Understanding sleep for prevention of chronic disease

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Circadian rhythmicity and sleep

- All living creatures have processes characterized by circadian rhythmicity governed by endogenous clocks.
- Between need to rest and to adjust to changes in physical environment (celestial mechanics) lead to Darwinian pressures to evolve in relation to the solar day.
- Circadian rhythms occur independent of external cues but can be entrained by zeitgebers (time-givers), light being primary one.

Circadian disruption: Voigt et al., Alcohol Res 2013:35:87-96

Considering that sleep is a state that negates gathering of nutritional resources, precludes active social interaction, and renders vulnerability to predation, it is perhaps the most perplexing of all organismic behaviors. On these grounds, there should have been significant evolutionary pressure to select against such a brain and behavioral state of apparent inactivity (Abel et al., Current Biol 2013).

Functions of sleep

- Energy-saving function
- Restoration of energy resources and repairing of cell tissue
- Thermoregulation
- Metabolic regulation
- Adaptive immune function

Sleep definition: Natural and reversible state of reduced responsiveness and relative inactivity, accompanied by a loss of consciousness.

Sleep is important for brain plasticity (from the Greek word ‘plastos’ meaning molded - refers to the extraordinary ability of the brain to modify its own structure and function following changes within the body or in the external environment.)

Role of sleep in mood regulation

The Yin and Yang of Sleep and Attention
Knaftskii & Selinodin; Trends in Neurosciences 2015
Effects of sleep deprivation

Acute: Mood changes including irritability, difficulty concentrating, sleepiness, fatigue, disorientation – perceptual distortions and hallucinations – paranoid thoughts (up to 112 hours)

Psychomotor impairment: Long, monotonous, without feedback, externally paced, newly learned and have a memory component (Driving)

Sleep restriction as the fundamental duration of sleep below which waking deficits accumulate.

Chronic (sleep disorders, work schedules and modern lifestyle): Cognitive performance and inability of subject to perceive actual deficits. Sleep propensity, driving safety, mood and physiologic conditions (obesity, increased mortality less than 6.5 hrs/night, increased coronary events, altered immune response to vaccination)

Prolonged: Animals deprived of sleep for several weeks show temperature and weight dysregulation and ultimately die of infections and tissue lesions

Understanding of sleep as a brain state

Awake state

• Restorative sleep

NREM sleep

• Memory consolidation

REM sleep

• Mood regulation

Neurobiology of sleep-wake states

(Espana and Scammell. SLEEP 2011;34(7):845-848)

• Diffuse array of neurons within the brainstem, BF and hypothalamus that project to the cortex to maintain wakefulness, different sleep states and transitions between states.

• Patterns of EEG activity and consciousness arise from subcortical systems, thalamus and cortex.

• Many arousal systems (Ach, NE, HA, DA, 5-HT and orexin) can independently promote wakefulness but they work together. Injury to one rarely causes loss of wakefulness.

• Each arousal system important in specific aspects of behavioral arousal
  - NE, HA and Ach enhance attention and responding to novel, stressful stimuli.
  - DA particularly when individual is physically active or motivated.
  - Orexin sustaining wakefulness.
Normal sleep

- SWS serves as an offline period during which newly encoded hippocampal declarative memories are encoded into neocortical knowledge networks.
- Rather than providing a passive storage, memories that have relevance for an individual's future are actively consolidated.

“... particularly intriguing aspect of the latter function is that sleep appears to prime the transformation of implicitly encoded information into explicit knowledge, i.e. something that is not conscious before sleep enters consciousness through sleep.”

Sleep and brain plasticity and emotional regulation (Walker M. Ann NY Acad. Sci 2009)

Brain plasticity
- Refers to the ability of the brain to modify its structure and function according to genetic information and environmental changes.
- Role in neural development: REM sleep occupies a large portion of time during early development and the amount of REM sleep declines to a low adult level when rapid brain maturation is completed (newborns more than 50% of 16-18 hours sleep is occupied by REM sleep). REM sleep-deprived animals show reductions in brain cortex and long-lasting changes such as weight, despair and alcohol dependence. REM sleep important in consolidation of visual traces during critical periods of experience-dependent cortical plasticity in vivo.

Emotional regulation
- Sleep deprivation associated with instability and increased volatility.

Why do we sleep? Namely "you should sleep on problem" and when troubled "get to bed, you will feel better in the morning."
Sleep in the 21st century

• What is adequate sleep?

• What is optimal sleep quality?

• What is optimal sleep schedule?

What is adequate duration of sleep?

Technological evolution and human sleep
Sleep durations in the current millennium

<table>
<thead>
<tr>
<th>Age</th>
<th>Sleep Needs</th>
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</thead>
<tbody>
<tr>
<td>Newborns (0 to 2 months)</td>
<td>10.5 to 14.0 hours</td>
</tr>
<tr>
<td>Infants (3 to 11 months)</td>
<td>8.5 to 11.0 hours</td>
</tr>
<tr>
<td>Toddlers (1 to 3 years)</td>
<td>7.0 to 8.0 hours</td>
</tr>
<tr>
<td>Preschoolers (4 to 5 years)</td>
<td>7.0 to 10.0 hours</td>
</tr>
<tr>
<td>School-aged Children (6 to 12 years)</td>
<td>8.5 to 9.5 hours</td>
</tr>
<tr>
<td>Teens (13 to 17 years)</td>
<td>9.5 to 10.5 hours</td>
</tr>
<tr>
<td>Adults</td>
<td>7.0 to 9.0 hours</td>
</tr>
<tr>
<td>Older Adults</td>
<td>7.0 to 9.0 hours</td>
</tr>
</tbody>
</table>

National sleep foundation surveys of sleep habits

<table>
<thead>
<tr>
<th>Number of Hours Slept per Night on Weekdays (past two weeks)</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 6 hours</td>
<td>23%</td>
<td>24%</td>
<td>24%</td>
<td>24%</td>
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<tr>
<td>6 to 8 hours</td>
<td>31%</td>
<td>31%</td>
<td>31%</td>
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</tr>
<tr>
<td>8 or more hours</td>
<td>45%</td>
<td>45%</td>
<td>45%</td>
<td>45%</td>
</tr>
<tr>
<td>Mean (h of sleep)</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>Median (h of sleep)</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
</tr>
</tbody>
</table>

What is optimal quality of sleep?
Optimal quality of sleep

• Difficult to ascertain with any objectivity

• Often understood in the context of disorders that disrupt sleep and lead to disease

  - Sleep apnea
  - Myriad other disorders of sleep disruption and sleep deprivation (restless legs syndrome, insufficient sleep, disorders of sleep regulation such as narcolepsy, parasomnias etc.)

Measuring sleep in the laboratory: POLYSOMNOGRAPHY

Obstructive sleep apnea
Sleep apnea: high prevalence and morbidity

- Disease affecting nearly 10-30% of adults
- Snoring a cardinal symptom
- Affects virtually organ system within the human body
- Associated with wide-ranging problems: research focused on
  - Cardiovascular disease
  - Metabolic syndrome
  - Neurodegenerative disease
  - Risk of cancer

Trend towards testing for sleep apnea at home and therapy with CPAP

What is optimal sleep schedule?
Mammalian clocks: genetic bases

Central and peripheral clocks
Circadian rhythm genes comprise of up to 3-10% mRNA transcription within cells.

Circadian disruptions in chronic disease
Dysynchronisation / Disruption / Decay of circadian system

Trends Endocrinol Metab 2013;24:229
Impact of Shift Work Disorder

- Decreased alertness and cognitive functioning
- Cardiovascular disease: Hypertension and CAD
- Gastrointestinal issues
- Mood disorders
- Cancer

Conclusion

- Sleep an important pillar of health and prevention of disease
  - Brain function (Memory, mood and personality)
  - Prevention of cardiovascular, neurologic, immunologic and metabolic disease

Sleep health as important maintenance of physical function and nutrition: active efforts to understand personal sleep patterns to improve overall health.