Sleep Science: 
Sleep, Sleepiness, and Sleeplessness

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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
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\% \text{ sleep}
  – N2 \approx 80\% \text{ sleep}
  – drowsy afternoon \approx 20\% \text{ sleep}

• drowsy before we go to sleep and after we wake up
  – sleep inertia: it can take 2 \text{ 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°F
  - body cools at bedtime
  - 60-68°F 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
9:00  Highest testosterone secretion
8:30  Bowel movement likely
7:30  Melatonin secretion stops
6:45  Sharpest rise in blood pressure
4:30  Lowest body temperature
2:00  Deepest sleep
10:00 High alertness
14:30 Best coordination
15:30 Fastest reaction time
17:00 Greatest cardiovascular efficiency and muscle strength
18:30 Highest blood pressure
19:00 Highest body temperature
21:00 Melatonin secretion starts
22:30 Bowel movements suppressed
18:30
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 Tmin: phase delay
- after Tmin: 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
sleepiness ↓
reaction time ↑
cognitive efficiency ↑

sleepiness ↑

midafternoon dip

sleepiness ↑
reaction time ↓
cognitive efficiency ↓
Circadian Rhythm

temperature

cortisol

melatonin

HI
LO

7 am noon 6 pm 11 pm 7 am

sleep
Sleep Wake Regulation: Two Process Model

Sleep Homeostasis - Process S

Circadian Alerting - Process C

9am          3pm         9pm         3am          9am

Sleep Wake Regulation:

- Tmin, about 2.5 hr before natural awakening
- Peak alertness: 6-8 pm
- Peak drowsiness: 2-4 pm

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

Still alert

Delayed Sleep Phase

Very sleepy

Advanced Sleep Phase

Cannot sleep

Difficult to wake up
Light Manipulations: Phase Advances and Phase Delays

Clock shifts earlier in time  Clock shifts later in time

Melatonin (pg/ml)

Time of day (h)

Phase Advance

Phase Delay
Circadian Phase Shifts

Owls

Alert
Sleep Tendency
Sleepy

Long objective sleep latency
Sleepy in the morning
Alert in Evening

Time (days-nights)

Delayed Sleep Phase Syndrome

Circadian Sleep Tendency
Desired Schedule
Circadian Phase Shifts

Larks

- Alert
- Sleepy in Evening
- Sleepy in Morning
- Alert in Evening
- Alert in Morning
- Early Morning Arousal
- Advanced Sleep Phase Syndrome

Time (days-nights)

Circadian Sleep Tendency
Desired Schedule
circadian rhythms and public health
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

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.
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

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