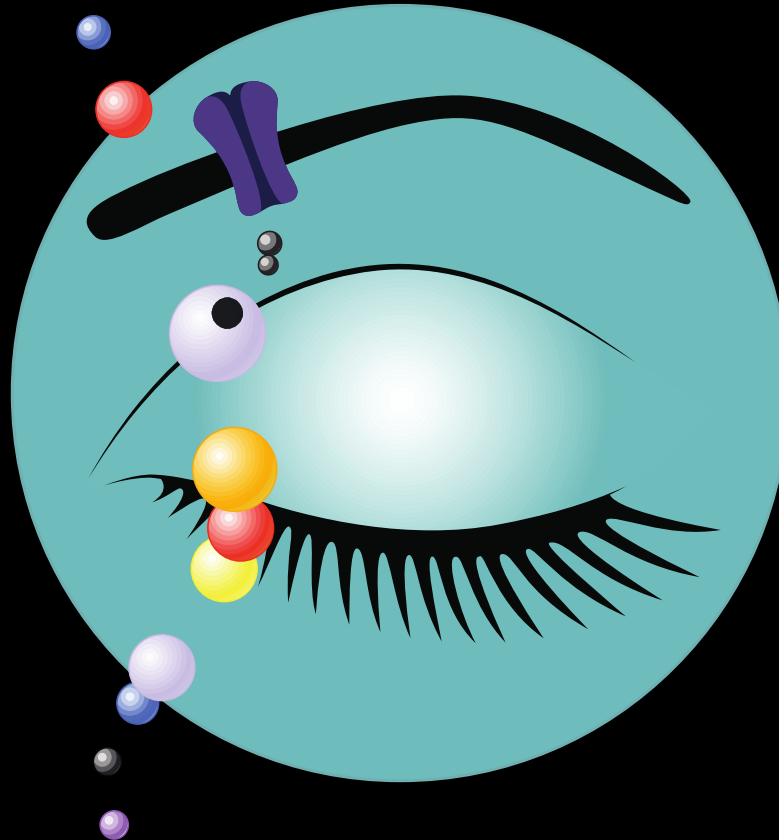


# Sleep Disruption and the Brain: Implications for Cognition and Brain Health



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# Human Performance Clinical Research Laboratory

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Boulder**

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Innovative Seed Grant Program**



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**USA Cycling**

# WHY SLEEP?



- sleep and circadian disruption are hallmarks of aging;
- associated with elevated risk for aging-related diseases (Type 2 diabetes, CVD, dementia and Alzheimer's Disease);
- the links between sleep and circadian physiology and system-wide disease processes remain incompletely understood.

HUMANS ARE DEFINED BY OUR  
CURIOSITY, OUR HUNGER FOR ANSWERS.

WE ALL SPEND A THIRD  
OF OUR LIVES LYING DOWN  
WITH OUR EYES CLOSED  
AND NOBODY KNOWS WHY.

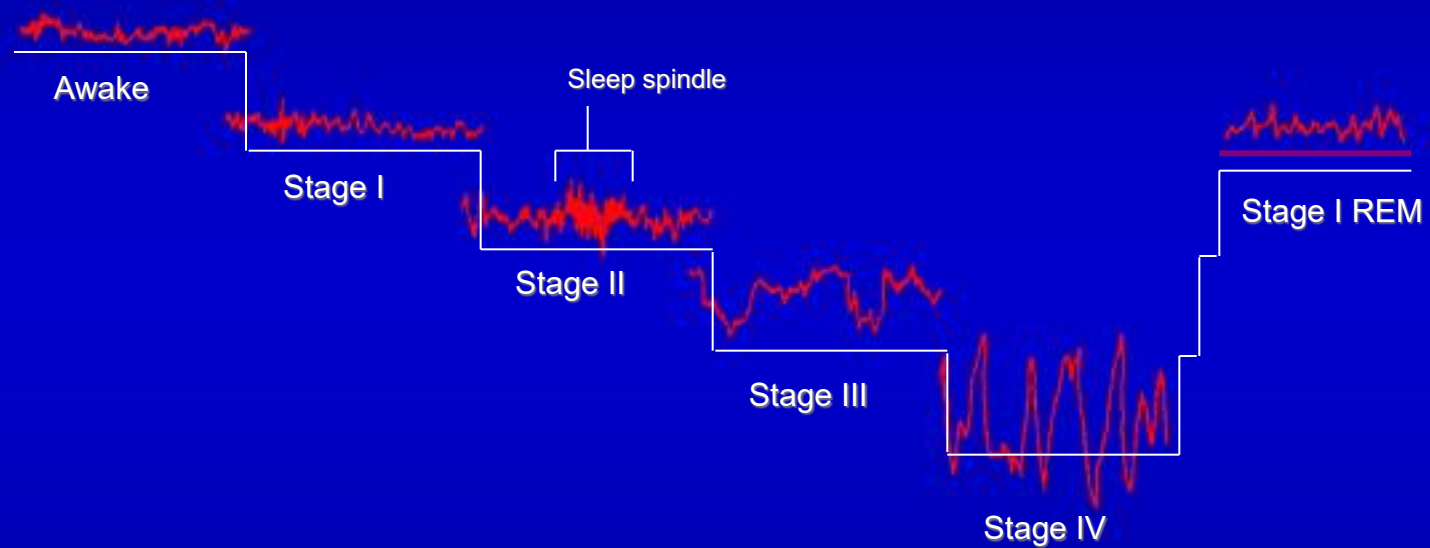
...TOUCHÉ.



<https://xkcd.com>

# SLEEP STAGES

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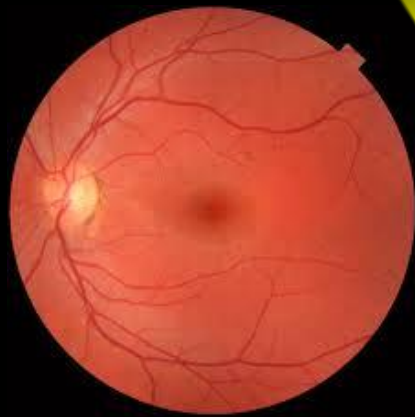
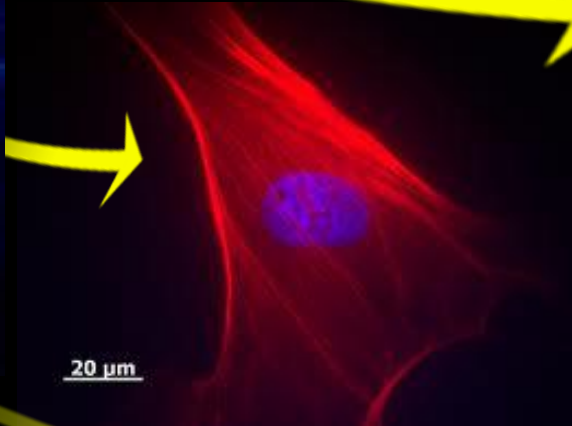
EEG: electroencephalogram

Measures electrical activity of large groups  
of cortical neurons across the scalp

Hobson, J. A. (1995)

# All animals sleep

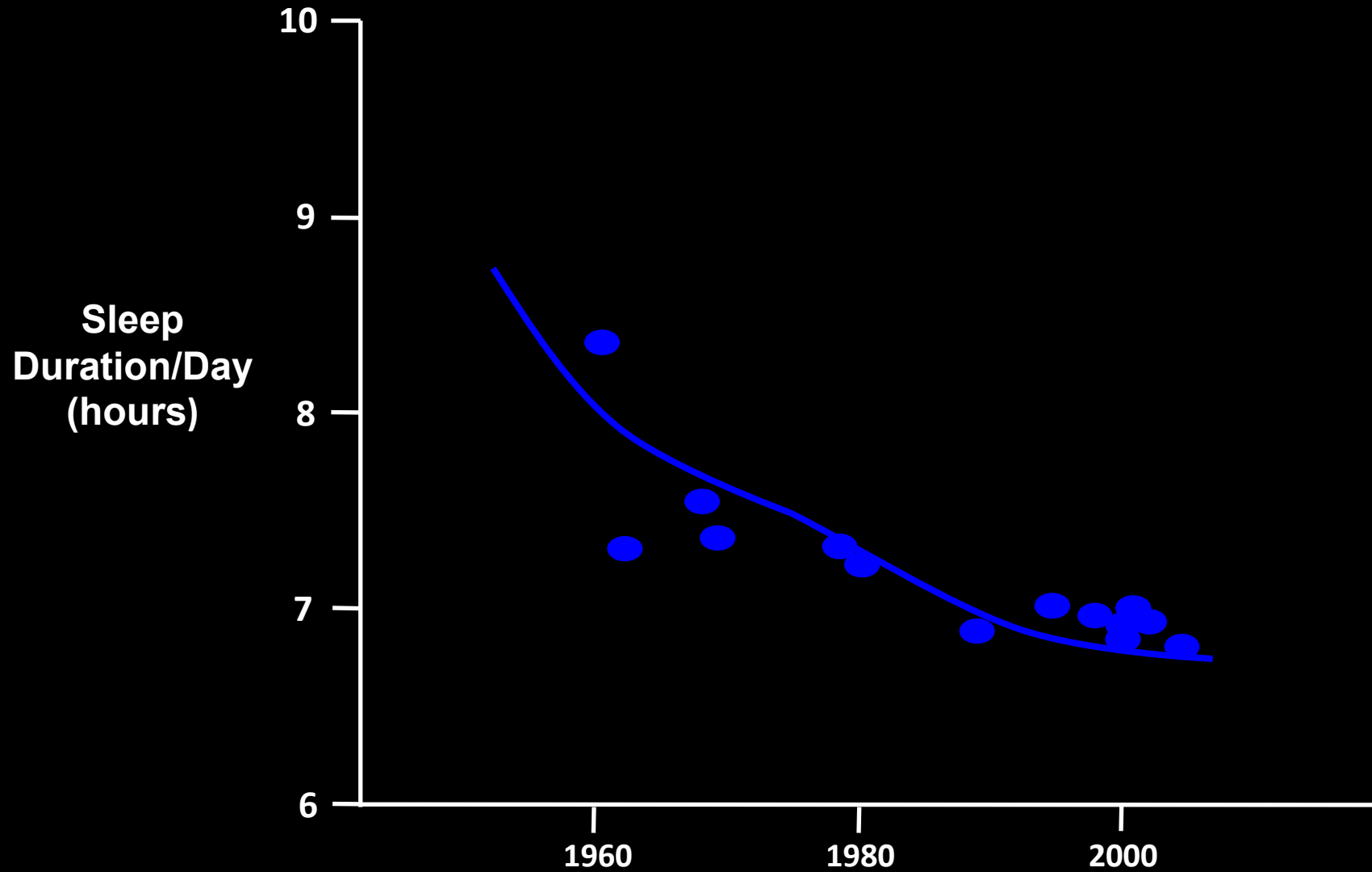








# Self-Reported Sleep Duration (in the US)



*Adapted from McAllister et al, Crit Rev in Food Nutr & Sci, 49: 868-913, 2009*



# What is the function of sleep?

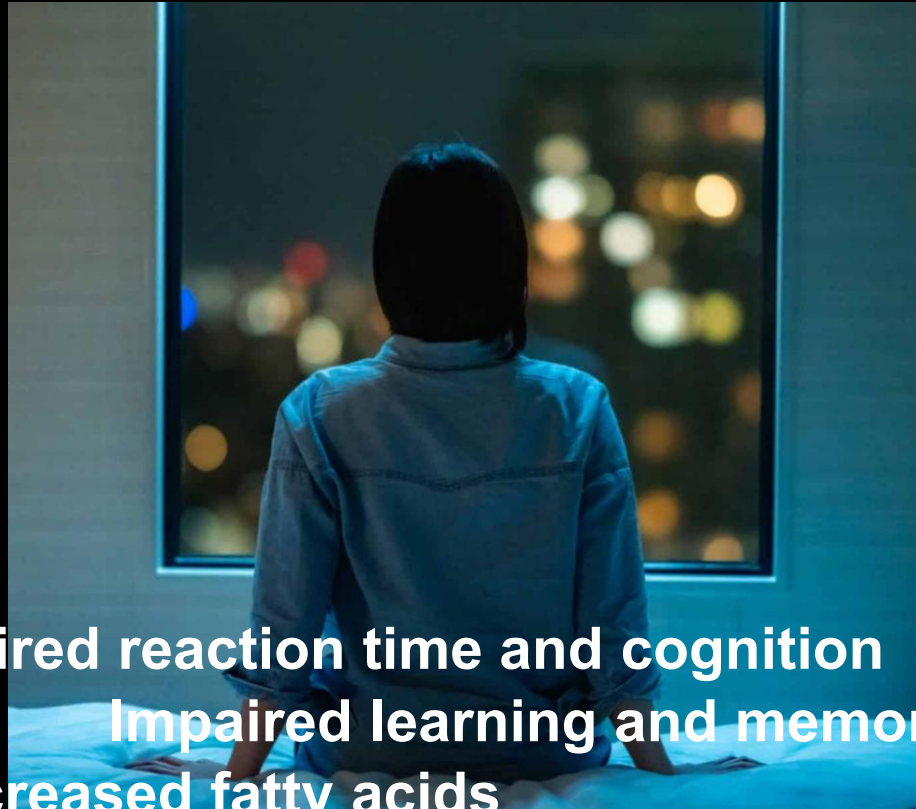
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- ~1/3 of human life is spent asleep.
- Total sleep deprivation is fatal.
- Function of sleep is *unknown*.



# Sleep and circadian disruption in humans, dogs and tissues

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**Impaired reaction time and cognition**  
**Impaired learning and memory**  
**Increased fatty acids**  
**Impaired glucose metabolism**  
**Altered hunger hormones**  
**Increased BP**



**Metabolism  
comparable  
to chronic  
high fat diet**



**Impaired adipose  
insulin signaling**

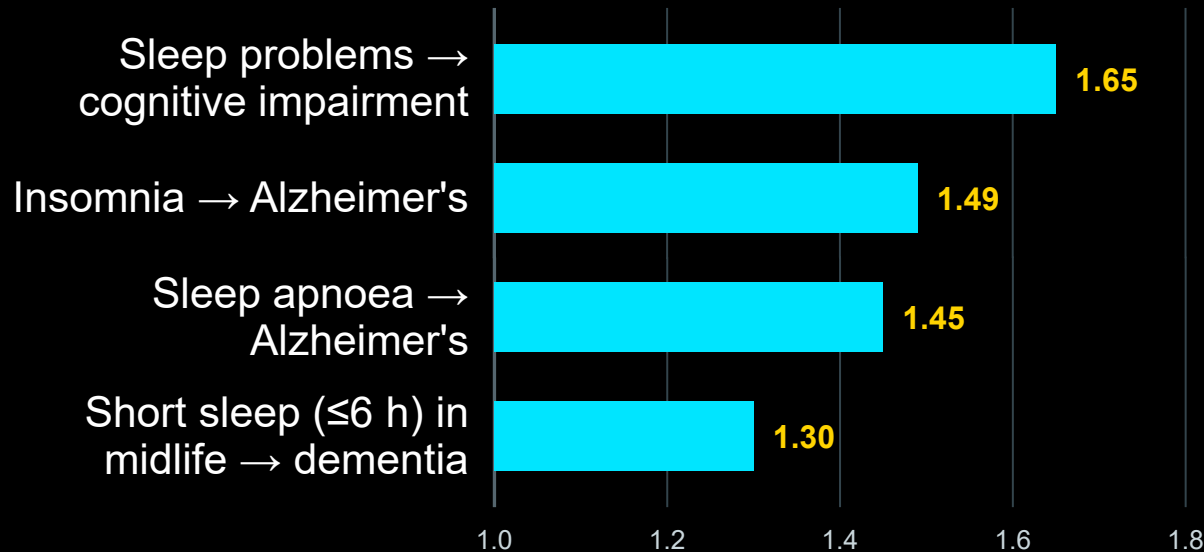
*Brouwer...Broussard, Diabetologia, 2020.*

*Broussard et al. Diabetologia. 2015 Apr;58(4):791-8.*

*Broussard et al, Ann Intern Med. 2012;157(8):549-557.*

# Sleep and circadian disruption and neurodegenerative disease

## Pooled relative risk of dementia vs. good sleepers

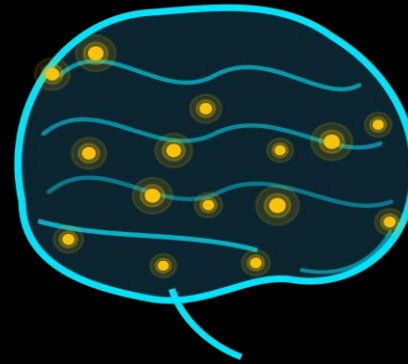


Persistent short sleep at ages 50, 60 and 70 carried a 30% higher dementia risk over 25 years of follow-up

Fragmented rest–activity rhythms predict incident dementia and faster brain atrophy in older adults

Night and shift work are linked to poorer late-life brain health

**Sleep disruption is one of the few modifiable dementia risk factors**



**~15%**

of Alzheimer's disease in the population may be attributable to sleep problems

### Bidirectional

Sleep changes emerge years before diagnosis, then worsen as pathology spreads

### Treatment may matter

Sleep apnea patients treated with CPAP had dementia risk similar to matched peers

*Sabia et al. Nat Commun. 2021;12:2289.*

*Bubu et al. Sleep. 2017;40(1):zsw032.*

*Shi et al. Sleep Med Rev. 2018;40:4-16.*

*Sleep disorders and dementia meta-analysis. GeroScience. 2025.*

# Study Aim

- Determine the impact of sleep and circadian disruption across a variety of physiological systems in otherwise healthy young adults.

# Inclusion criteria

- 18-35 years old
- BMI 18.5-25.5 kg/m<sup>2</sup>
- Habitually sleep 7-9h/night
- No clinically significant unstable medical or surgical conditions within the last year
- No evidence of clinically significant sleep disorders (as assessed by the Sleep Disorder Questionnaire)
- Non-smokers; medication and drug free
- No travel outside of MST in past 3 weeks
- Must have lived at Denver/Fort Collins altitude for >3 months
- Weight stable (<5 lb change in past 6 months)

# Exclusion criteria

- Any medication except oral contraceptives (non-hormonal IUDs allowed)
- Excessive caffeine use (>400 mg per day)
- Excessive alcohol (males > 14 drinks/week; females > 7 drinks/week)
- Irregular menses (for female participants)

# ***Subject Demographics***

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n=18 healthy, lean, sedentary men and women

Pre-study conditions

- 9h sleep schedule 1 week prior to study

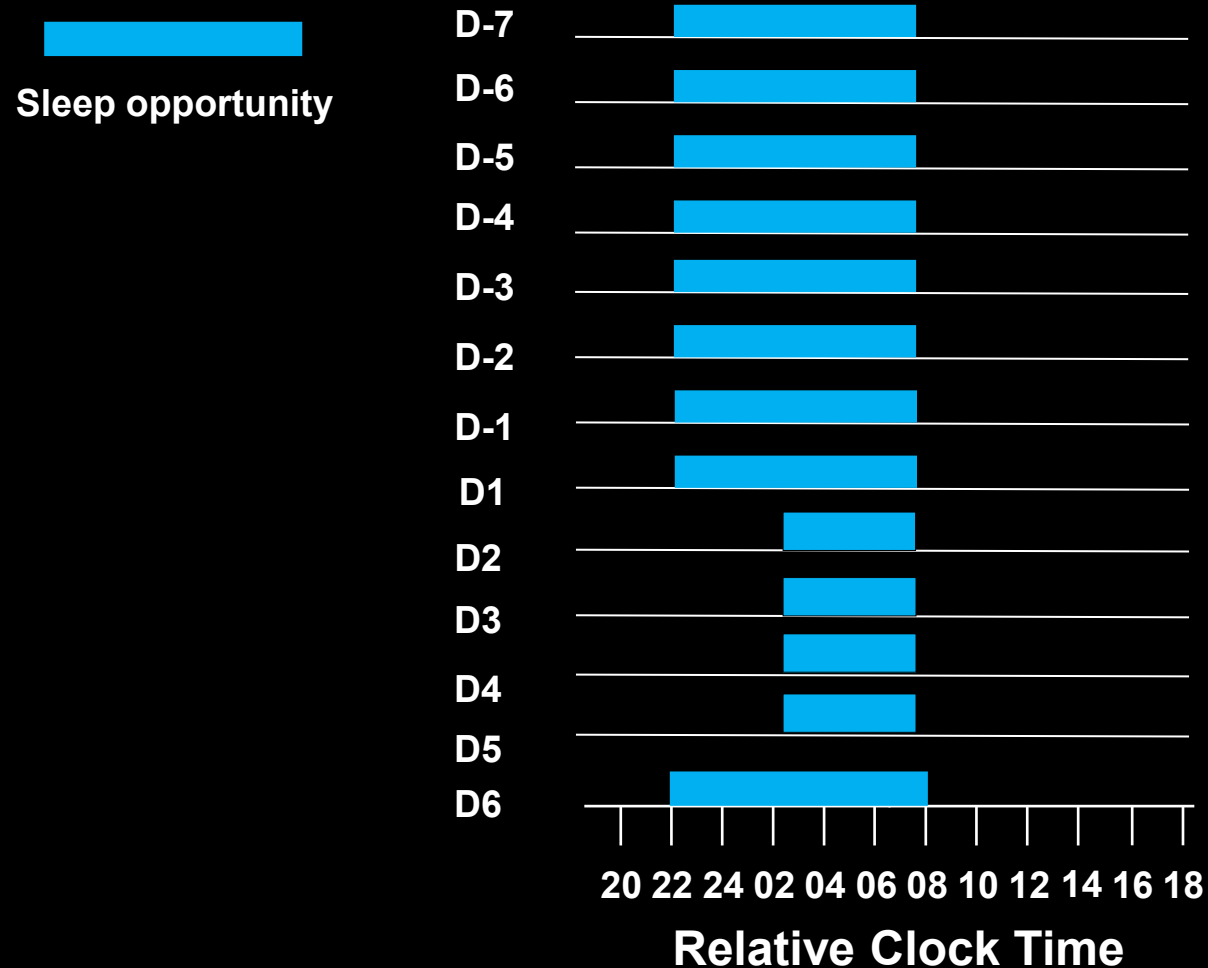
  - Based on habitual sleep schedule

- Energy balanced diet 3 days prior to study (no exercise)

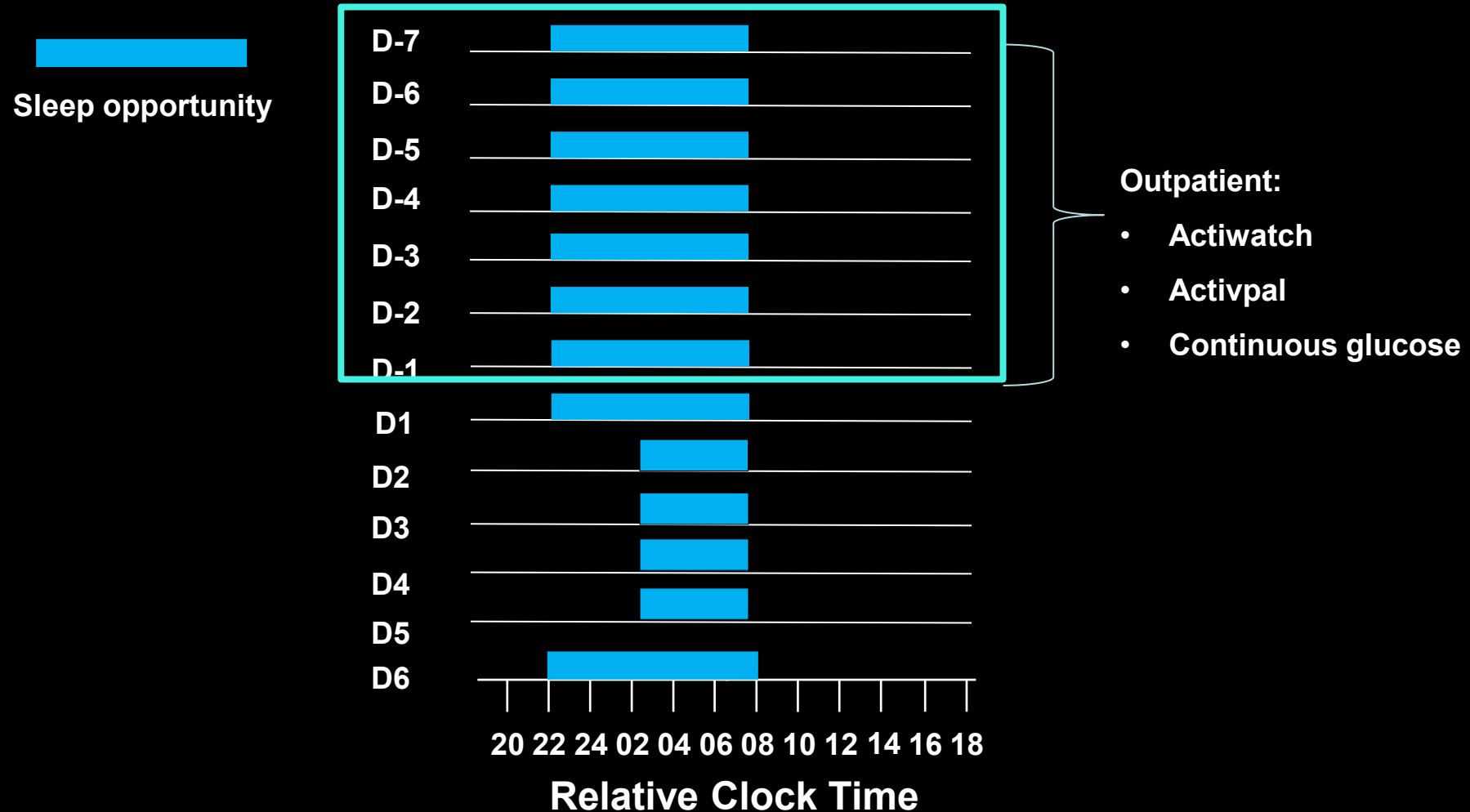


# Protocol: Insufficient sleep

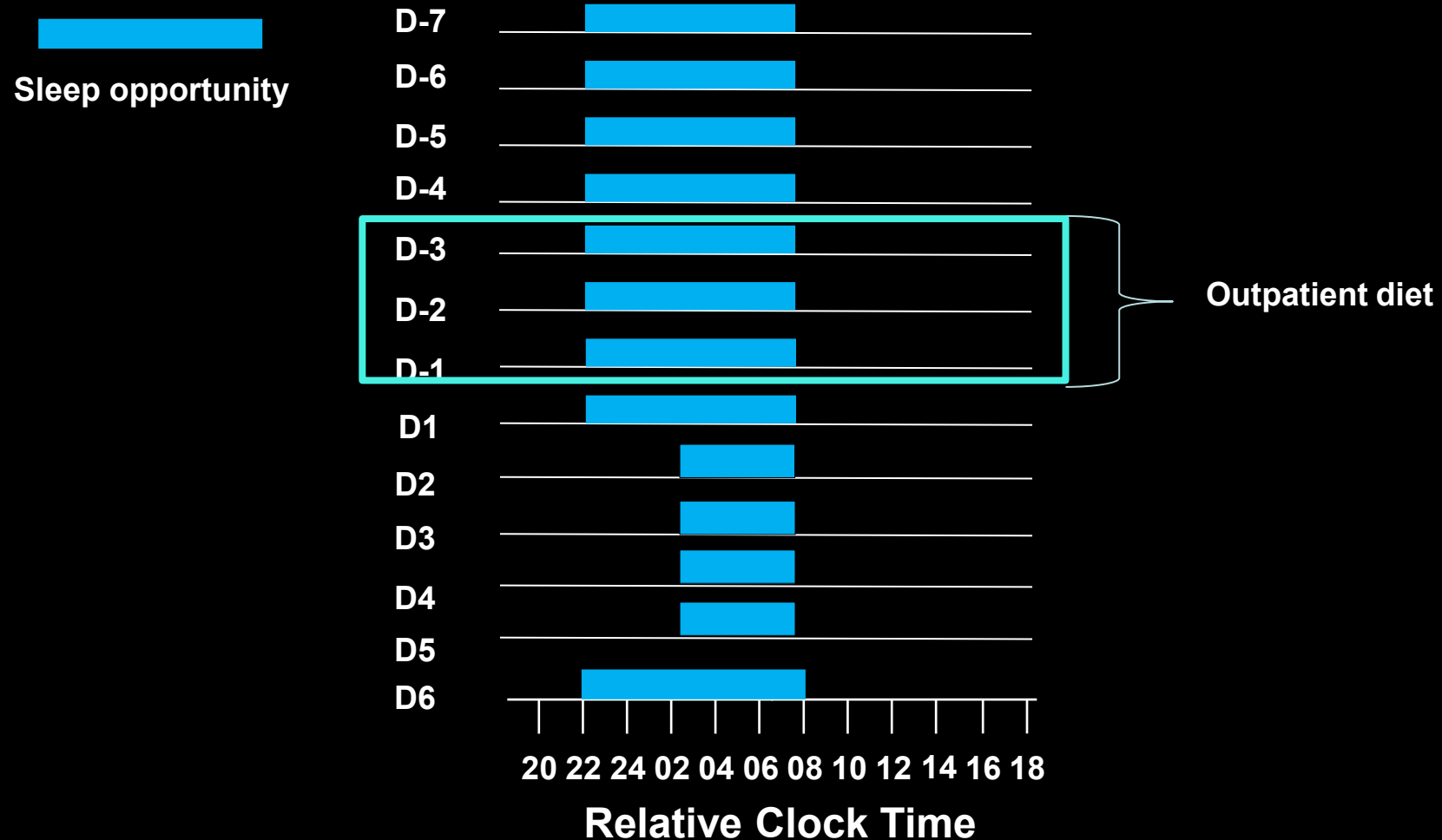
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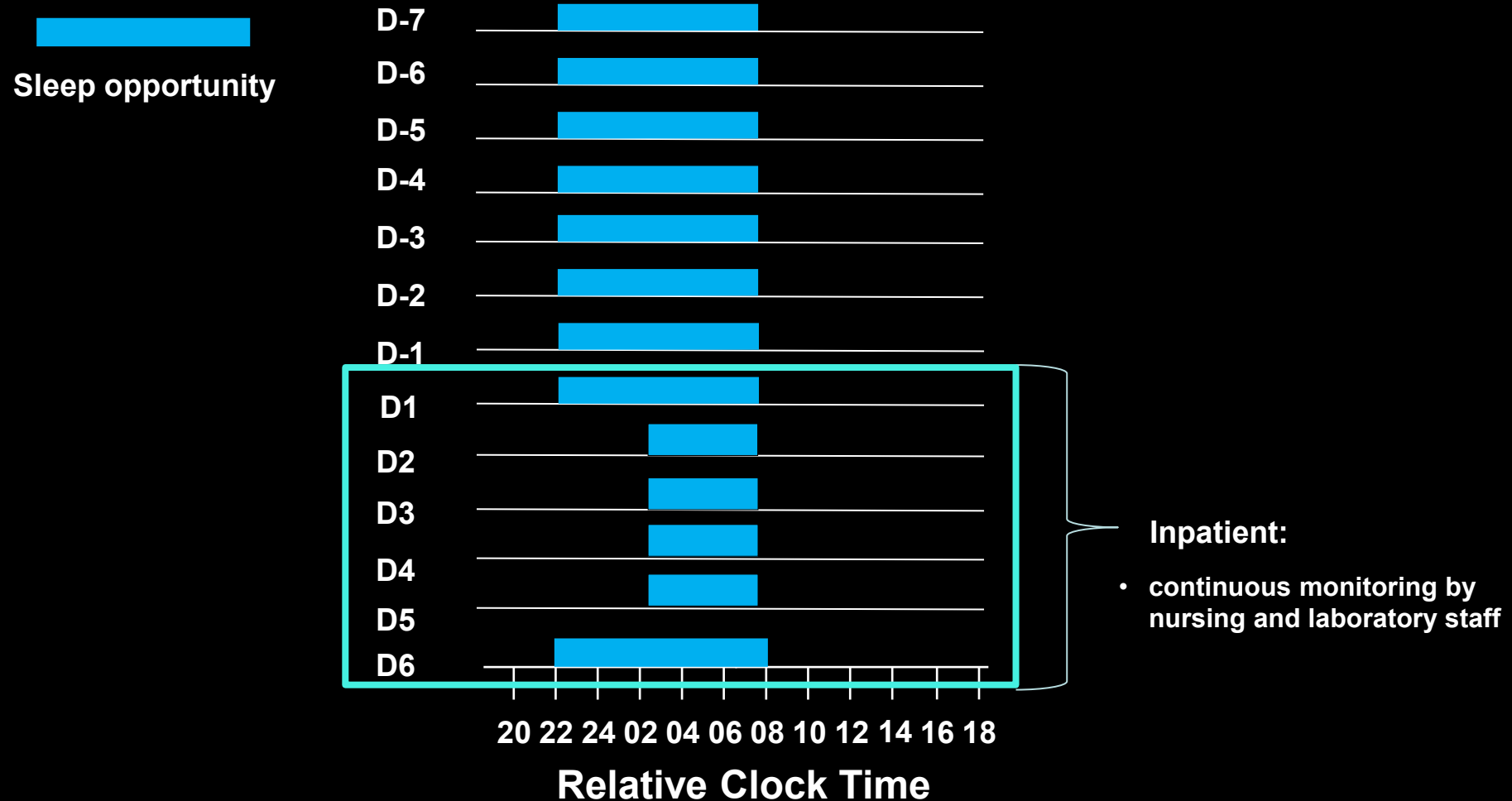
# Protocol: Insufficient sleep



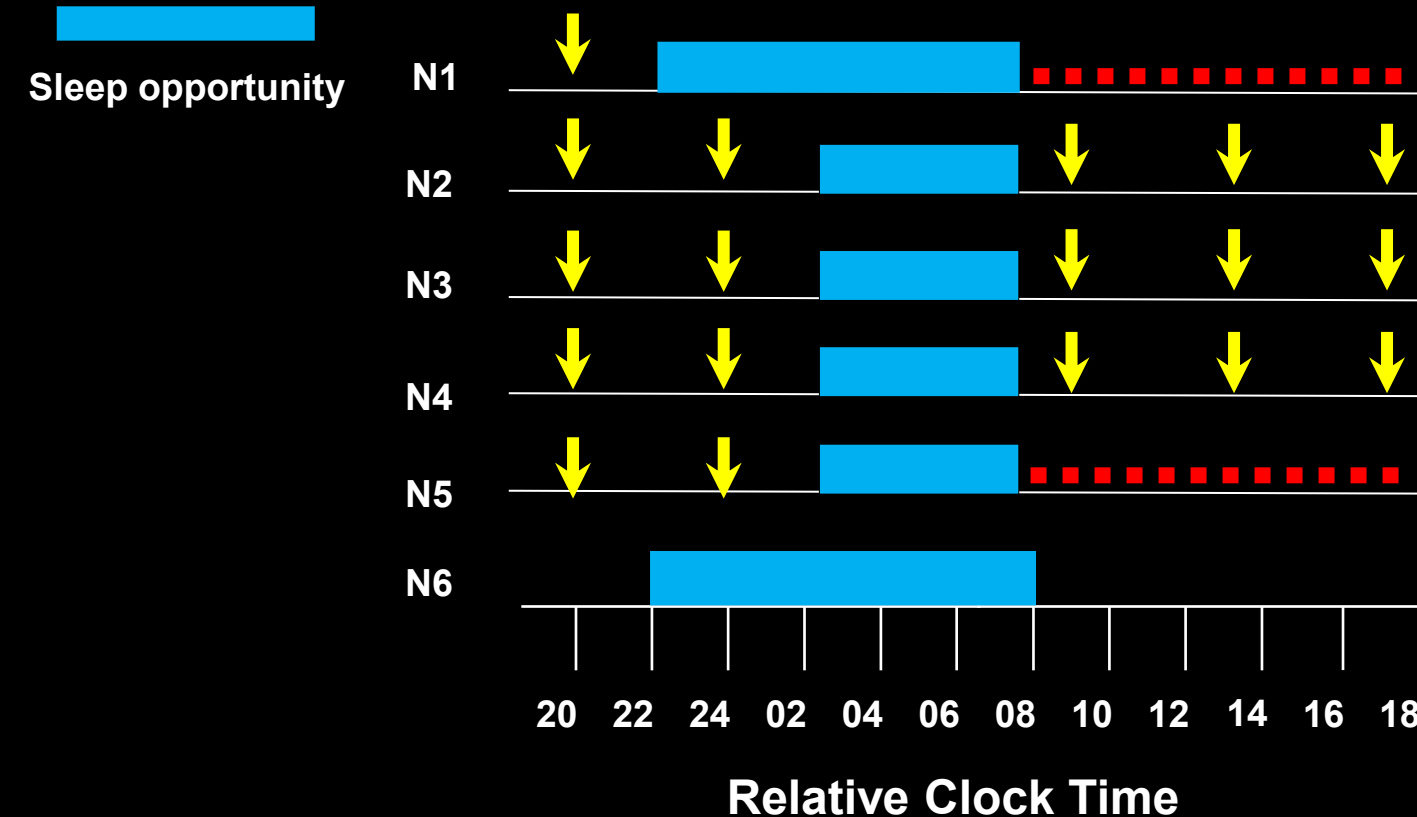
# Protocol: Insufficient sleep



# Protocol: Insufficient sleep



# Protocol: Insufficient sleep

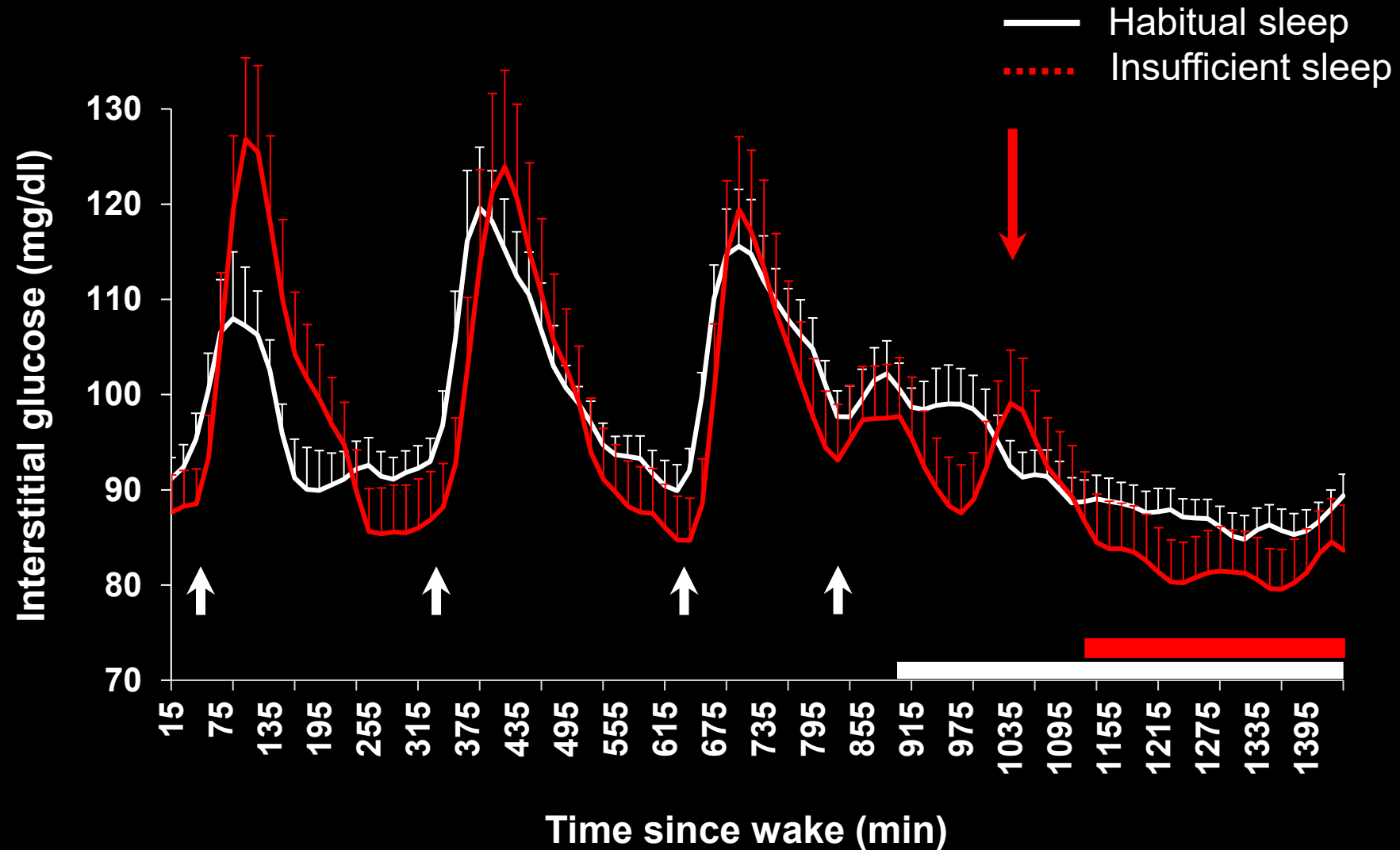


- frequent blood draws,
- 24-hour blood pressure,
- flow-mediated dilation,
- muscle biopsy,
- hyperinsulinemic euglycemic clamp

↓ Meals  
■ ■ ■ Intensive testing days

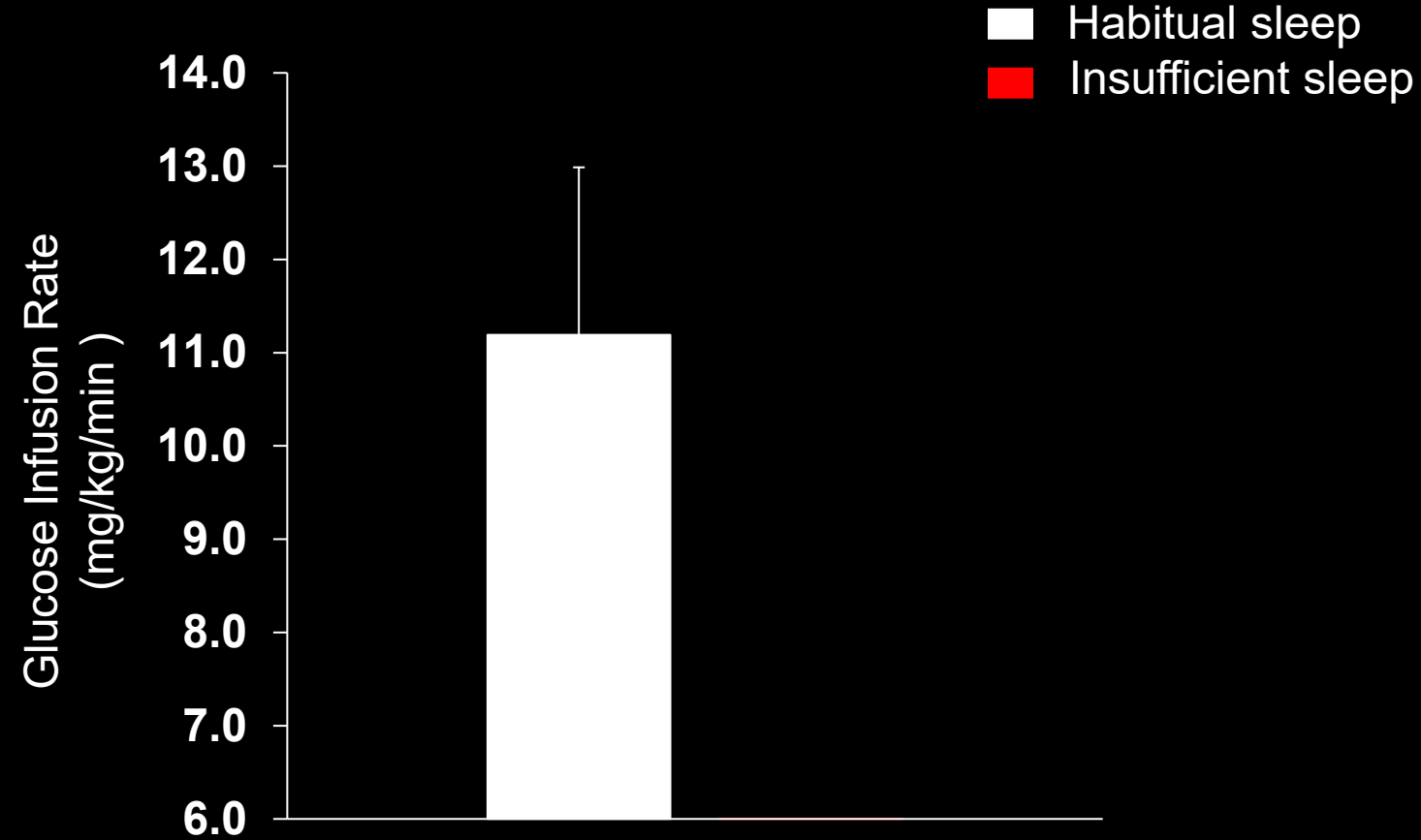
# Results

# Insufficient sleep and interstitial glucose



# Insufficient sleep and insulin sensitivity

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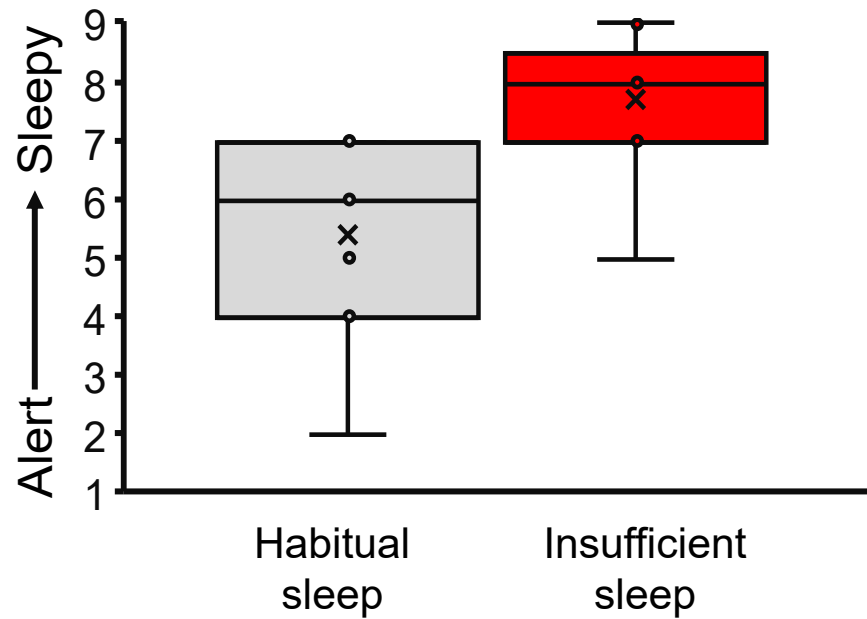


*unpublished data*

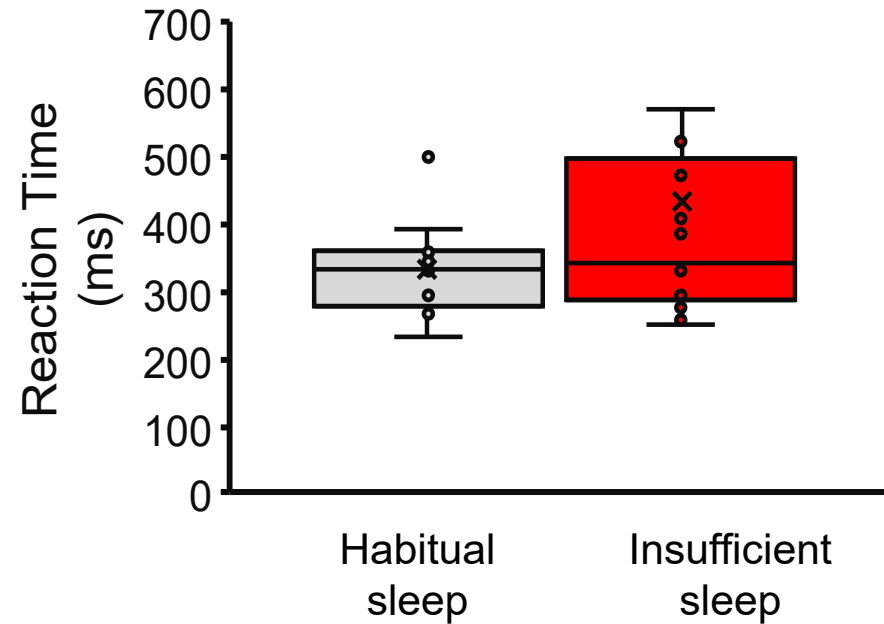
# Insufficient sleep and markers of reaction time

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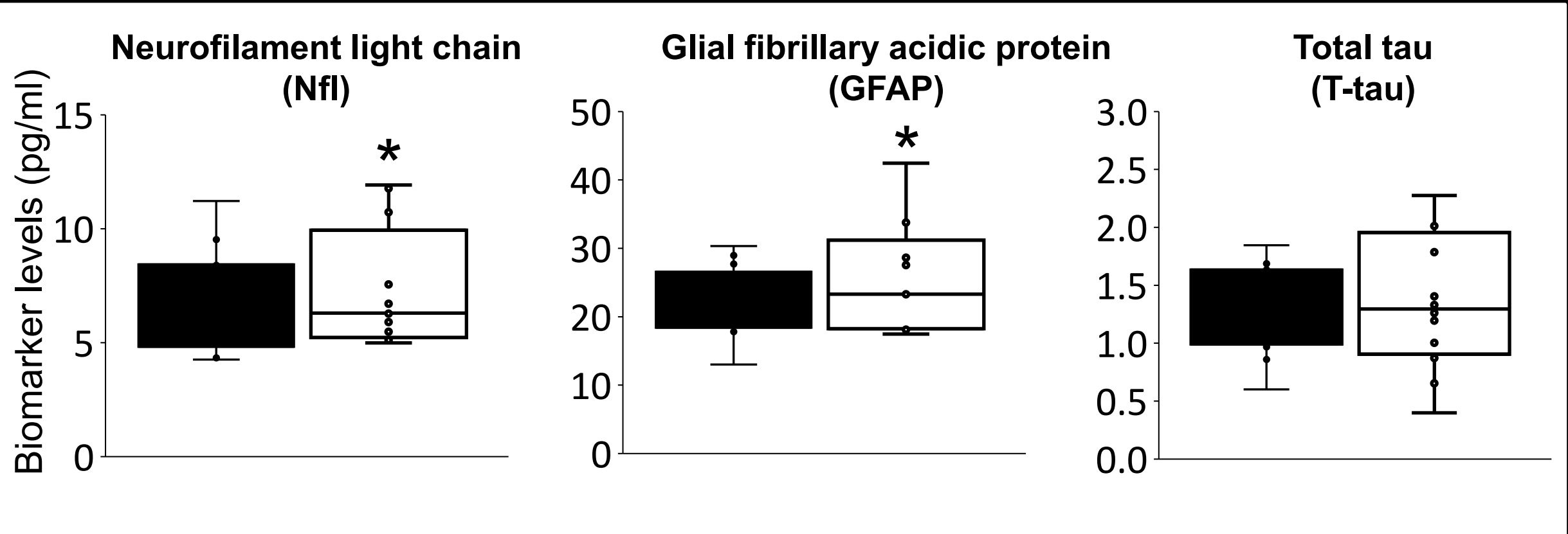
Karolinska Sleepiness Scale



Psychomotor Vigilance Test



# Insufficient sleep and markers of brain injury and neuroinflammation



# Summary

Sleep and circadian disruption lead to:

- an increase in interstitial glucose levels and impaired insulin sensitivity;
- increased skeletal muscle species of lipids including 1,2-DAGs, ceramides and dihydroceramides;
- elevations in circulating markers of brain injury and neuroinflammation.

# Conclusion

- Sleep and circadian disruption impair multiple physiological processes;
- may represent an experimental model of neuroinflammation and neurodegeneration;
- may provide potential mechanistic insights and generate hypotheses linking sleep and circadian disruption to neurodegenerative diseases.

Thank you; see you  
in the panel for Qs!

