

SLEEP SCIENCE:  
SLEEP, SLEEPINESS, AND SLEEPLESSNESS

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# macular degeneration and sleep

## ⌘ Tsai et al., 2019

- Followed 108,255 subjects for 5 years. Insomnia patients were more likely to have subsequent macular degeneration than those without insomnia (2.5% versus 1.8%,  $p < 0.001$ ).

## ⌘ Keenan et al., 2017

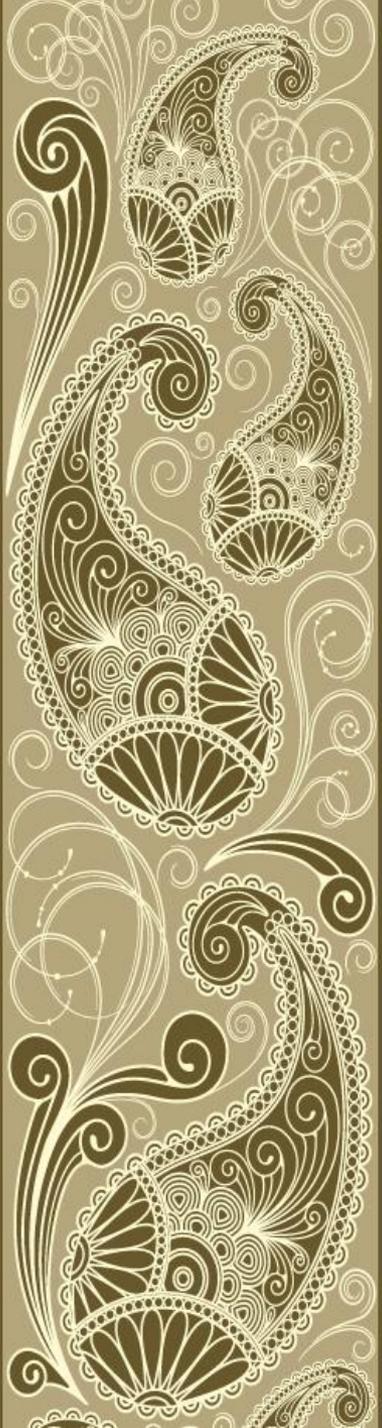
- Studied 2,751,917 people. Rate of macular degeneration in those with sleep apnea was 44% higher than in those without.

## ⌘ Khurana et al., 2016

- Studied 1,003 consecutive patients in an ophthalmology practice. People who slept  $> 8$  hours were 7 times more likely to have macular degeneration than shorter sleeping people.

## ⌘ Pérez-Canales et al., 2016

- Studied 165 subjects (57 patients with macular degeneration and 108 controls). People who slept  $< 6$  hours were 3 times more likely to have macular degeneration than longer sleeping people.



# sleepiness

circadian rhythms:  
the body's symphony

# Topics

- ❧ basic circadian concepts
- ❧ normal sleep rhythm
- ❧ disordered sleep rhythm
- ❧ sleep deprivation
- ❧ blindness
- ❧ treating circadian disorders
- ❧ jet lag
- ❧ social jet lag
- ❧ shiftwork

# basic circadian concepts

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# General Description

- "About a day"
- Circadian rhythms are generated by an internal clock: suprachiasmatic nucleus (SCN)
- 3 primary characteristics
  - repeat  $\approx$  24 hours
  - endogenous, not dependent on external cues
  - entrainable

# central and peripheral clocks

- SCN
  - central master clock
  - signals and coordinates peripheral clocks
- peripheral clock
  - every cell in the body has a clock mechanism
  - large deviations from routine, e.g., temperature, meal schedule, & jet lag can cause desynchrony
    - ❖ awkward feeling, bowel movement in the middle of the night

# sleep/wake transition: sleep/wake is not binary

- the brain is often not 100% asleep or 100% awake
  - N1  $\approx$  60% sleep
  - N2  $\approx$  80% sleep
  - drowsy afternoon  $\approx$  20% sleep
- drowsy before we go to sleep and after we wake up
  - sleep inertia: it can take 2 hr to fully wake up after a night's sleep

# SCN driven circadian functions

## ☞ SLEEP

- ☞ melatonin [↑ during sleep]
- ☞ temperature [↓ during sleep]
- ☞ cortisol [↓ during sleep]
- ☞ urine volume [↓ during sleep]
- ☞ thyroid hormone TSH [↓ during sleep]
- ☞ growth hormone HGH [↑ during N3]
- ☞ blood pressure dipping [↓ during sleep]
- ☞ many others

# sleep rhythm factors

## ☞ melatonin

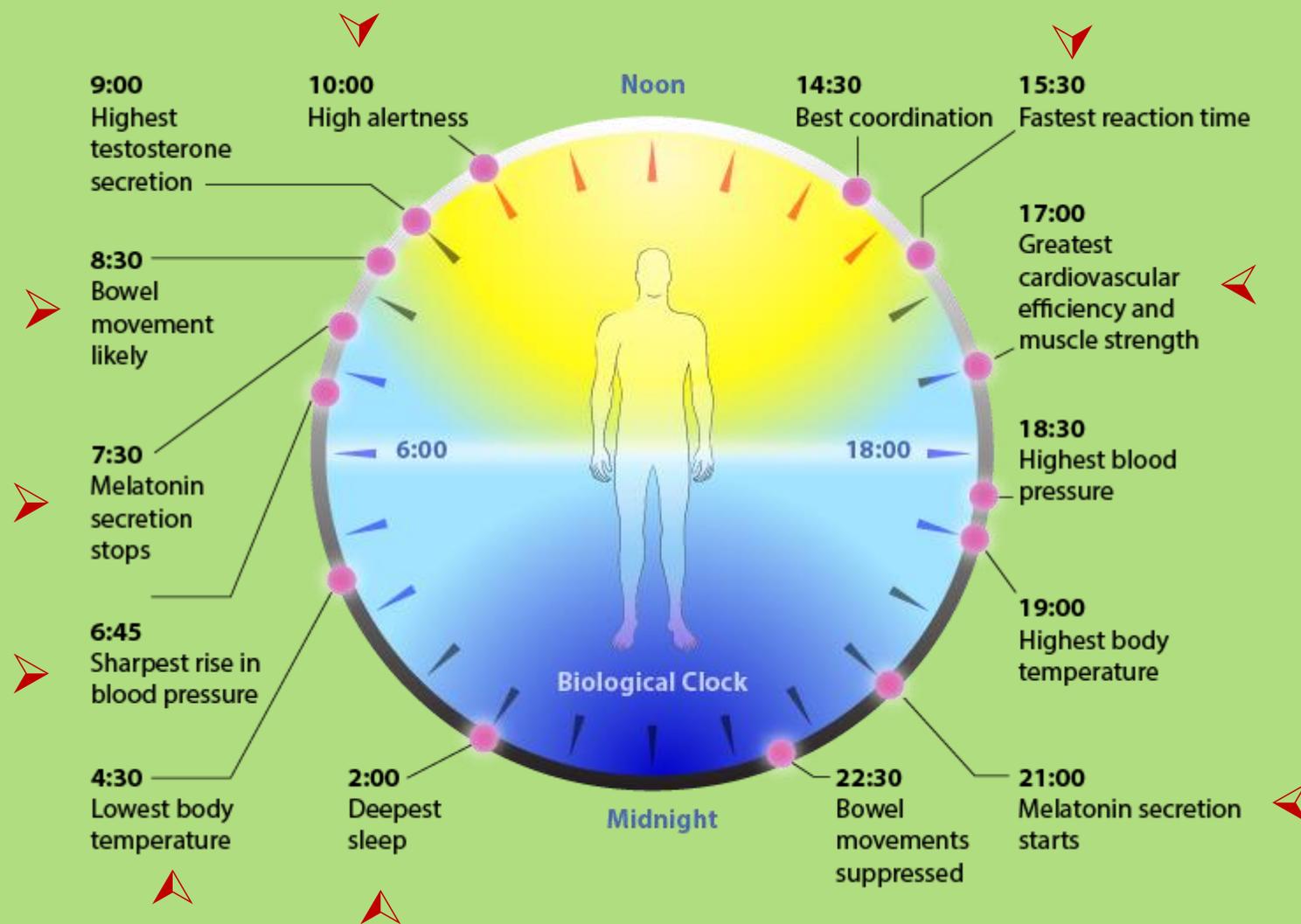
- hormone
- pineal gland
- causes drowsiness
- causes lowering of body temperature
- inhibited by light to the retina and permitted by darkness
- dim-light melatonin onset (DLMO) about 2 hours prior to natural bedtime

## ☞ temperature

- varies between 97-99°
- body cools at bedtime
- 60-68° Fahrenheit room temperature aids sleep
- Tmin about 4 hours after sleep

## ☞ cortisol

- hormone
- adrenal gland (located atop kidney)
- released in response to stress
- activates body's strength capacity: part of fight or flight response



# entrainment

- ❧ Circadian rhythms can synchronize to external cues: entrainment.
- ❧ The external cues that entrain rhythms are called zeitgebers [time-giver].
- ❧ Light is the strongest zeitgeber.
  - before T<sub>min</sub>: phase delay
  - after T<sub>min</sub>: phase advance
- ❧ 1 hr of exercise
  - 5 hr before natural bedtime: phase advance
  - 2 hr before natural bedtime: phase delay

normal sleep rhythm



# natural bedtime/natural wake time

## ☞ favorite time to go to bed

- no atypical alerting experiences
  - ❖ late heavy, meals
  - ❖ late exercise
  - ❖ bright light in evening
- no atypical sedating experiences
  - ❖ poor sleep the night before
  - ❖ weak exposure to bright light during the day
  - ❖ sedating drugs at night

## ☞ favorite time to wake up

- good night's sleep
- no pressure to wake early

**11 pm – 7 am ± 1 hr**

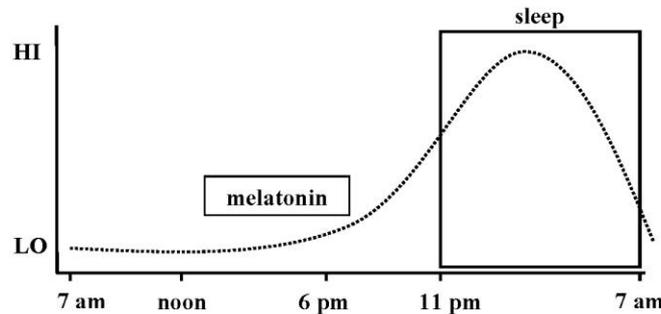
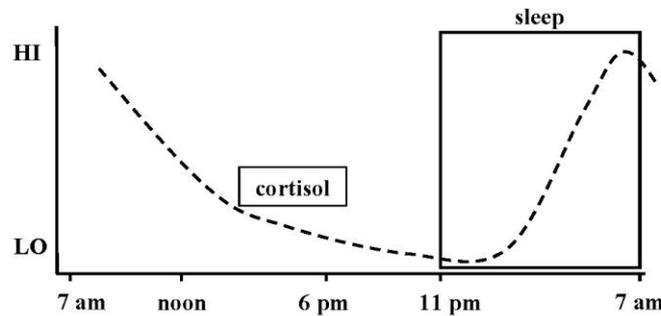
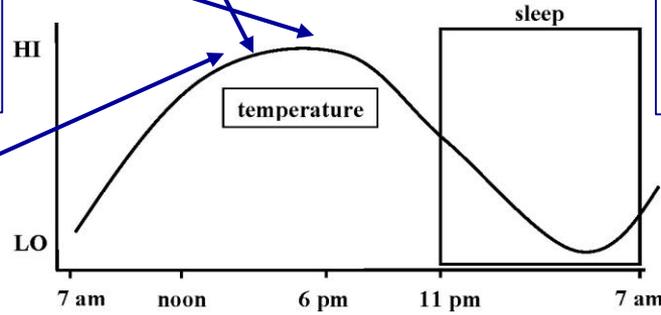
# midafternoon dip

sleepiness ↓  
reaction time ↑  
cognitive efficiency ↑

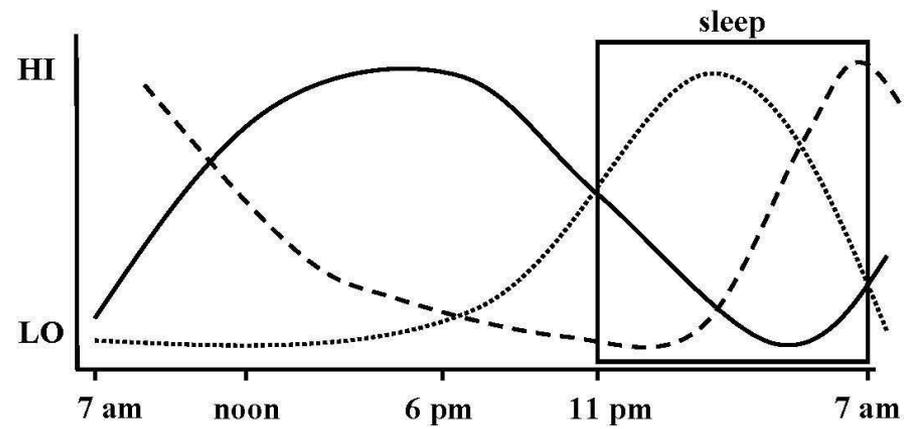
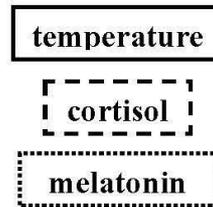
sleepiness ↑  
reaction time ↓  
cognitive efficiency ↓

sleepiness ↑

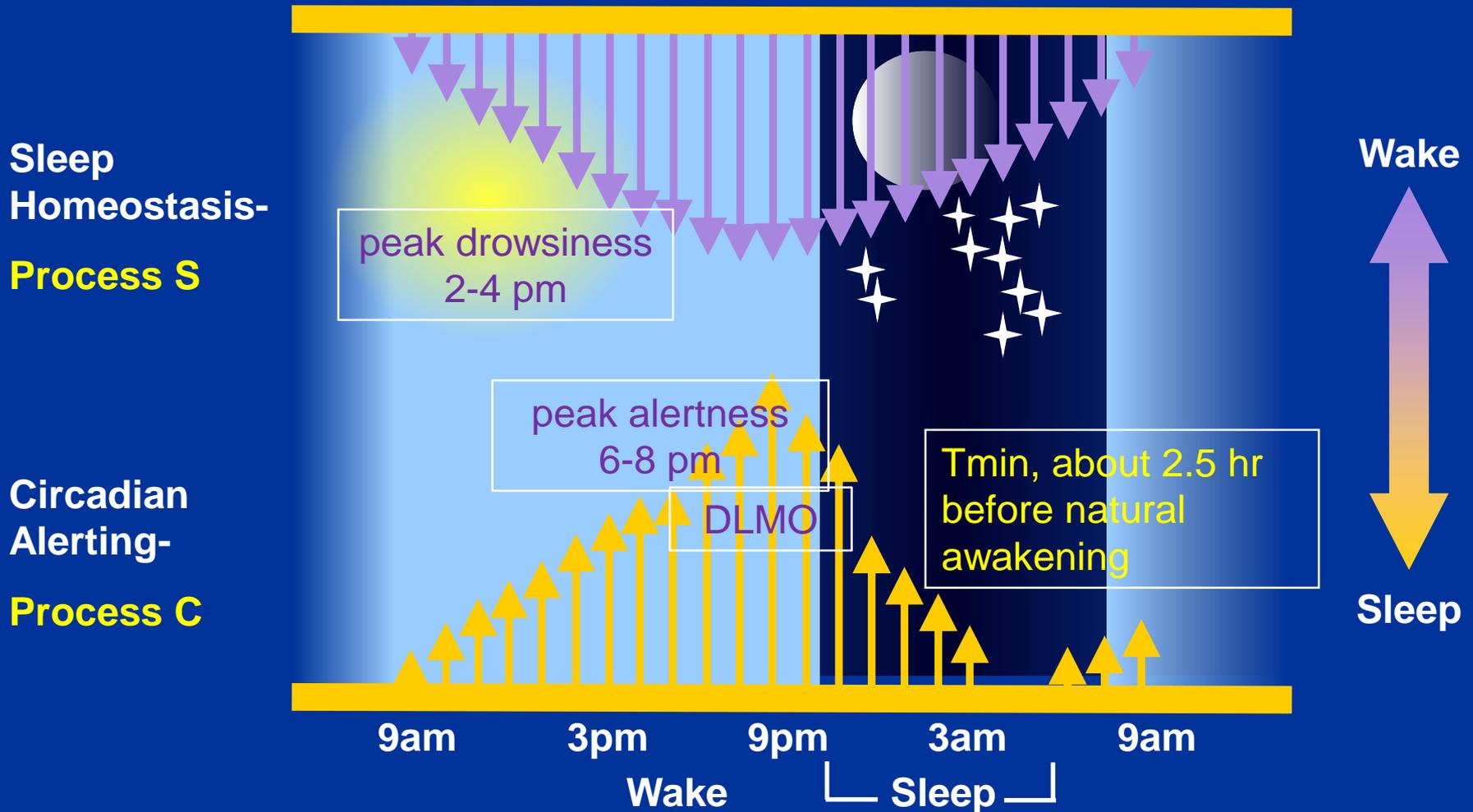
Circadian Rhythm



# Circadian Rhythm

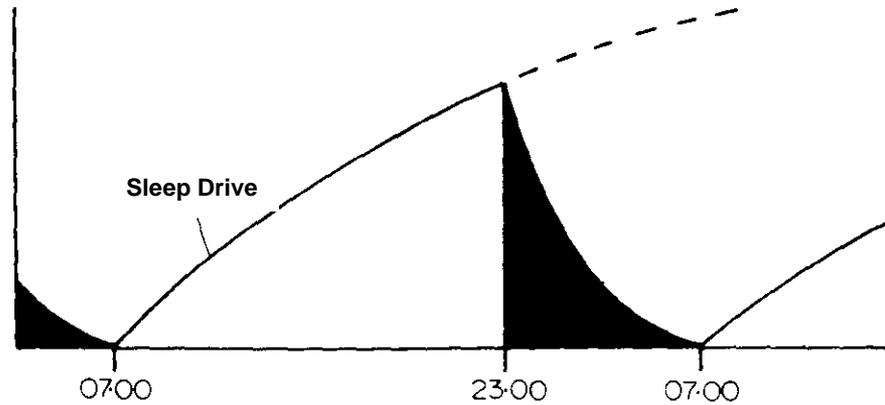


# Sleep Wake Regulation: Two Process Model

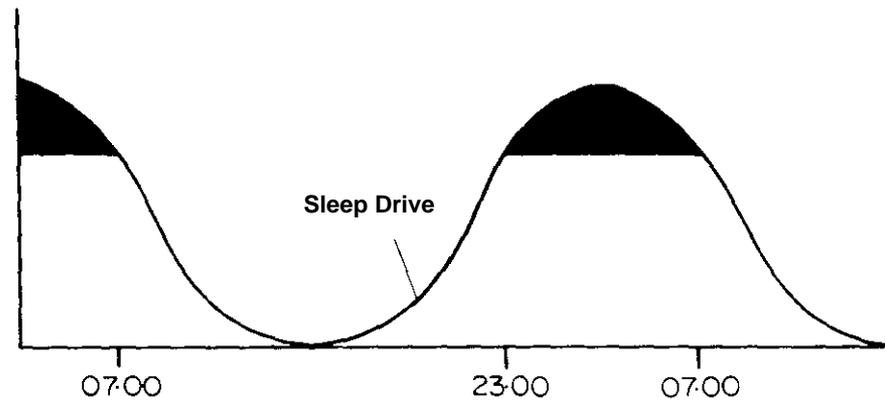


# 2-process model of sleep

process S



process C



disordered sleep rhythm



# Circadian Rhythm Tendencies

## Owls

- ❖ Difficulty waking up in the morning and/or prolonged time to feel fully awake
- ❖ Difficulty falling asleep before very late into the night and/or difficulty disengaging from nighttime activities

## Larks

- ❖ Early bedtime and involuntary evening “naps”
- ❖ Early wake-up times

preferred sleep time:  
lark or owl?



# Chronotype: lark or owl?



Normal Sleep Phase  
Tmin↓

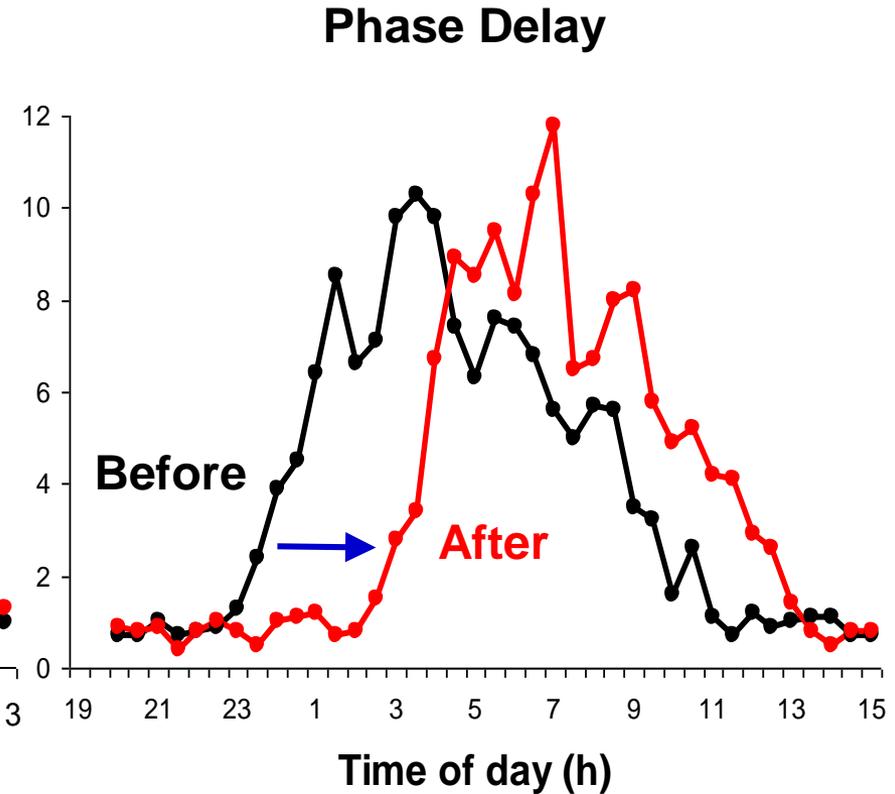
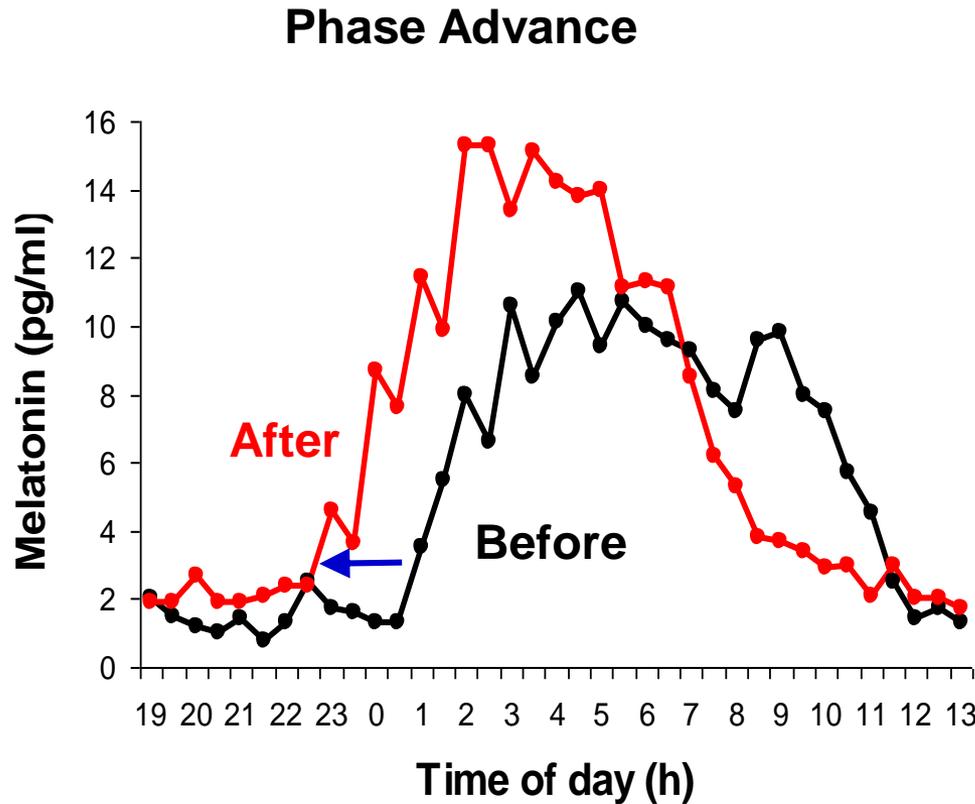


Still alert	Delayed Sleep Phase Tmin↓	Difficult to wake up
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Very sleepy	Advanced Sleep Phase Tmin↓	Cannot sleep
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# Light Manipulations: Phase Advances and Phase Delays

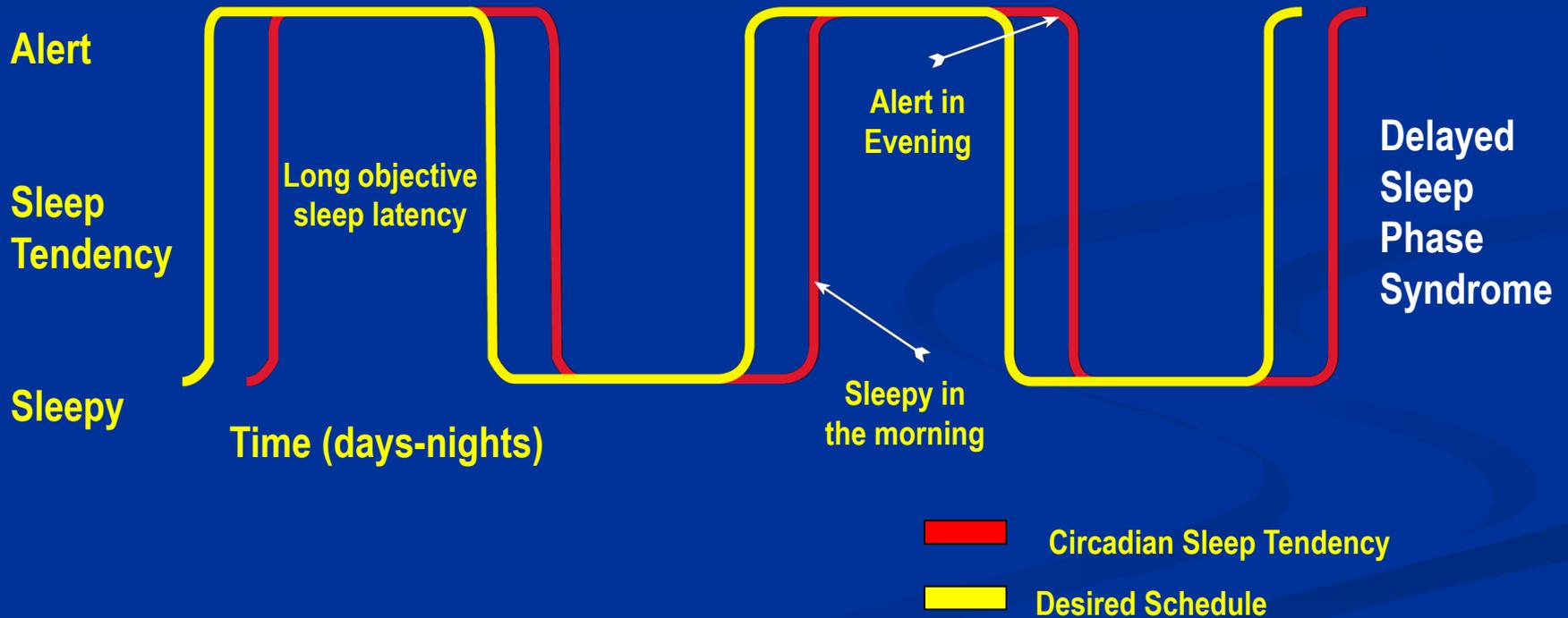


Clock shifts **earlier** in time

Clock shifts **later** in time

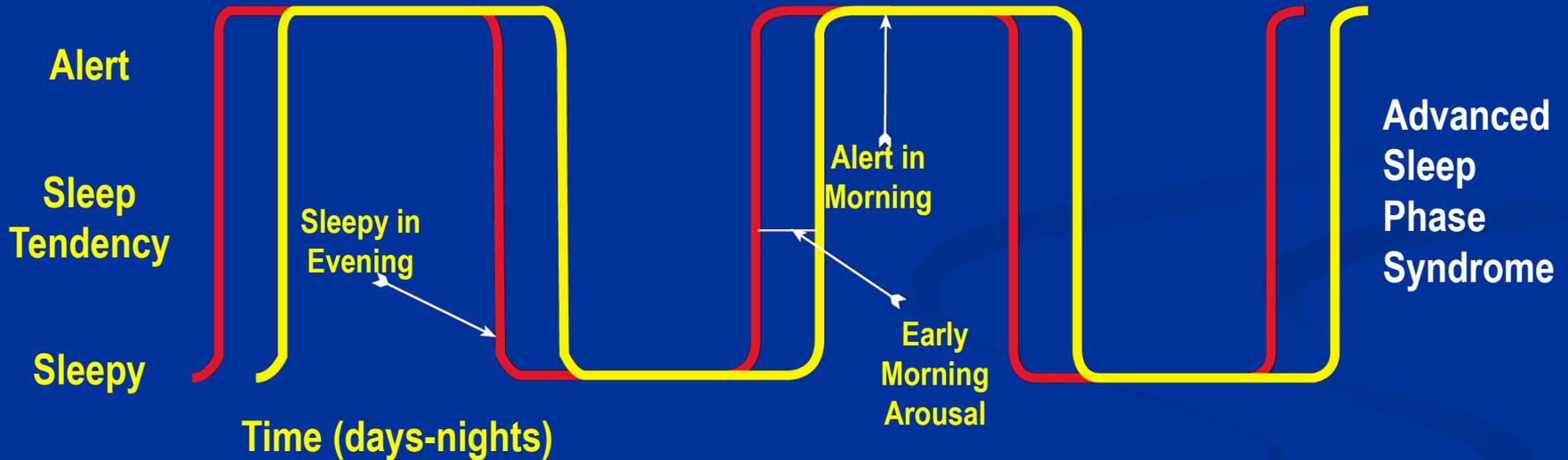
# Circadian Phase Shifts

## Owls



# Circadian Phase Shifts

## Larks



 Circadian Sleep Tendency

 Desired Schedule

circadian rhythms  
and public health

# Los Angeles Times

October 13, 2019

## California becomes first state in the country to push back school start times

- middle schools start  $\geq 8$  am
- high schools start  $\geq 8:30$  am



# **Will Nashville public schools change high school start times?**

Dec. 27, 2018, The Tennessean

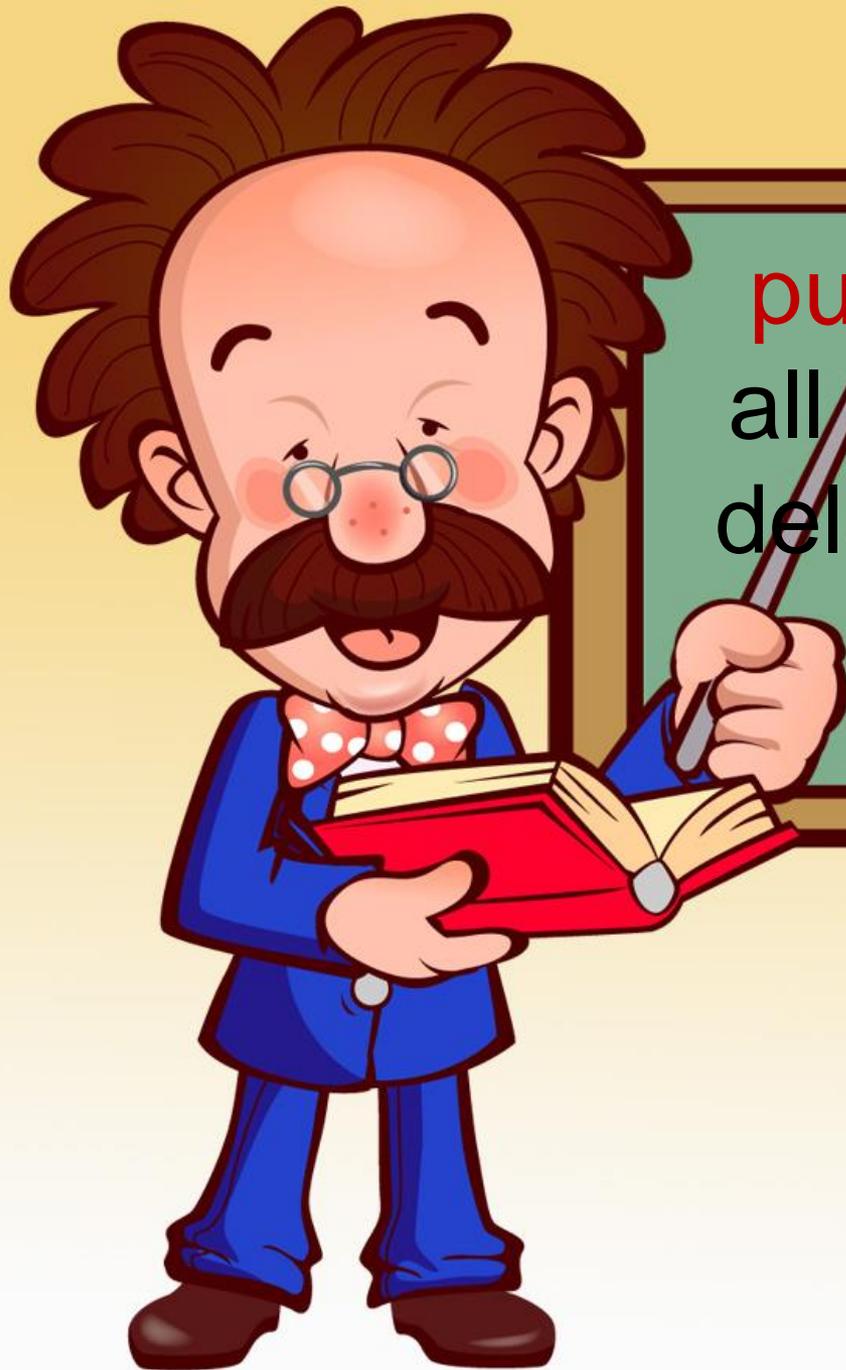
Exploring whether Nashville public schools should start high school later in the morning could again become a topic for the district's board.

# delayed sleep phase in adolescents

- ❧ adolescent delayed sleep phase observed 30 years ago (Carskadon, 1990)
- ❧ in the early-mid 1990s, later high school start time was introduced in some schools in Minnesota and Rhode Island
- ❧ resistance by schools and parents
- ❧ American Medical Association
  - start time no earlier than 8:30 am
- ❧ American Academy of Pediatrics
  - start time no earlier than 8:30 am

# benefits of delayed start time for 18 million students

- ☞ currently, some schools in 45 states have adopted delayed start times
- ☞ academic benefits of later start times
  - truancy ↓
  - tardiness ↓
  - grades ↑
  - graduation rate ↑
- ☞ health benefits of later start times
  - depression ↓
  - suicidal ideation ↓
  - car wrecks ↓
  - substance abuse ↓



public health prediction:  
all high schools will have  
delayed start times within  
10 years

even in the south

circadian rhythm in distress

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SLEEP DEPRIVATION

# sleep deprivation (SD) research

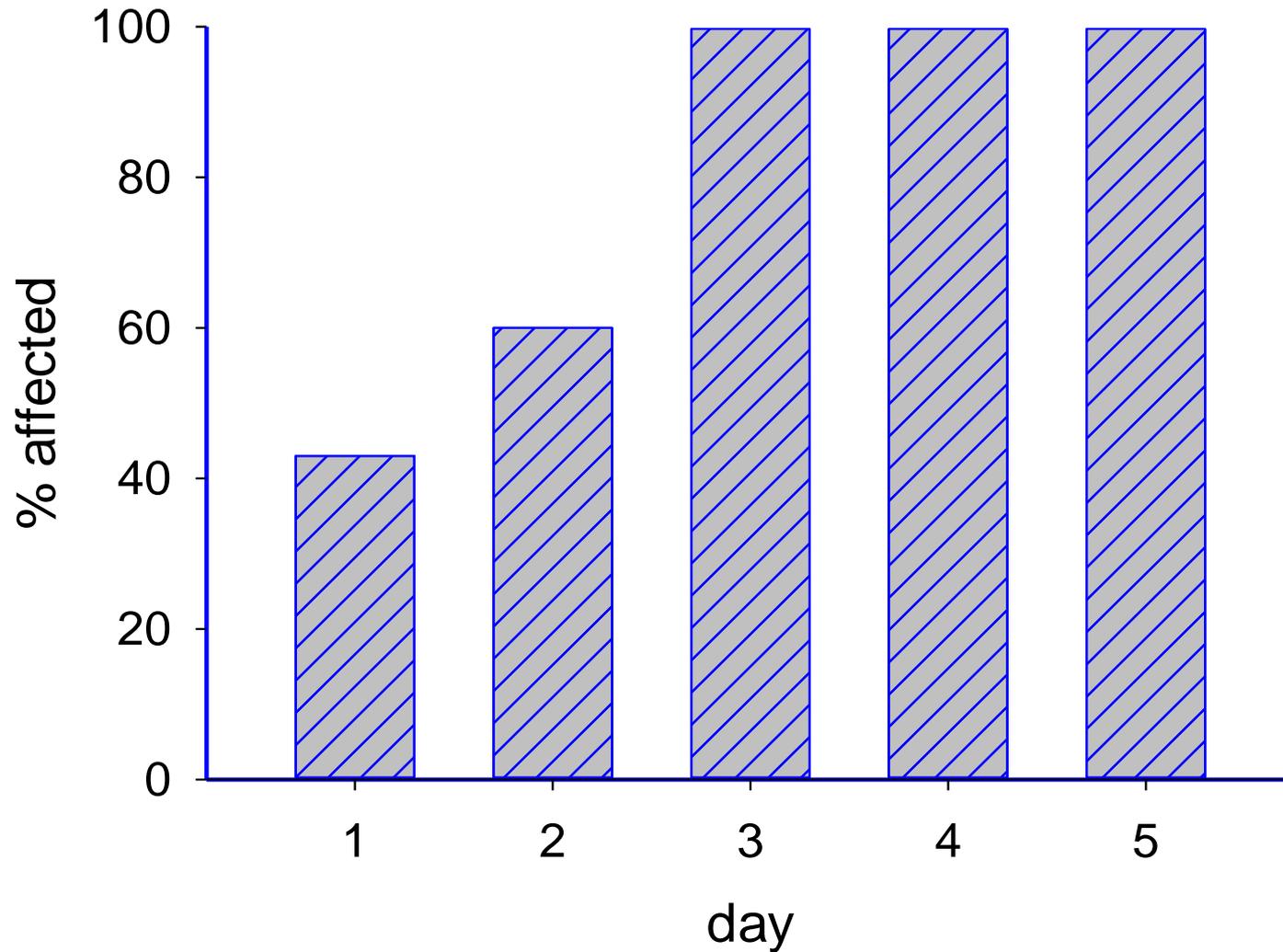


- ❧ 21 studies under laboratory control
- ❧ most conducted prior to 1970
- ❧ healthy subjects
- ❧ mostly males
- ❧ longest SD was 11 days

In the middle ages, accused **witches** were tortured by depriving them of sleep.

**Medical residents** work 36-hour shifts with little or no sleep.

# SD: mood, cognitive impairment, and hallucinations



# sleep deprivation

## ❧ impairment sets in within 36 hrs of wakefulness

- cognitive impairment ↑
  - ❖ constructive thinking
  - ❖ memory
  - ❖ false memories
- emotional instability ↑
  - ❖ anger, anxiety, depression
- microsleeps, 2-10 sec ↑

## ❧ within 3 days of wakefulness

- visual hallucinations ↑
- auditory and tactile distortions ↑
- paranoid delusions ↑

## ❧ recovery

- sleep for 50% of hours awake
- for example, awake for 40 hours requires 20 hours of sleep over a few days

# chronic partial sleep deprivation

☞ we are normally awake 16-18 hrs/day

- extending wake time beyond this is partial deprivation or sleep restriction
- routine sleep restriction: socializing, work demands, medical conditions
- 35% of US adults regularly sleep less than 7 hrs on week days
- restricted sleep over several days produces cumulative effects
  - ❖ errors, accidents, injuries, personal conflicts, impaired health

☞ restriction vs deprivation

- restricting sleep to 4 hrs/day for 2 weeks = deficits of 3 days of total sleep deprivation, 72 hours

☞ habitual sleep restriction, 4-7 hrs/day

- health risk: obesity, diabetes, hypertension, heart disease, cognitive decline, all-cause mortality
- pancreas/insulin ↓, ghrelin ↑, immunity ↓, chronic arousal ↑

# recovery from sleep deprivation

- ❧ dependent on the degree of sleep deprivation
  - number of continuous hours
  - severity of sleep restriction: amount and days
- ❧ after 7 nights of 5 hr sleep, near complete recovery occurs after:
  - 2 nights of 10 hr sleep
  - 3 nights of 8 hour sleep
- ❧ N3 rebound greater than any other sleep stage

circadian rhythm in distress

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BLINDNESS

# blindness: does light get through?

## ☞ different types of blindness

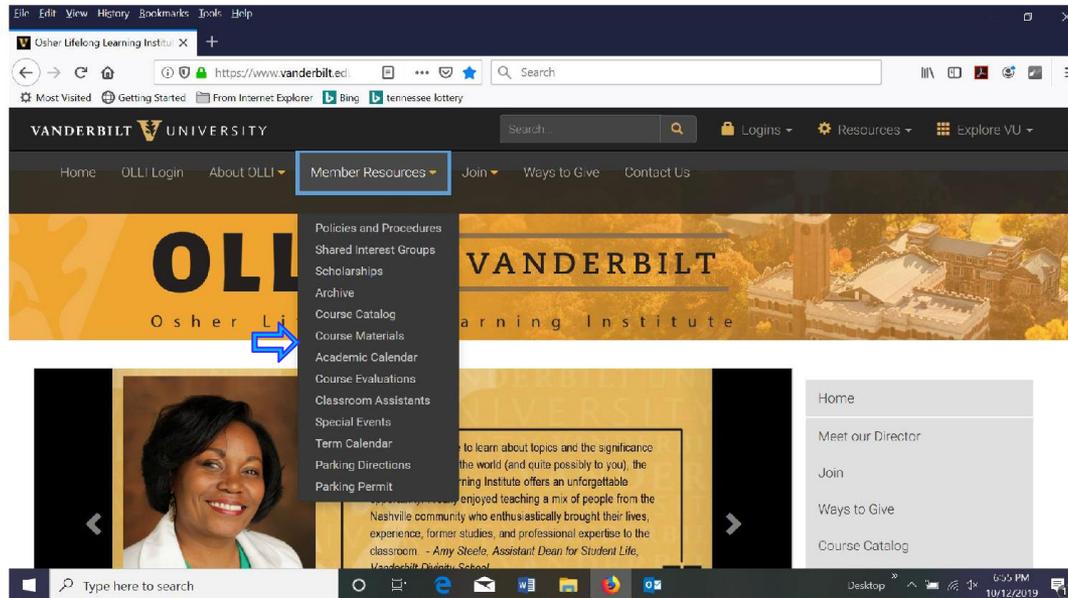
- melanopsin response is critical
- varies between individuals with blindness
- 80% of blind people have some sight
- partial sight blind people have far less sleep problems than "totally" blind
- 70% of "totally" blind people have poor sleep

## ☞ circadian impairment

- human circadian rhythm averages 24 hr, 15 min
  - ❖ environmental entraining creates the appearance of 24 hr rhythm
- non-entrained circadian rhythm
  - ❖ unresponsive to zeitgebers
  - ❖ disruptive to work and leisure activities
  - ❖ often accompanied by depression

# blindness: sleep diagnosis & treatment

- ❧ Non-24-Hour Sleep-Wake Rhythm Disorder (free-running disorder)
  - progressive sleep onset delay
  - sleep-onset insomnia, EDS
  - rare in sighted people, common in people with blindness
    - ❖ severity of disorder dependent on degree of departure of circadian rhythm from 24 hr
  - present in 50% of “totally” blind people
- ❧ fixed scheduling of available zeitgebers
  - meals
  - physical activity
- ❧ drugs having some success
  - oral melatonin
  - tasimelteon, melatonin receptor agonist



- for lecture 4
- select Course Materials
- scroll down to this course
- select 1 mg Melatonin Schedule and print

to be continued