How do we measure sleep in humans and animals?

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Summer SWIM:
Sleep and Circadian Workshop on Indispensable Methods
August 10-14, 2020
Measuring sleep in humans

- “A recurring, reversible neuro-behavioral state of relative perceptual disengagement from and unresponsiveness to the environment.
- Sleep is typically accompanied (in humans) by postural recumbence, behavioral quiescence, and closed eyes.”

Carskadon & Dement, PPSM, 2005.
Lots of methods out there! What’s your question? Your budget? Is it for clinical or research purposes?

Ibáñez (2018) PeerJ
Sleep Health Framework

Sleep health is a multidimensional pattern of sleep-wakefulness, adapted to individual, social, and environmental demands, that promotes physical and mental well-being. Buysse, *SLEEP*, 2014

**SLEEP HEALTH DIMENSIONS: RU-SATED**

1. Regularity
2. Satisfaction
3. Alertness
4. Timing
5. Efficiency
6. Duration
Self-Report Questionnaires

- Rely on subjective reports
  - Bias and demand characteristics, and retrospective accuracy, as with all self-report measures
  - However, perceptions are important!

<table>
<thead>
<tr>
<th>Sleep questionnaire</th>
<th>Acronym</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini Sleep Questionnaire</td>
<td>MSQ</td>
<td>Insomnia and hypersomnia</td>
</tr>
<tr>
<td>Pittsburgh Sleep Quality Index</td>
<td>PSQI</td>
<td>Sleep quality and patterns of sleep in adults</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale</td>
<td>ESS</td>
<td>Level of daytime sleepiness. Average sleep propensity in daily life</td>
</tr>
<tr>
<td>Insomnia Severity Index</td>
<td>ISI</td>
<td>Nature, severity, and impact of insomnia. Treatment response in adults</td>
</tr>
<tr>
<td>Sleep Disorders Questionnaire</td>
<td>SDQ</td>
<td>Sleep disturbance and usual sleep habits during the past month only</td>
</tr>
<tr>
<td>Sleep apnea clinical score</td>
<td>SACS</td>
<td>Sleep apnea</td>
</tr>
<tr>
<td>Functional Outcomes of Sleep Questionnaire</td>
<td>FOSQ</td>
<td>Impact of excessive sleepiness on daily life</td>
</tr>
<tr>
<td>Calgary Sleep Apnea Quality of Life Index</td>
<td>SAQLI</td>
<td>Quality of life associated with sleep apnea</td>
</tr>
<tr>
<td>Oviedo Sleep Questionnaire</td>
<td>OSQ</td>
<td>Insomnia and hypersomnia in the last month</td>
</tr>
<tr>
<td>Berlin Questionnaire</td>
<td>BQ</td>
<td>Sleep apnea</td>
</tr>
</tbody>
</table>
Sleep diary

- Collected daily over multiple days
  - Good and bad days collected
  - Less subject to retrospective recall errors, though still subjective
  - Less reliant on memory as questions completed in the morning upon awakening

- Many different versions exist
  - Pittsburgh Sleep Diary (Monk et al., 1994)
  - Consensus Sleep Diary (Carney et al., 2012)
    - Developed during the 2005 Pittsburgh Assessment Conference (Buysse et al., 2006)
  - Diaries can be completed via paper, or electronically (better accuracy)
  - Now, many sleep tracking apps also exist
### SLEEP DIARY

<table>
<thead>
<tr>
<th></th>
<th>Noon</th>
<th>p.m.</th>
<th>Evening</th>
<th>Midnight</th>
<th>a.m.</th>
<th>Morning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
<td></td>
<td>12</td>
<td>1</td>
<td></td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>M</td>
<td>T</td>
<td>W</td>
<td>Th</td>
<td>F</td>
<td>Sa</td>
<td>Su</td>
</tr>
</tbody>
</table>

**Instructions:** Use the symbols below to indicate your sleep times in the grid. Rate your sleep quality each night from 0 (poor) to 10 (excellent).

- \( \downarrow \) = Go to bed
- \( \uparrow \) = Get out of bed
- \( \_ \) = Actual sleep
- Blank = Awake

**Comments**

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
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</tbody>
</table>
Actigraphy

- **Objective measure – most of the time**
  - …but of activity, not sleep per se
  - Uses accelerometers in the X, Y, Z plane to get activity counts
  - Algorithm to detect sleep vs. wake
    - Still may require extensive cleaning / processing of data, which sometimes feels more art than science.

- **Commercial devices now widely available**
  - Validation studies?
    - Underestimate sleep disruptions and overestimate total sleep time and sleep efficiency in normal subjects
  - Proprietary sleep detection algorithms (that can change over time)
  - May not be possible to extract the raw activity data
Actigraphy: Is it accurate for detecting sleep / wake?

- **Sensitivity:**
  Ability to correctly identify sleep

- **Specificity:**
  Ability to correctly identify wake

<table>
<thead>
<tr>
<th></th>
<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>P-value</td>
<td>Estimate</td>
</tr>
<tr>
<td>Overall</td>
<td>0.865</td>
<td>n/a</td>
<td>0.965</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.854</td>
<td>0.428</td>
<td>0.962</td>
</tr>
<tr>
<td>Female</td>
<td>0.893</td>
<td></td>
<td>0.971</td>
</tr>
<tr>
<td>Time of Sleep</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day</td>
<td>0.866</td>
<td>0.105</td>
<td>0.972</td>
</tr>
<tr>
<td>Night</td>
<td>0.865</td>
<td></td>
<td>0.963</td>
</tr>
<tr>
<td>Insomnia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.833</td>
<td>0.516</td>
<td>0.946</td>
</tr>
<tr>
<td>No</td>
<td>0.869</td>
<td></td>
<td>0.967</td>
</tr>
</tbody>
</table>

These models are adjusted for age. The findings for age are presented in Figure 2. The P-values for the effect of age on accuracy, sensitivity and specificity were not significant.

Marino et al. (2013). *SLEEP.*

For commercial devices:
Sensitivity reported is in the interval 86%–98%,
Specificity is in the interval 20%–54%
Polysomnography (PSG) – “the gold standard”
Stages of Sleep

- Relaxed wakefulness
- Alpha waves

Stage N1
- Theta waves
- K-complex

Stage N2
- Sleep spindles

Stage N3
- Delta waves

REM or dreaming sleep

Hypnogram
- PSG needed to diagnose certain sleep disorders
  - Periodic Limb Movements
  - Sleep apnea
  - Narcolepsy

- Sleep architecture
  - Macrostructure
    - Sleep stages
      - Non-REM: N1, N2, N3
      - REM
  - Microstructure
    - Arousals
    - Sleep spindles
    - Etc.
Polysomnography - Cons

- More invasive / high burden for the participant

- Expensive
  - Equipment
  - Staff involvement
    - Collect the studies (overnight!)
    - Score & process, and manage the data

- EEG is mainly a measure of cortical activity, and does not measure sub-cortical sleep generating regions.
Polysomnography-PET studies: Design

PET Scans and EEG

State
Awake
Sleep

Location
Bedroom
PET Center

Time (min)
-20 0 20 40 60 80 100

Emission scans
Transmission scan
Venous blood samples

Stage 2 NREM
18F-FDG injection
Maximum 18F-FDG uptake

Sleep Onset
0800
2300
0800

PET = Positron Emission Tomography

Nofzinger, Brain Res Protocols, 1998
Hyperarousal: Whole Brain Metabolism during Wake and NREM Sleep in Normal Controls & Insomnia Patients

Whole brain metabolism

State: F=31.5, p<0.001
Group: F=6.79, p=0.017
State by Group Interaction: F=0.77, p=0.39

Nofzinger, Am J Psychiatry, 2004