



# The Importance of Sleep for Health and Well-Being

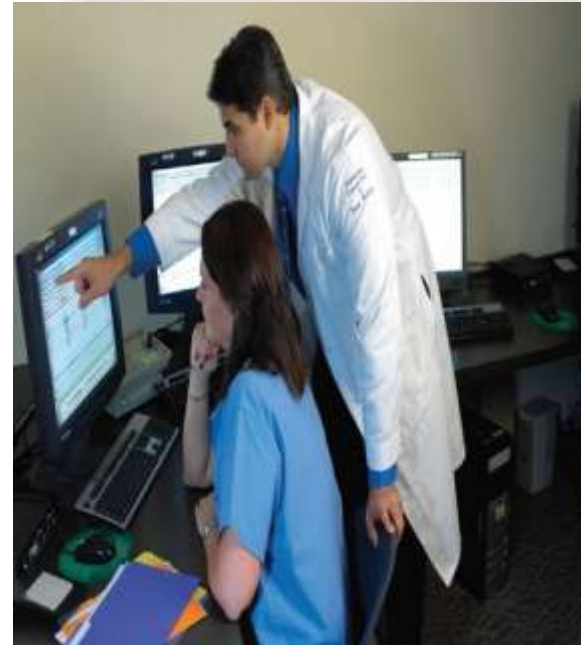
**Karl Doghramji, MD, FAASM, DFAPA**

Professor of Psychiatry, Neurology, and Medicine

Director, Jefferson Sleep Disorders Center

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# Jefferson Sleep Disorders Center





### Karl Doghramji MD

Jefferson University Physician  
Academic Title: Professor

- SPECIALTIES
- Sleep Medicine



### Zhanna Fast MD

Jefferson University Physician  
Academic Title: Clinical Assistant Professor

- SPECIALTIES
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### Ritu G Grewal MD

- Jefferson University Physician
- Academic Title: Associate Professor



### Dimitri Markov MD

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- Sleep Medicine



- SPECIALTIES
- Pulmonology Sleep Medicine



### Saoirse L Owens CRNP



### Mary E Pollice CRNP

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OFFICE LOCATIONS



### Maurits S Boon MD

Jefferson University Physician  
Academic Title: Associate Professor

- OFFICE LOCATIONS

SPECIALTIES

Otolaryngology



### Colin Huntley MD

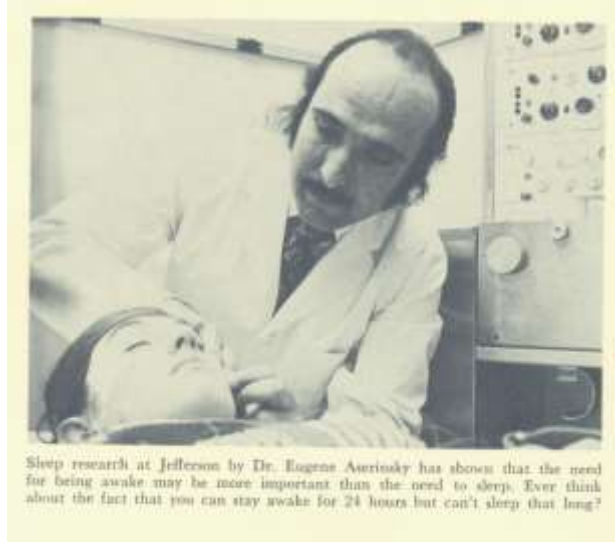
Jefferson University Physician  
Academic Title: Assistant Professor

- SPECIALTIES
- Otolaryngology



# Legacy in Sleep Science at Jefferson

Eugene Aserinsky, PhD, discovered REM sleep, Chair of Physiology 1954-



Sleep research at Jefferson by Dr. Eugene Aserinsky has shown that the need for being awake may be more important than the need to sleep. Ever think about the fact that you can stay awake for 24 hours but can't sleep that long?



Albert Biele, MD, Professor of Psychiatry 1947-1978. Seminal research on dreams



First sleep laboratory in Philadelphia in 1978: NIH Grant



# Sleep is essential to health



Sleep is essential to health: an American Academy of Sleep Medicine position statement



National Sleep Foundation sets the standard for sleep as a vital sign of health

The New York Times

The Sleep Debt Collector Is Here

THE WALL STREET JOURNAL

What a Good Night's Sleep Can Do for Your Heart



Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives, Protecting People™

“...Getting enough sleep is not a luxury—it is something people need for good health...”<sup>5</sup>

Age Group <sup>6</sup>		Recommended Hours of Sleep Per Day
Newborn	0-3 mo	14-17 hours (National Sleep Foundation) No recommendation (AASM)
Infant	4-12 mo	12-16 hours per 24 hours (including naps)
Toddler	1-2 yr	11-14 hours per 24 hours (including naps)
Preschool	3-5 yr	10-13 hours per 24 hours (including naps)
School Age	6-12 yr	9-12 hours per 24 hours
Teen	13-18 yr	8-10 hours per 24 hours
Adult	18-60 yr	≥7 hours per night
	61-64 yr	7-9 hours
	≥65 yr	7-8 hours

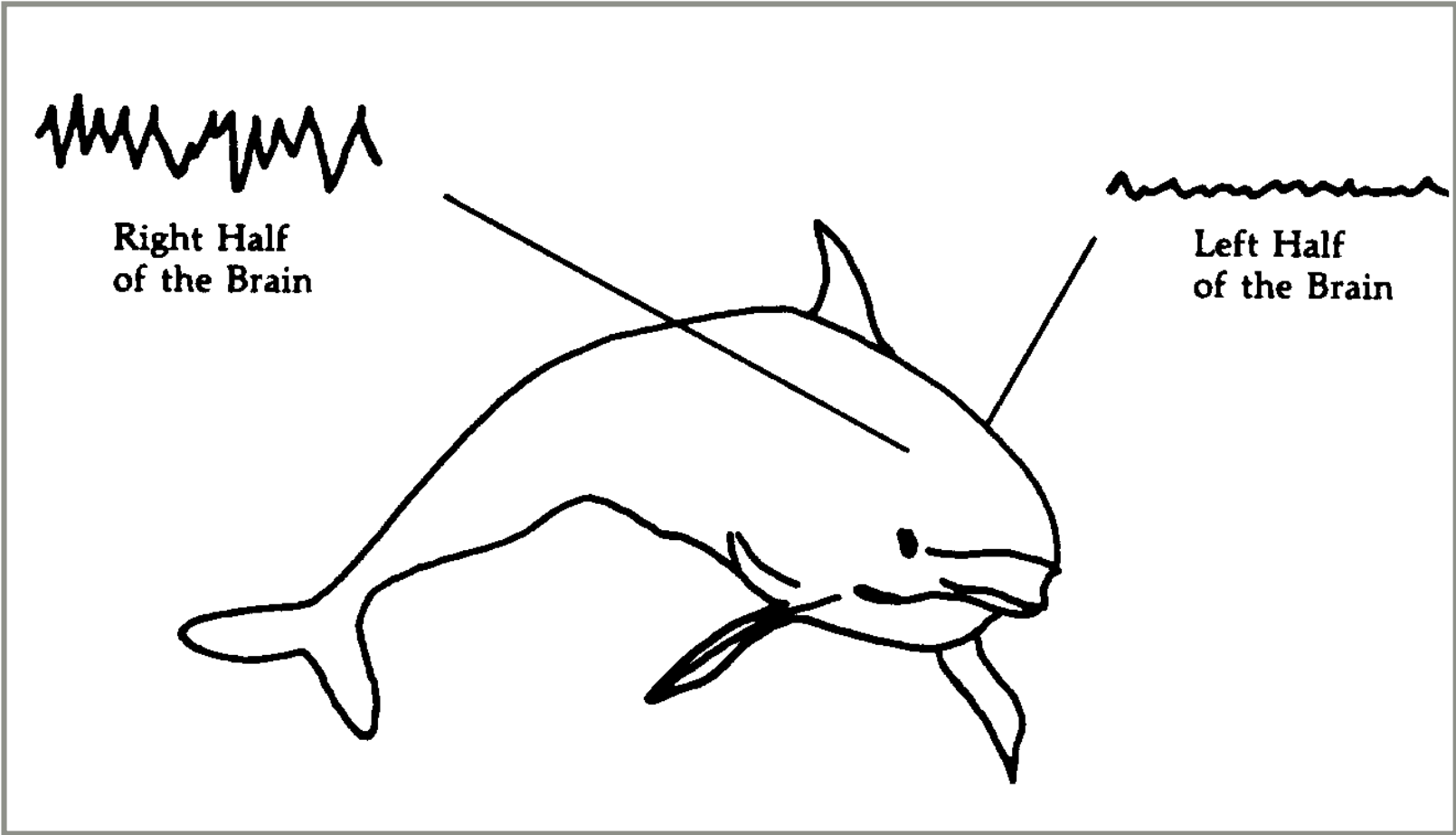
1. Ramar K, et al. *J Clin Sleep Med*. 2021;17(10):2115-2119. 2. Ojile J. *Sleep Health*. 2017; 3(4):226. doi: 10.1016/j.sleh.2017.05.009. 3. Whang, O. *The New York Times*. June 24, 2022. Accessed January 10, 2023. <https://www.nytimes.com/2022/06/24/health/sleep-debt-health.html>. 4. Morris B. *The Wall Street Journal*. July 17, 2022. Accessed January 6, 2022. <https://www.wsj.com/articles/what-a-good-nights-sleep-can-do-for-your-heart-11658066400>. 5. Centers for Disease Control and Prevention. 2022. Accessed January 6, 2023. [www.cdc.gov/sleep/about\\_sleep/how\\_much\\_sleep.html](https://www.cdc.gov/sleep/about_sleep/how_much_sleep.html). 6. Centers for Disease Control and Prevention. 2022. Accessed January 6, 2023. <https://www.cdc.gov/sleep/index.html>



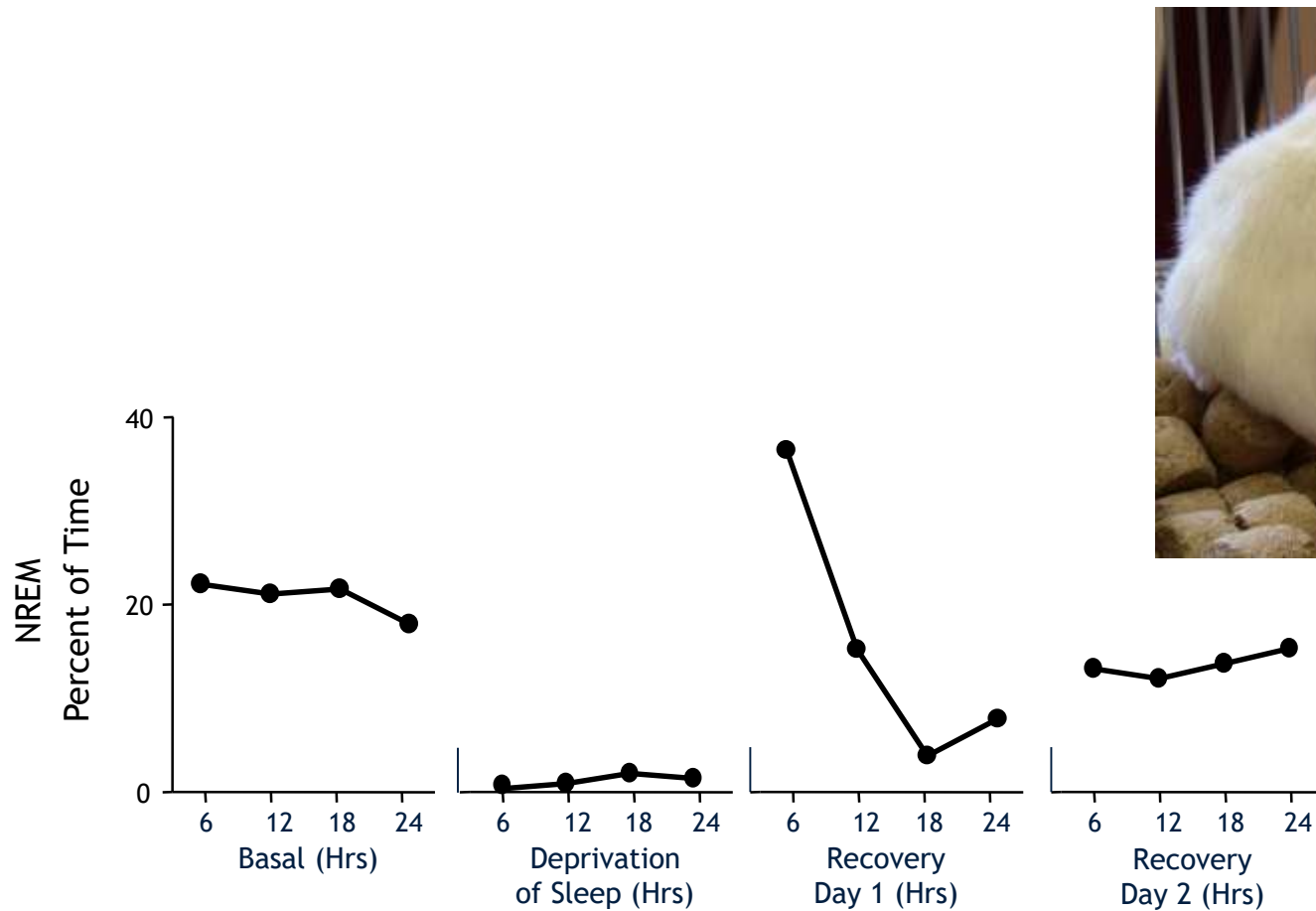




# Unihemispheric Sleep in the Dolphin



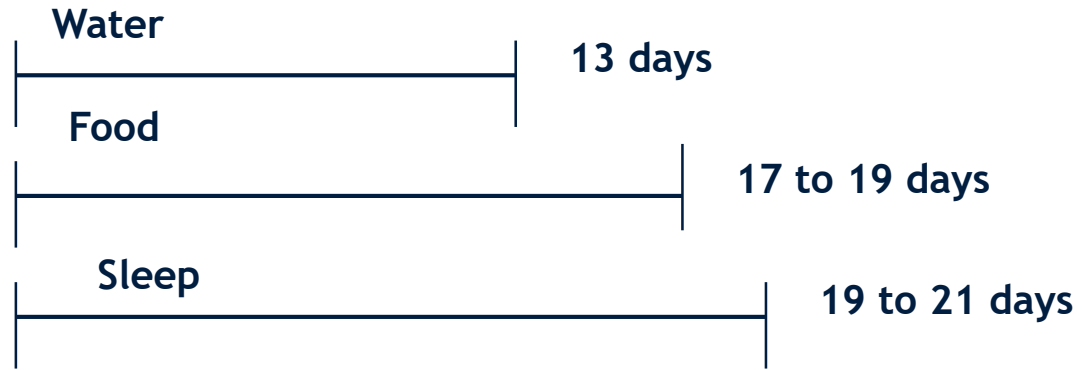
# Sleep Homeostasis: Highly Regulated



Rebound sleep stages after sleep deprivation

# Survival During Deprivation of Basic Needs

## Rat



## Human



# Sleep is Critical for Survival

Puppies



Dogs (adult)



Rabbits



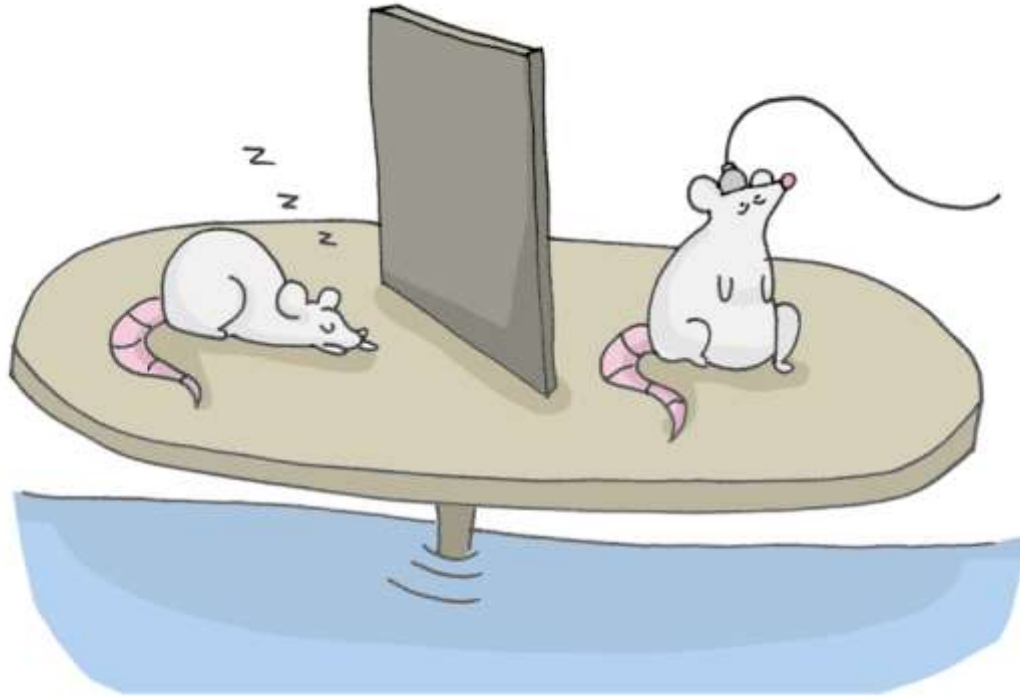
Rats



Human



# Sleep is Critical for Survival



- Hypoxemia
- Malnutrition
- Starvation
- Dehydration

# Cognitive Impact of Sleep Curtailment in Humans

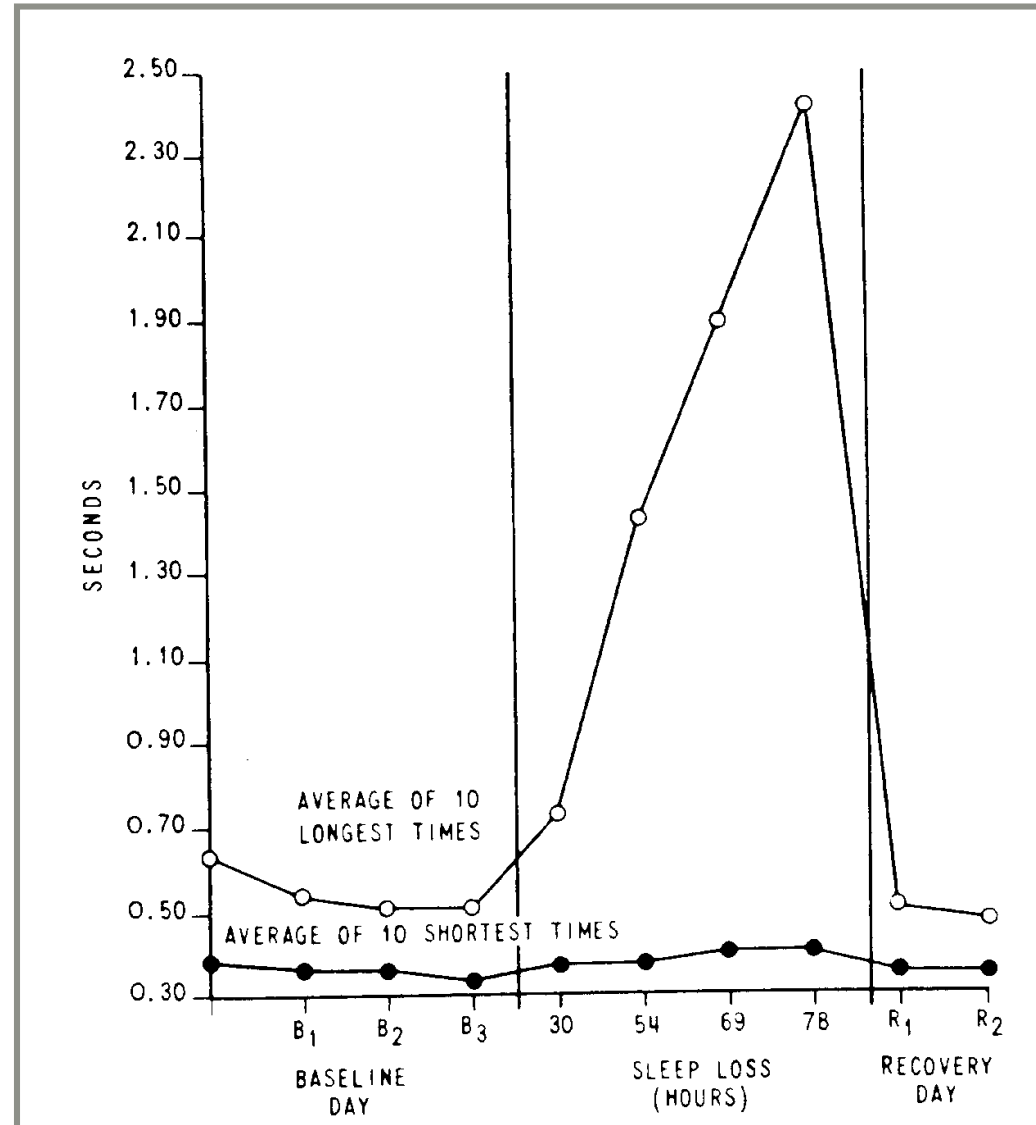
- Slower response time
- Errors of omission and commission
- Decline in memory
- Reduced learning
- Diminished concentration
- Lapses in attention due to microsleeps
- Diminished insight into subtle meanings
- Diminished subjective awareness

Dinges D. Clin Psychiatry News. 2002;5:5

Wagner U, Gais S, Haider H, et al. Nature 427, 352 – 355, 2004

# Slower Response Time

Changes in reaction time with sleep loss





# Physician Errors in Detection of Cardiac Arrhythmias

Medical Interns	Non-Sleep Deprived	Sleep Deprived
Sleep Amount in Prior 32 h	7.0 h (5.5 – 8.5 h)	1.8 h (0 – 3.8 h)*
Errors on ECG Sustained Attention Task	5.21 ± 0.93	9.64 ± 1.41*

\*p<.0001

Friedman et al., N Engl J Med 1971

# Trucking Accidents



# 200,000 Auto Accidents/Year Attributed to Excessive Sleepiness



# Accidents and Catastrophes



Challenger explosion, 1986



Three Mile Island Meltdown, 1979



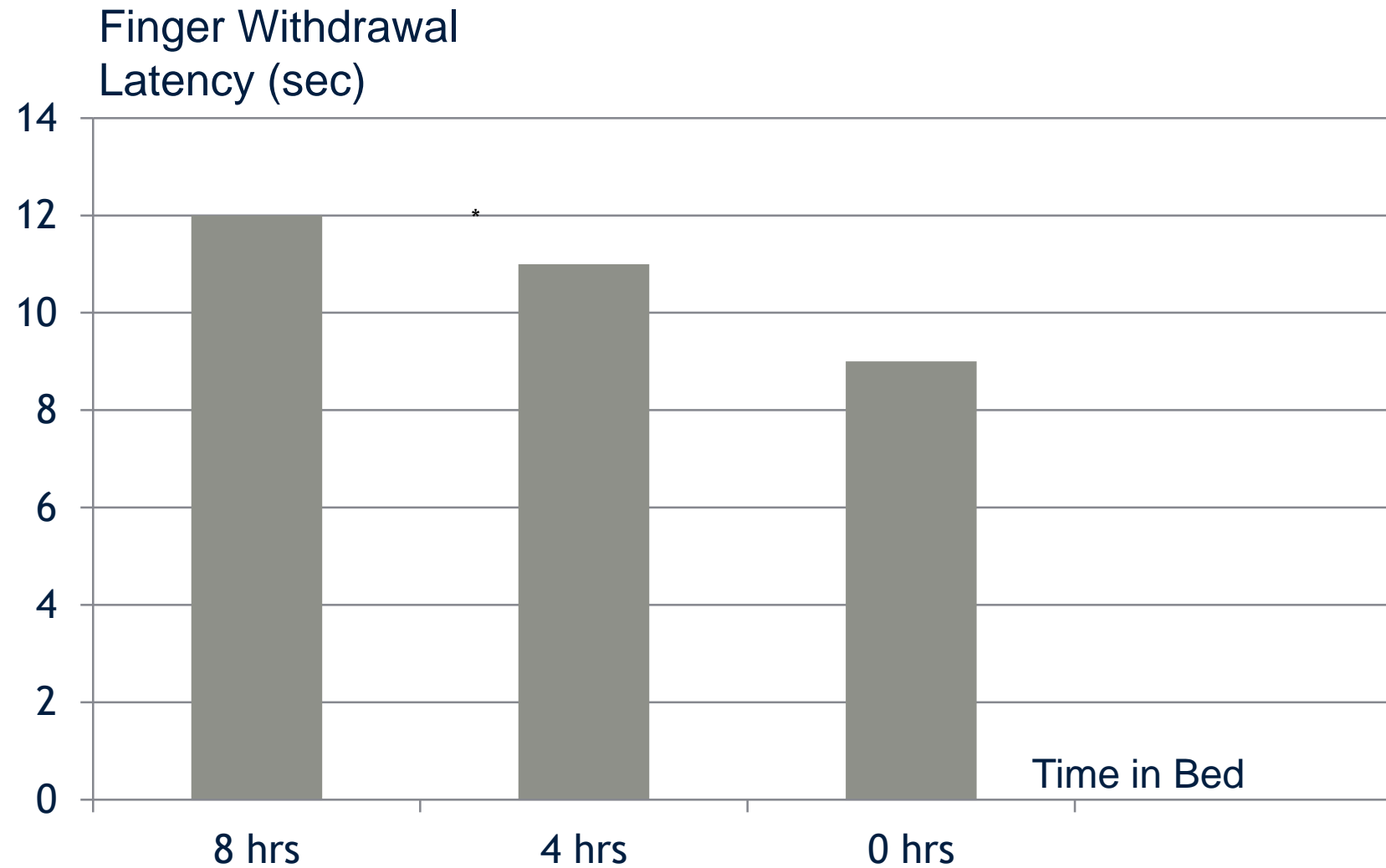
Air India, 2010

- Mellinger GD , et al. Arch Gen Psychiatry 1985 ; 42 (3): 225 – 232
- National Sleep Foundation, 2001 “Sleep in America Poll”

# Systemic Consequences of Sleep Curtailment in Humans

- Increased pain sensitivity
  - Major depression
  - Aggravate hypoxemia
  - Cardiovascular
    - Increase BP, CRP, pro-inflammatory cytokines
  - Metabolic
    - Increase hunger for high-calorie foods
    - Decrease adipose weight loss during dieting
    - Decrease glucose tolerance/increased insulin resistance
    - Decrease leptin, increase ghrelin
- Mullington JM et al. *Prog Cardiovasc Dis.* 2009;51:294-302; Nedletcheva AV et al. *Ann Int Med.* 2010;153:435-441; Leproult R, Van Cauter E. *Endocr Dev.* 2010;17:11-21; Banks S et al. *J Clin Sleep Med.* 2007;3:519-528

# Sleep Loss is Hyperalgesic



Roehrs T, et al. SLEEP 2006;29(2): 145-151

# Sleep Extension Reduced Pain Sensitivity

- 18 sleepy yet healthy subjects
- 4 nights of extended bedtime (10 hr) or 4 nights of habitual bedtime (8 hr)
- During extended bedtimes
  - Subjects slept 1.8 hr more/night
  - Were less sleepy during the day
  - Had reduced pain sensitivity

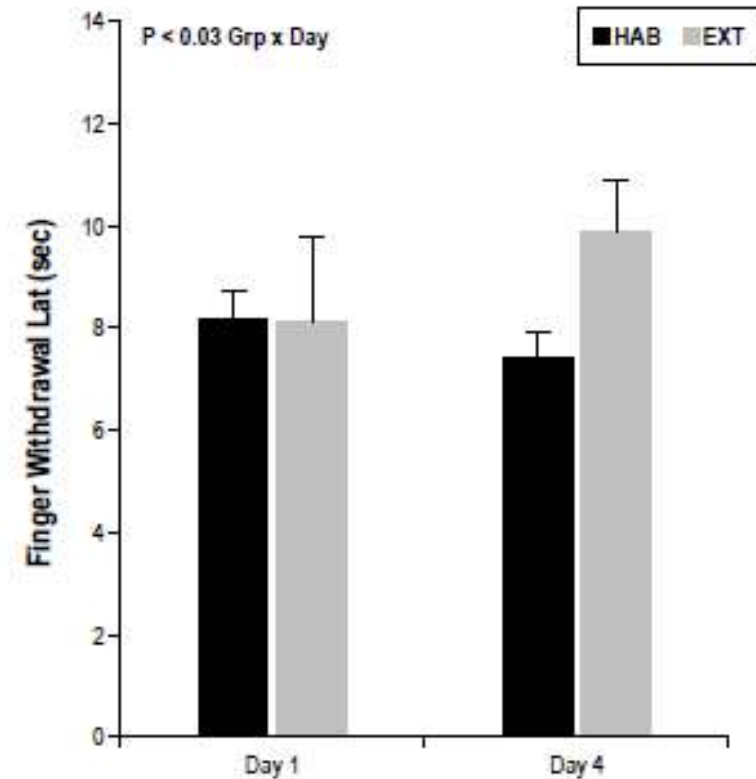
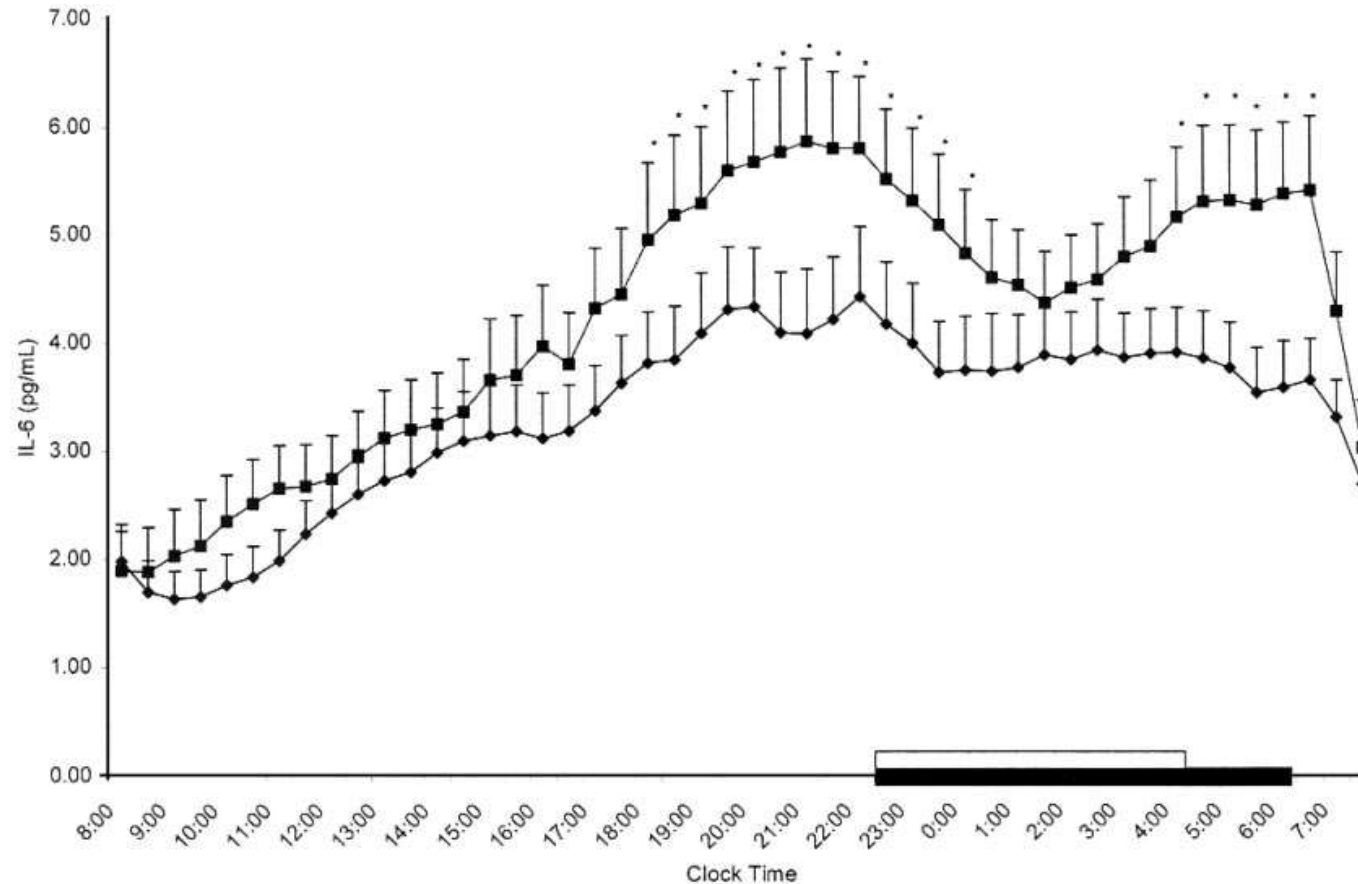


Figure 2—Average finger withdrawal latency to a radiant heat stimulus tested at 10:30 and 14:30 hr and conducted on experimental day 1 and 4 for the habitual (HAB) and sleep extension (EXT) groups. Finger withdrawal latency increased over the four days in the EXT, but not the HAB group.

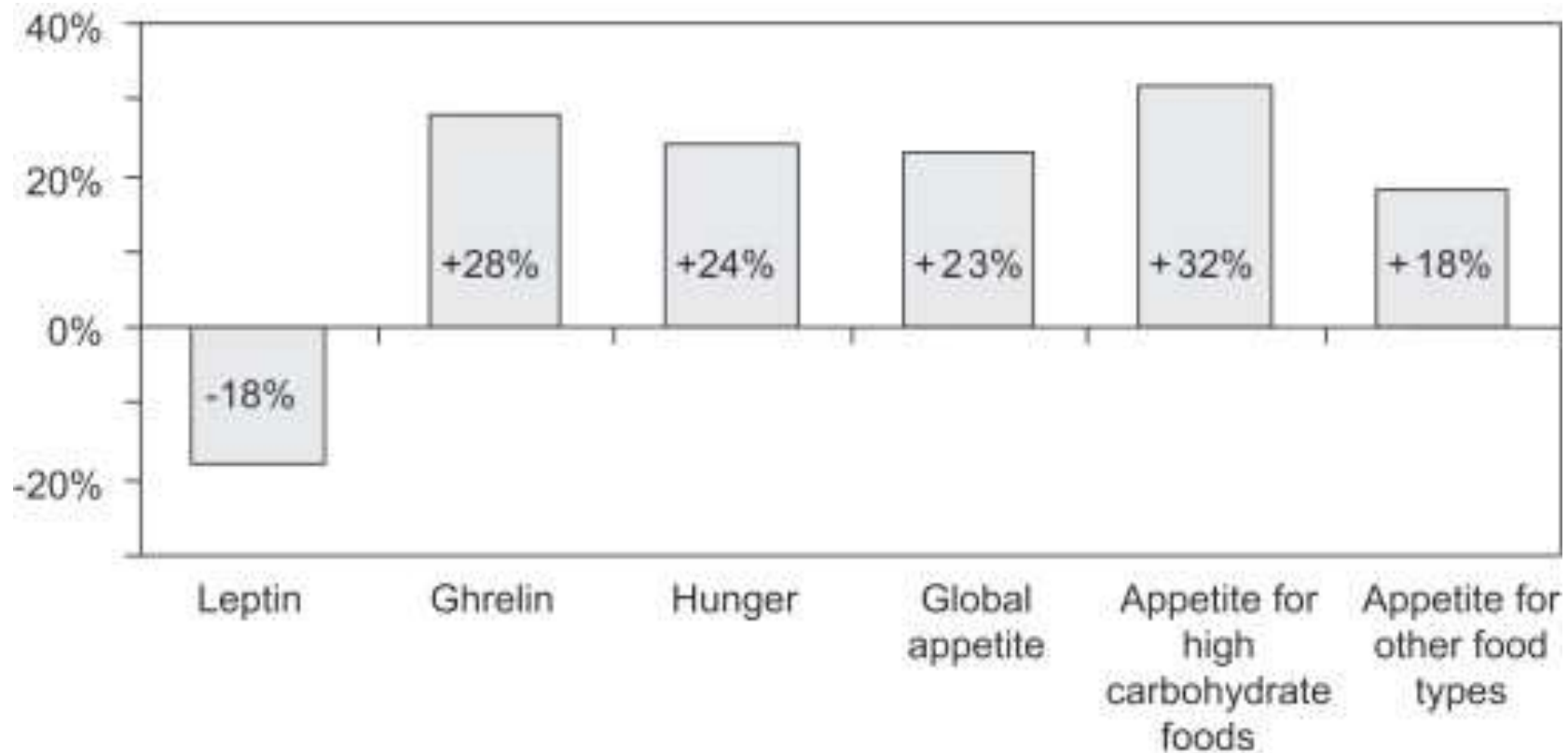
# Sleep Reduction From 8 to 6 Hours/Night for 1 Week Results in Increase in Secretion of Inflammatory Cytokines



IL-6 before (lower graph) and after (upper graph) partial sleep restriction. *Bar*: SE. *Thick black bar*: Sleep period at baseline; *open bar*: Sleep period during partial sleep restriction. \*,  $P < 0.05$ .

Vgontzas AL, et al. J Clin Endocrinol Metab 89: 2119–2126, 2004

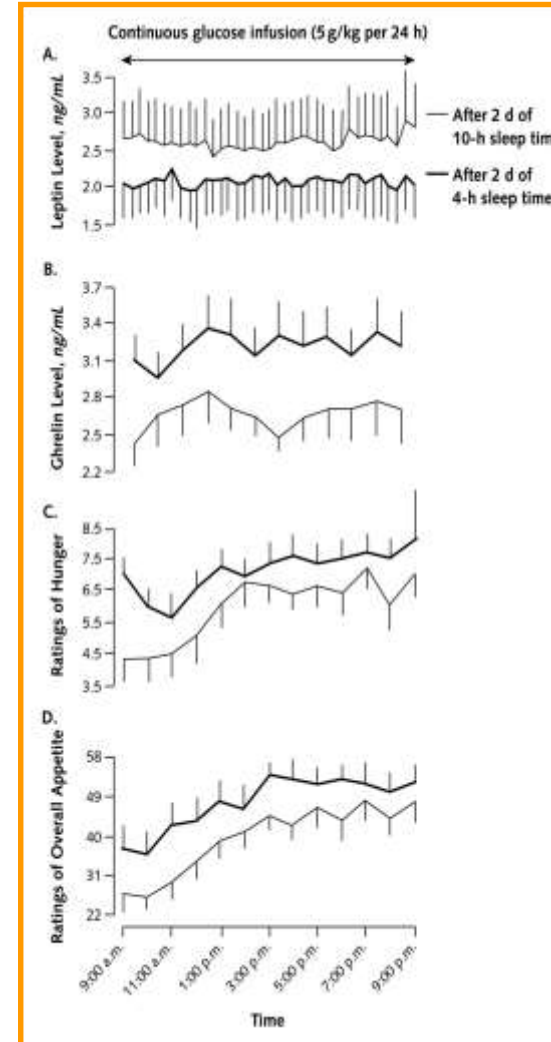
# Sleep and Metabolism



- Knutson KL, Spiegel K, Penev P, Van Cauter E. The metabolic consequences of sleep deprivation. *Sleep Med Rev.* 2007 Jun;11(3):163-78. Epub 2007 Apr 17. Review.

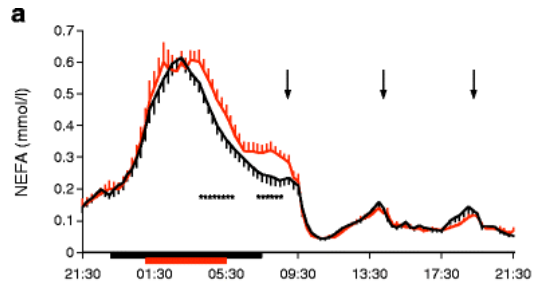
# Appetite

- PSD produces insulin resistance
  - 6 nights with 4 hours TIB
- PSD affects leptin and ghrelin
  - 2 nights 4 hours TIB ↓ leptin and ↑ ghrelin
  - Leads to ↑ hunger and appetite
- Reduced TIB (potential PSD) associated with ↑ BMI

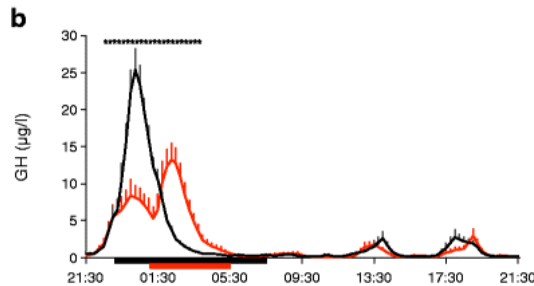


Modified from Spiegel et al., *Ann Internal Med*, 2004

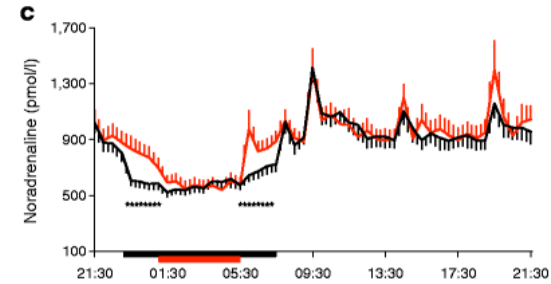
# Sleep Restriction Increases Free Fatty Acids in Healthy Men



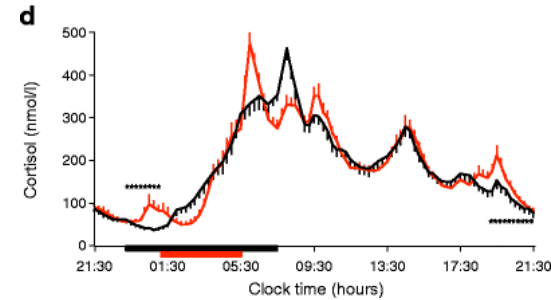
Free fatty acids



Growth Hormone



Noradrenaline



Cortisol

— Sleep restricted  
— Normal sleep

- Broussard JL, et al. Diabetologia. 2015;58(4):791-798.

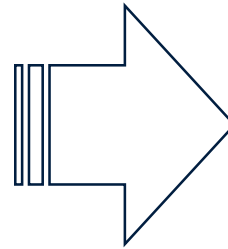
# Poor Sleep is Associated with Cardiovascular Conditions



American  
Heart  
Association.

## Life's essential 8<sup>1</sup>

In 2022, **added sleep** as an essential component of cardiovascular health



**HYPERLIPIDEMIA<sup>2,a</sup>**

**HYPERTENSION<sup>2,a</sup>**

**STROKE<sup>2,a</sup>**

**MYOCARDIAL  
INFARCTION<sup>2,a</sup>**

Habitual short sleep affects the ANS, endothelial function, inflammation, and coagulation<sup>3</sup>

<sup>a</sup>US-based EPIC study of patients with insomnia disorder based on the DSM-5. N = 3911.

ANS = autonomic nervous system.

1. Lloyd-Jones DM, et al. *Circulation*. 2022;146:e18–e43. doi: 10.1161/CIR.0000000000001078 2. Kalmbach DA, et al. *Sleep*. 2016;39(12):2101-2111. 3. Tobaldini E et al. *Nat Rev Cardiol*. 2019;16(4):213-224.

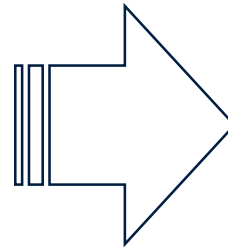
# Poor Sleep is Associated with Diabetes



## Standard of Care in Diabetes 2023<sup>1</sup>

Recommendation 5.55

**Screen for sleep health** in  
people with diabetes



**DIABETES MELLITUS<sup>2,a</sup>**

Habitual short sleep affects insulin secretion, leptin and ghrelin balance, and energy expenditure<sup>3</sup>

<sup>a</sup>US-based EPIC study of patients with insomnia disorder based on the DSM-5. N = 3911.

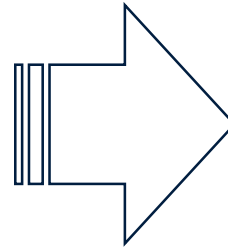
1. ElSayed NA, et al. *Diabetes Care*. 2023;46(Suppl. 1):S68-S96. 2. Kalmbach DA, et al. *Sleep*. 2016;39(12):2101-2111. 3. Tobaldini E et al. *Nat Rev Cardiol*. 2019;16(4):213-224.

# Poor Sleep is Associated with Depression

**Sleep** is part of **depression classification** and **assessments**<sup>1-4</sup>



PHQ-9  
HAM-D



**DEPRESSION**<sup>5,a</sup>

VA/DoD Clinical Practice Guideline for the management of major depressive disorder

Beck Depression Inventory

Insomnia is a common residual symptom of remitted depression, suggesting that insomnia and depression may be linked, but separate conditions<sup>6</sup>

DoD = US Department of Defense. DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> ed. HAM-D = Hamilton Depression Rating Scale. PHQ-9 = Patient Health Questionnaire, 9. VA = US Department of Veterans Affairs <sup>a</sup>US-based EPIC study of patients with insomnia disorder based on the DSM-5. N = 3911.

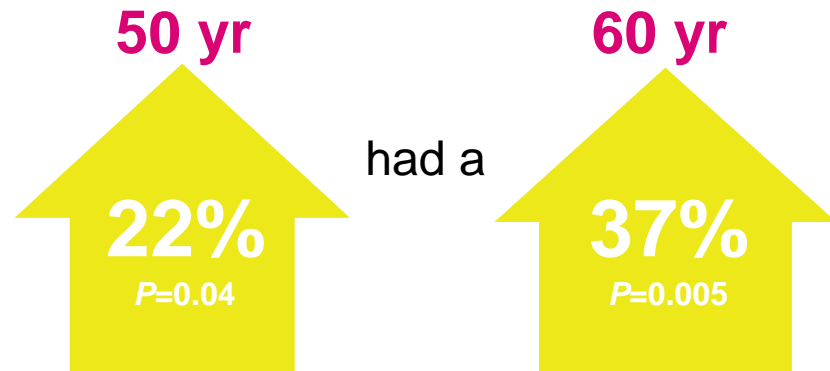
1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC: American Psychiatric Association; 2013. 2. VA/DoD Clinical Practice Guideline. *The Management of Major Depressive Disorder*, Ver 4. 2022. 3. American Psychological Association. 2019. Accessed January 10, 2023. <https://www.apa.org/depression-guideline/assessment>. 4. Beck AT, et al. *Arch Gen Psychiatry*. 1961;4:561-571.

5. Kalmbach DA, et al. *Sleep*. 2016;39(12):2101-2111. 6. Nierenberg AA, et al. *Psychol Med*. 2010;40(1):41-50.

# Short Sleep Later in Life Increases the Risk for Dementia

British civil servant cohort followed for 30 years (N=7959)

Patients with a sleep duration of  $\leq 6$  hrs at ages



**increased risk of dementia**

Independent of sociodemographic, behavioral, and cardiometabolic factors vs 7 hr sleepers

Patients with **persistent short sleep** ( $\leq 6$  hr) between ages 50 and 70 yr had a



**increased risk of dementia**

Independent of sociodemographic, behavioral, and cardiometabolic factors vs 7 hr sleepers

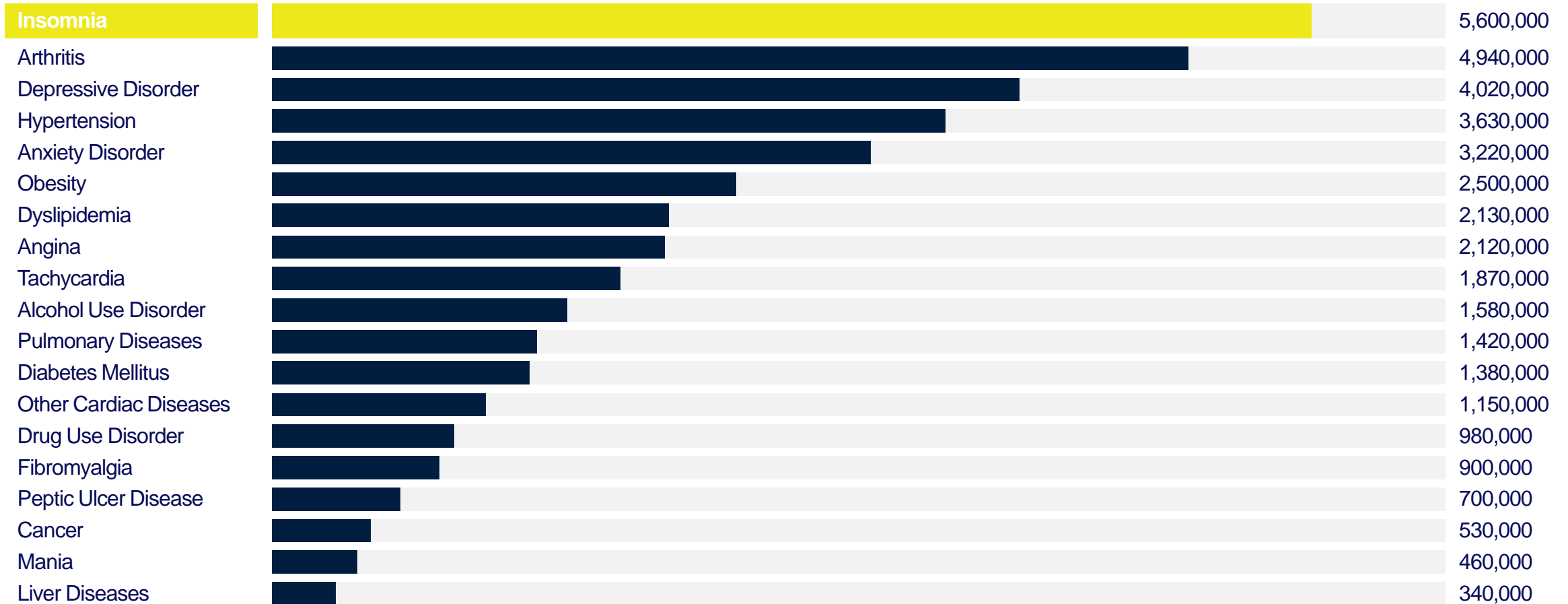
Whitehall II study of British civil servants aged 35-55 years in 1985-1988. 521 patients developed dementia. Sleep duration was assessed using a questionnaire. Hazard ratios were estimated from an adjusted cox regression model. N=7959. Sabia S et al. *Nature Commun.* 2021;12(1):2289.

# Sleep, Cognitive impairment, and Alzheimer's disease: A Systematic Review and Meta-Analysis

- 69,216 participants, 27 observational studies
- Results: Individuals with sleep problems had a 1.68 times higher risk for the combined outcome of cognitive impairment and/or AD








# The Burden of Insomnia

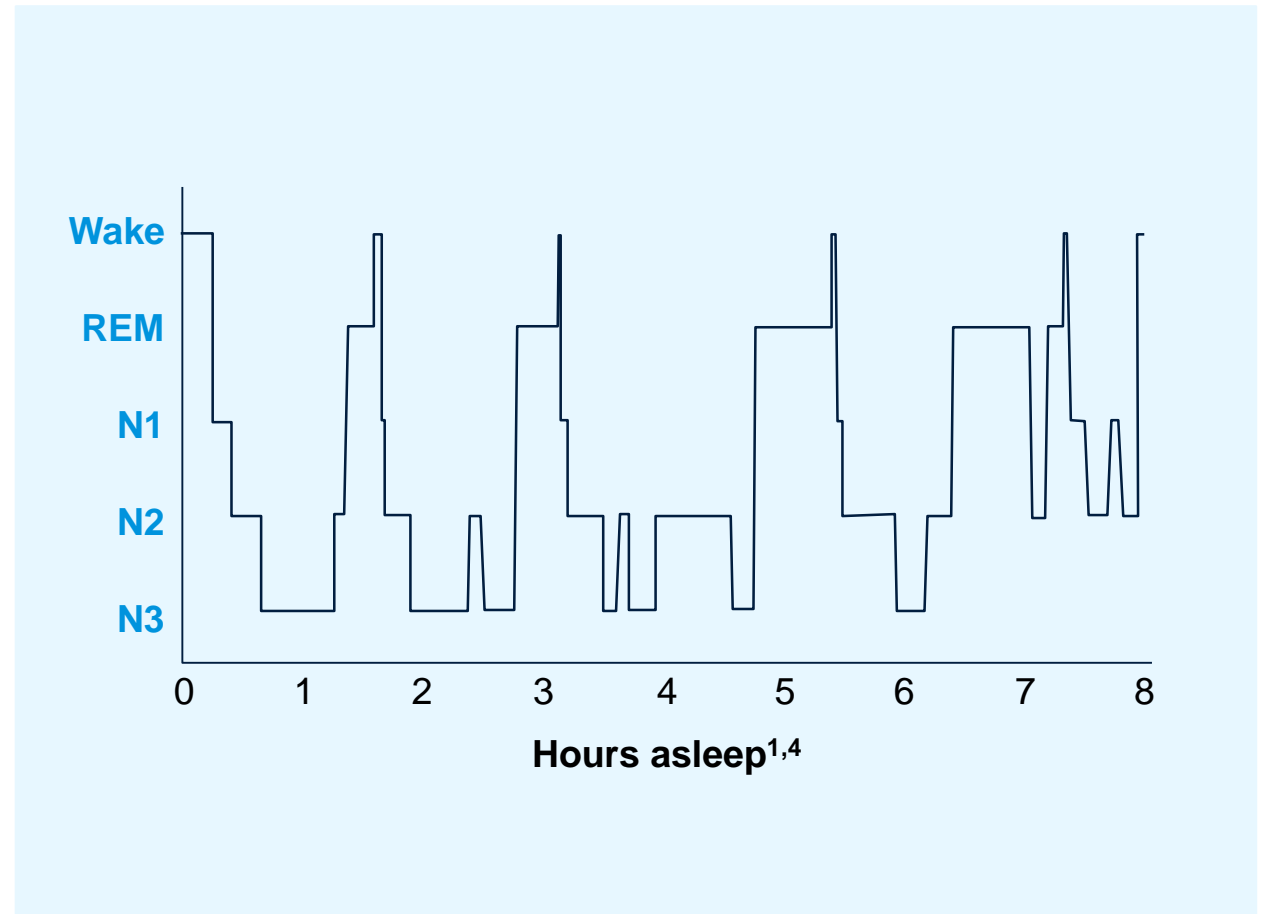
Estimated Quality-adjusted Life Years (QALY) Loss for the US Population



NESARC-III study; N=34,712; insomnia defined as patient-reported problems falling or staying asleep in the last 12 months. Estimated population QALY loss was adjusted for age, sex, and race/ethnicity. GI = gastrointestinal; NESARC-III = National Epidemiologic Survey on Alcohol and Related Conditions-III. Olfson M, et al. *J Clin Psychiatry*. 2018;79(5):17m12020.

# Sleep is an Active Process<sup>1-4</sup>

Stage	EEG Pattern
Wake <sup>2</sup>	Beta waves 
	Alpha waves 
N1 <sup>2</sup>	Theta waves 
N2 <sup>1,2</sup>	Sleep spindle 
	K-complex 
N3 <sup>1,3</sup>	Delta waves 
REM <sup>1,4</sup>	Fast, random 



EEG = electroencephalogram; REM = rapid eye movement.

1. Kryger MH, et al, eds. *Principles and Practice of Sleep Medicine*. 6th ed. Elsevier; 2017. 2. Purves D, et al, eds. Cortical states. In: Purves D, et al, eds. *Neuroscience*. 6th ed: Sinauer Associates; 2018. 3. Iber C, et al. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*. American Academy of Sleep Medicine; 2007. 4. Colten HR, Altevogt BM, eds. Sleep physiology. In: Colten HR, Altevogt BM, eds. *Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem*. National Academies Press; 2006:33-54.

# Why Do We Need Sleep?



**Energy  
conservation<sup>1</sup>**



**Clearance of  
metabolic  
waste from the  
brain<sup>2</sup>**



**Macromolecule  
synthesis<sup>3</sup>**



**Modulation of  
inflammation<sup>4,5</sup>**



**Memory  
consolidation<sup>1</sup>**

1. Purves D, et al, eds. *Neuroscience*. 6th ed. Sunderland, MA: Sinauer Associates; 2017. 2. Xie L, et al. *Science*;342(6156):doi:10.1126/science.1241224. 3. Landolt HP, et al, eds. *Sleep-Wake Neurobiology and Pharmacology*. Cham, Switzerland: Springer, Cham; 2019. Barrett JE, ed. *Handbook of Experimental Pharmacology*; vol 253. 4. Marshall L, et al. *Int Rev Neurobiol*. 2002;52:93-131. 5. Irwin MR, et al. *Biol Psychiatry*. 2016;80(1):40-52.

# Why Do We Need Sleep?

Glymphatic clearance occurs during sleep<sup>1</sup>

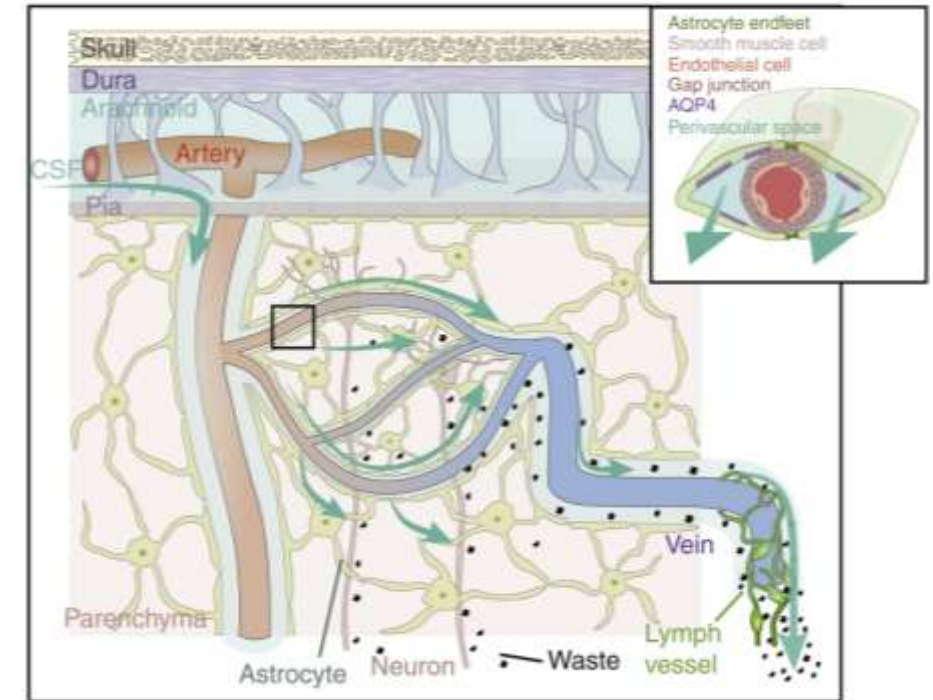
## Sleep Drives Metabolite Clearance from the Adult Brain

Lulu Xie,<sup>1\*</sup> Hongyi Kang,<sup>1\*</sup> Qiwu Xu,<sup>1</sup> Michael J. Chen,<sup>1</sup> Yonghong Liao,<sup>1</sup> Meenakshisundaram Thiyagarajan,<sup>1</sup> John O'Donnell,<sup>1</sup> Daniel J. Christensen,<sup>1</sup> Charles Nicholson,<sup>2</sup> Jeffrey J. Iliff,<sup>1</sup> Takahiro Takano,<sup>1</sup> Rashid Deane,<sup>1</sup> Maiken Nedergaard<sup>1†</sup>

The conservation of sleep across all animal species suggests that sleep serves a vital function. We here report that sleep has a critical function in ensuring metabolic homeostasis. Using real-time assessments of tetramethylammonium diffusion and two-photon imaging in live mice, we show that natural sleep or anesthesia are associated with a 60% increase in the interstitial space, resulting in a striking increase in convective exchange of cerebrospinal fluid with interstitial fluid. In turn, convective fluxes of interstitial fluid increased the rate of  $\beta$ -amyloid clearance during sleep. Thus, the restorative function of sleep may be a consequence of the enhanced removal of potentially neurotoxic waste products that accumulate in the awake central nervous system.

www.sciencemag.org **SCIENCE** VOL 342 18 OCTOBER 2013

## Brain glymphatic system<sup>2</sup>



1. Xie L, et al. *Science*;342(6156):doi:10.1126/science.1241224. 2. Hablitz LM, et al. *Curr Biol*. 2021;31(20):R1371-R1375.

# Selected Functions of REM Sleep

- Oculomotor activation for waking binocular activity (Berger)
- Brain rids itself of unwanted wake memory stores and organizing daytime experiences in memory (Crick & Mitcheson)
- Synthesis of unconscious psychological conflict (Freud)

# Sleep Disorders

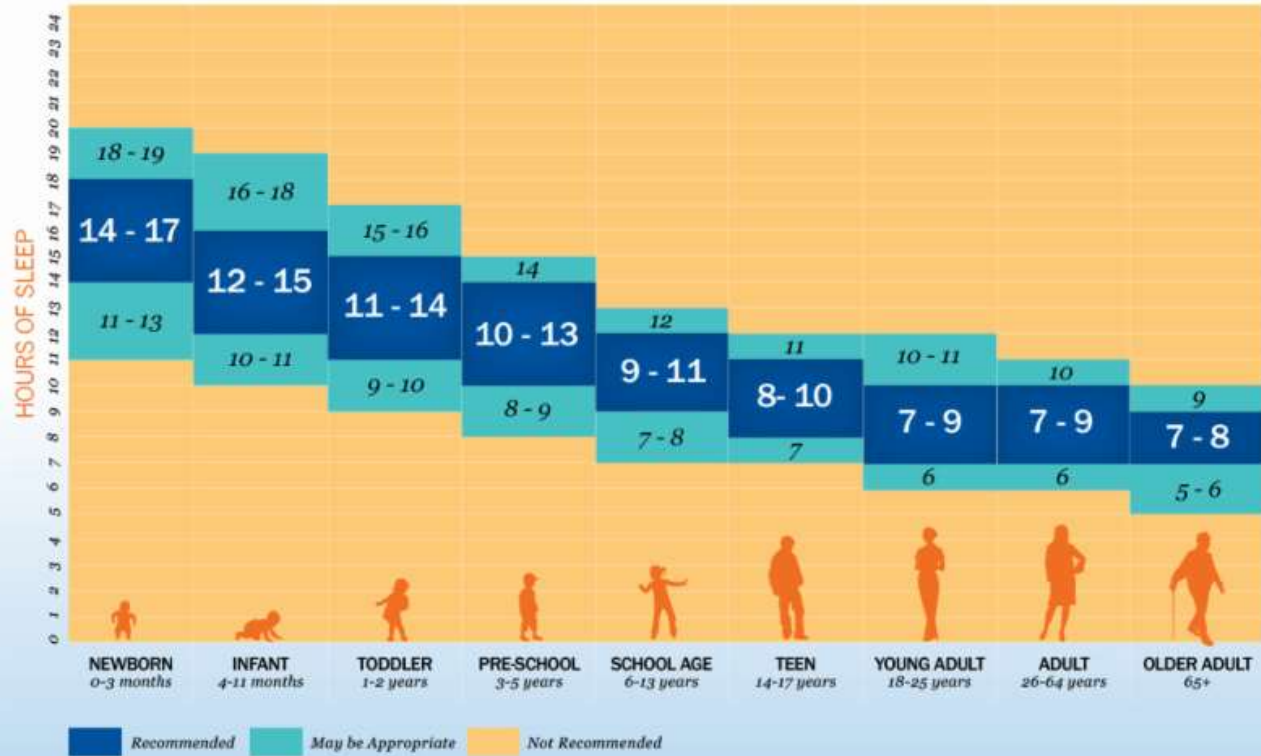
- Disorders
  - Sleep hygiene impairments (poor sleep practices)
  - Primary insomnia
  - Medical and psychiatric disorders
  - Primary sleep disorders: Emerge from sleep
    - Sleep apnea
    - Periodic limb movement disorder
  - Circadian misalignment: Trying to sleep when the body should be awake, trying to work when the body should be asleep
    - Shift work
    - Jet lag
- Sleep is disturbed by 2 basic mechanisms
  - Curtailed sleep quantity (sleep deprivation)
  - Impaired sleep quality (sleep fragmentation)

# The Dos of Sleep Hygiene

Do...

- Allow adequate time for sleep!
- Establish a daily activity routine
- Wake up at the same time every day
- Increase exposure to bright light during the day
- Decrease light exposure in the evening
- Exercise regularly in the morning and/or afternoon
- Set aside a worry time
- Do something relaxing prior to bedtime
- Try a warm bath

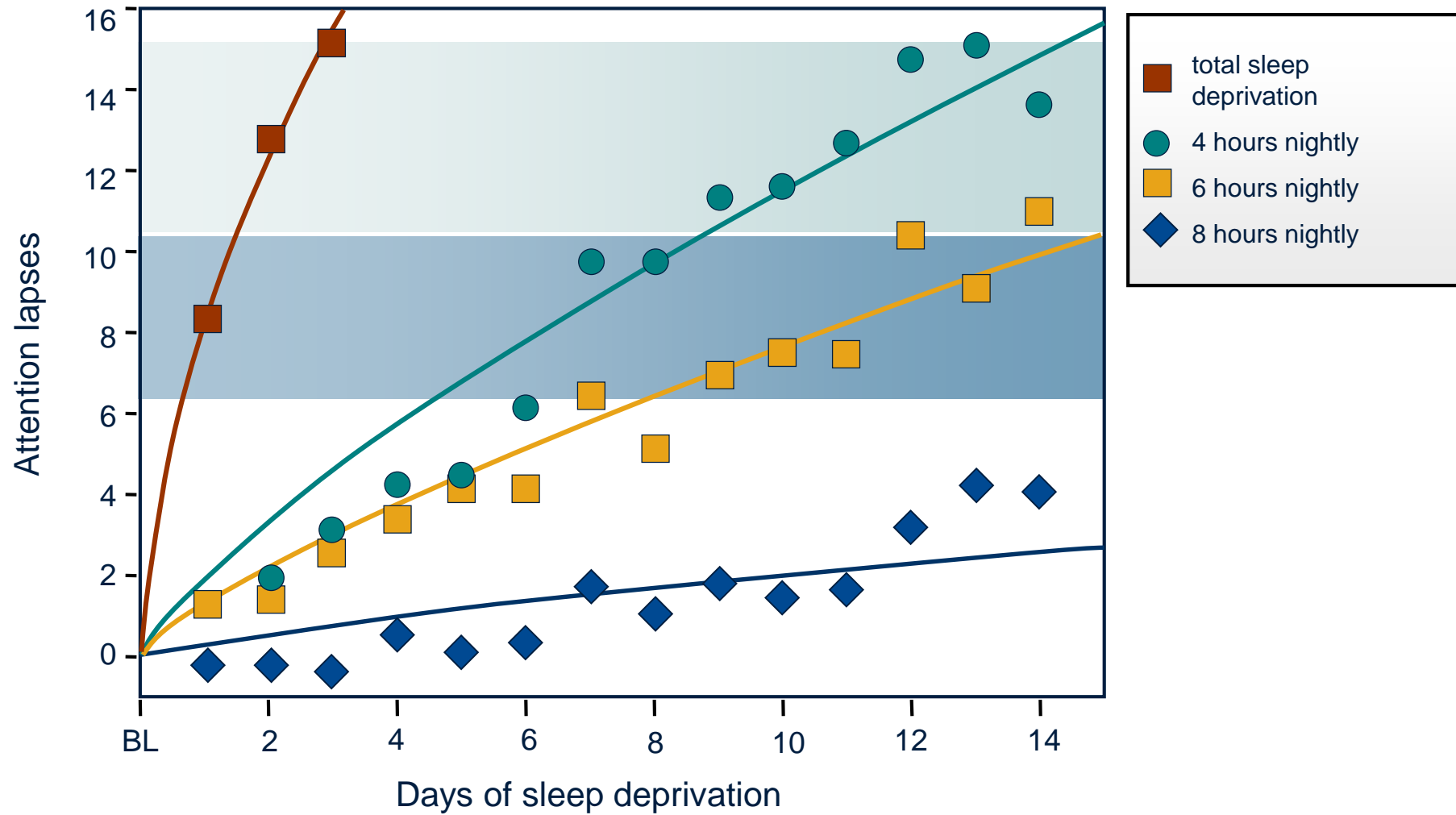
# SLEEP DURATION RECOMMENDATIONS



SLEEPFOUNDATION.ORG | SLEEP.ORG

Hirshkowitz M, The National Sleep Foundation's sleep time duration recommendations: methodology and results summary, Sleep Health (2015). <http://dx.doi.org/10.1016/j.sleh.2014.12.010>

# Acute and Chronic Sleep Deprivation



# Epworth Sleepiness Scale

Situation	Chance of dozing (0-3)			
Sitting and reading	0	1	2	3
Watching television	0	1	2	3
Sitting inactive in a public place—for example, a theater or meeting	0	1	2	3
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after lunch (when you've had no alcohol)	0	1	2	3
In a car, while stopped in traffic	0	1	2	3
0 = would never doze 1 = slight chance of dozing		2 = moderate chance of dozing 3 = high chance of dozing		<b>Total Score</b> <input type="text"/>

ESS total score  $\geq 10$  indicates possible excessive

# The Don'ts of Sleep Hygiene

## Avoid...

- Alcohol
- caffeine, nicotine, and other stimulants
- Heavy meals or drinking within 3 hours of bedtime
- Using your bed for things other than sleep (or sex)
- Watching the clock
- Staying in bed awake too long
- Napping, unless a shiftworker

# Conclusions

- Sleep is a vital function that is necessary proper health and well-being
- It affects social and occupational functioning and the status of many other body functions
- Sleep quality and quantity are affected by poor sleep practices, primary sleep disorders, and medical conditions
- Attention to proper sleep habits can address many sleep related complaints
- If symptoms persistent, underlying disorders can be identified and managed in medical settings



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