019

The Effects of Blue Light-Filtering Intraocular Lenses on the Protection and Function of the Visual System

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Affiliations – collapse

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PMID: 31824137 PMCID: PMC6901063 DOI: 10.2147/OPTH.S213280
Free PMC article

Abstract

Filtration of high-energy short-wave visible light (blue light) to improve vision and protect against damage has evolved both in aquatic animals and terrestrial species. In humans, pigments in the inner layer of the macula absorb wavelengths between 400 and 520 nm and function to improve visual performance. In patients who undergo cataract surgery, replacing cataractous lenses with artificial intraocular lenses (IOLs) that do not mimic normal healthy adult lenses could result in preventable negative visual effects, including glare disability. Blue light-filtering (BLF) IOLs were designed to filter short-wave light in addition to ultraviolet light and mimic the natural crystalline lens. Current studies indicate that BLF IOLs may provide protection from blue light-induced retinal damage and slow the development and progression of age-related macular degeneration. Additionally, BLF IOLs have been shown to improve chromatic contrast, reduce photostress recovery time, reduce glare disability and discomfort, and generally improve visual performance under glare conditions. Although a number of concerns have been raised about the relative risks versus the benefits of BLF IOLs, recent studies reported no adverse effects on visual function or contrast under photopic conditions, no long-term effects on color vision, and no detrimental effects on circadian rhythms with BLF IOLs. Based on the current understanding of the field, evidence suggests that BLF IOLs would be returning the eye to a more natural state compared with non-BLF lenses.

Keywords: blue light filtration; cataract surgery; intraocular lens.

Conflict of interest statement

B. R. Hammond received research funding from and was a consultant for Alcon. V. Sreenivasan and R. Suryakumar are Alcon employees. The authors report no other conflicts of interest in this work.

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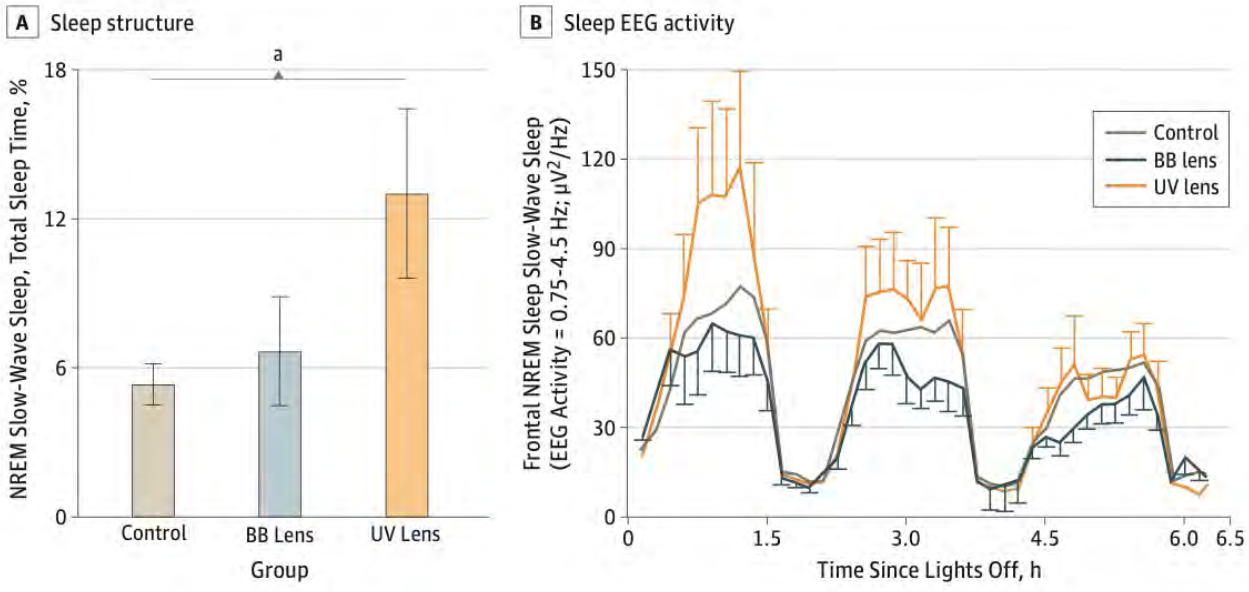
Chellappa et al., JAMA Ophthalmol 2019

Figure 3. Sleep Structure and Sleep Electroencephalographic (EEG) Activity



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