Sleep, Circadian Rhythm and the Impact of Insufficient and Poorly Timed Sleep

Julie Dahl, APRN, CNP
Minnesota Sleep Society President
president@mnsleep.net

Nobel Prize 2017
Awarded to Jeffrey C. Hall, Michael Rosbash and Michael W. Young for their discoveries of molecular mechanisms controlling the circadian rhythm

Outline
- Why we Sleep
- How we Sleep
- Timing of Sleep
- Shift Work

Results of Insufficient or Poorly Timed Sleep
- Performance & Public Safety
- Mental Performance
- Preventable Accidents
- Disease Risk
  - Mood disorders, obesity, diabetes, high blood pressure, heart disease, stroke, immune function, dementia, cancer

Why we Sleep
Sleep Rids the Brain of Toxic Cellular Waste.
Eiko Ojala

How we Sleep
4 stages of sleep
Two Process Model of Sleep Regulation

Alertness Level

Homeostatic Sleep Drive (accumulation of adenosine + other somnogens)

Circadian Wake Drive (melatonin)

Sleep

Circadian Nadir

6 am

3 pm

9 pm

3 am

6 am

Awake

Asleep

How we Sleep

Healthy Sleep Duration

The American Academy of Sleep Medicine recommends that you get the following hours of sleep on a regular basis for optimal health at each stage of life:

All-cause mortality

Proportion of deaths

1.00

1.10

1.20

1.30

1.40

1.50

1.60

95% confidence interval

Best fitting cubic spline

https://doi.org/10.1161/JAHA.117.005947

Journal of the American Heart Association. 2017;6:e005947

True or False

Adults need 8 hours of sleep each night

Sleep is for slackers!
The more tired you are, the less aware you are that you are tired.

In addition to a "master clock" in the brain, each cell in the body possesses a "circadian oscillator"/"clock" which must be synchronized with one another and the environment.

### The Timing of Sleep

In situations involving circadian misalignment:
- **Daylight Savings Time**
  - Increased incidence of car accidents
  - Increased incidence of heart attacks
- **Jet Lag**
  - The more time zones you cross, the more time it will take to recover
  - Traveling east is more difficult than traveling west

### Situations involving Circadian Misalignment

#### Yes or No

Are fluctuations in daily light necessary for daily rhythm?

Jean Jacques d'Ortous de Mairan work with mimosa plants in the 18th century shows there is an internal biologic clock.

The circadian clock anticipates and adapts our physiology to the different phases of the day.
Preferred Chronotype - Child to age 30

Late Chronotype associated with increased prevalence of morbidity and mortality

- Study done in the UK
- N=433,268, age 38-73, followed for an average of 6.5 years

Self Reported Chronotype

- Definite Morning: 27%
- Moderate Morning: 35%
- Moderate Evening: 28%
- Definite Evening: 9%

- Definite Evening types had a 10 percent increased risk of death compared to definite morning types and were more likely to have psychiatric disorders, diabetes and neurological disorders

Yes or No

Is it better to be a morning lark than a night owl?

Physiology of Circadian System

Diurnal depiction of neuroendocrine factors and airway dynamics associated with nocturnal asthma exacerbations

Evidence for Chronotherapy in Asthma Therapy

<table>
<thead>
<tr>
<th>Medication</th>
<th>Suggested Time</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montelukast (Singular)</td>
<td>Evening</td>
<td>Improved FEV1 when compared with morning dosing</td>
</tr>
<tr>
<td>Salmeterol (Serevent)</td>
<td>Evening</td>
<td>One evening dose is equivalent to BID dosing</td>
</tr>
<tr>
<td>Beclometasone (Qvar)</td>
<td>Afternoon</td>
<td>One afternoon dose is equivalent to BID dosing</td>
</tr>
<tr>
<td>Mometasone (Asmanex)</td>
<td>Evening</td>
<td>Increased FEV1, FVC while morning dose and placebo showed no difference</td>
</tr>
<tr>
<td>Oral Prednisone</td>
<td>3:00 pm</td>
<td>Significantly increased nocturnal FEV1 when compared with 8:00 am and 8:00 pm dosing</td>
</tr>
<tr>
<td>IV Methylprednisolone</td>
<td>3:00 pm</td>
<td>Greatest increase in PEF compared to 3:00 am, 7:00 am and 7:00 pm</td>
</tr>
</tbody>
</table>
Risk during heart surgery has morning-to-afternoon variation

- Reviewed prior AVR surgical cases: Almost double the amount of major cardiac events of the morning (18.1%) compared to afternoon (9.4%) patients.
- A year long study with 88 patients randomly assigned found afternoon surgery compared to morning had reduced short-term perioperative myocardial injury with the mechanism decreasing thromboembolic risk with.
- Cardiac troponin T release was lower in patients who underwent surgery in the afternoon.
- And hypoxia myocardium.
- Genetic analysis was done.

Montagne, Lancet 2018

---

Yes or No

Can you train your circadian clock?

**Rotating night shift work and risk of obesity and weight gain**

- Nurses Health Study (Pan, Schernhammer, Sun Hu PLOS Med 2011)

Late eating impairs glucose tolerance

- Higher concentration of glucose when eating 1 hour before habitual bedtime compared to 4 hours before habitual bedtime.
- The mechanisms is due to both mistimed eating, when melatonin levels are elevated and genetics.
  - Those with a MTNR1B genotype more strongly influenced glucose tolerance.
- Clinical relevance
  - The nightshift workers eating during their night shift.

Lopez-Minguez et al, Clin Nutr, 2017

---

Who is at risk for circadian misalignment

- TV Binge Viewers
- Teenagers
- Shift workers
- All of the above
Social Jet Lag

- Occurs when you go to bed and wake up later on weekends than during the week
- Increased risk for sleepiness and fatigue, insomnia and poor mood
- Increase likelihood of heart disease
  - Each hour of social jet lag also is associated with an 11-percent link with TV binge-watching: poorer sleep quality, more fatigue, and increased insomnia

Shift Work

- 8.6 million Americans work at night
- Are getting less daily sleep on average (30-60 minutes) and suffer more from insomnia than the general population
- At a higher risk for injury which increases over successive shifts:
  - 6% in the second night
  - 17% in the third night
  - 36% in the fourth night

Consequences of Shift Work Disorder

- Disruption of biological circadian rhythms & sleep/wake cycle
- Performance & safety (driving)
- Family & social issues
- Health disorders

Coping strategies for shift work

- Maintain a healthy lifestyle
  - Good nutrition, drink plenty of water, stay active, allow enough time for sleep, keep the sleep schedule as regular as possible
- Preparations for optimal environmental conditions for daytime sleep
  - Moderate caffeine and other substances that can affect sleep
  - Ready your room (cool, quiet, dark room)
- Timed light exposure in the work environment and light restriction in the morning
- Meal Timing

Recommendations for the Treatment of Shift Work Disorder

- Improve alertness:
  - Planned napping before or during the shift
  - Timed light exposure in the work environment (10,000 Lux) and light restriction in the morning
  - Modafinil (stimulant) use
  - Caffeine use
- Promote daytime sleep
- Administration of melatonin prior to the daytime sleep
- Hypnotic medication
Circadian misalignment possibilities

A lack of harmony with internal factors due to environmental, behavioral, social

- Light/Dark
- Behavioral
  - Rest/activity
  - Sleep/wake
  - Feeding/fasting
- Work/School demands

A lack of harmony on internal factors

- Clock
- Clock genes
- Cells
- Organs
- Peripheral (Organ) Clocks

In conclusion

- Physical sleep/wake cycles and biologic factors need to work in sync for one's health and well-being
- This requires adequate and well-timed sleep in line with one's internal clock
- Inadequate sleep and circadian misalignment increases morbidity and mortality risk
- Knowledge of cyclic body rhythms has clinical application as we can take advantage of peak performance times
- While we cannot change our circadian rhythm, we can develop behavioral strategies that help to cope with alteration in circadian rhythms