Beyond PSG: Sleep Assessment Endpoints, Considerations and Recommendations

A Physician-Engineer's Perspective

Justin Brooks, M.D., Ph.D.

Academic Appointments

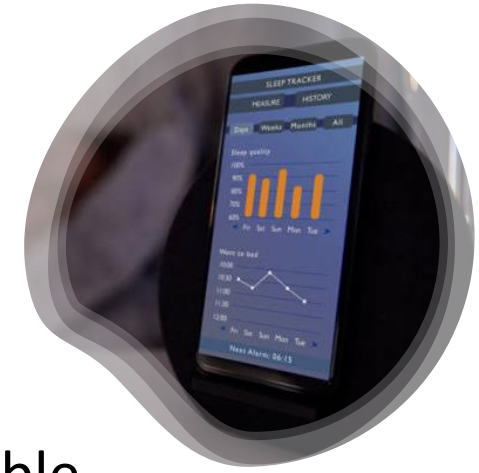
- Associate Professor, Department of Computer Science and Electrical Engineering, UMBC
- Director of Entrepreneurship and Creative Director, University of Maryland, Institute for Health Computing

UNIVERSITY OF MARYLAND
INSTITUTE FOR HEALTH COMPUTING
MPOWERING THE STATE

Company Affiliations

- D-Prime LLC, Scientific Advisor
- Tanzen Medical Inc, Scientific Advisor
- Clinilabs Inc., Scientific Advisory Board Member

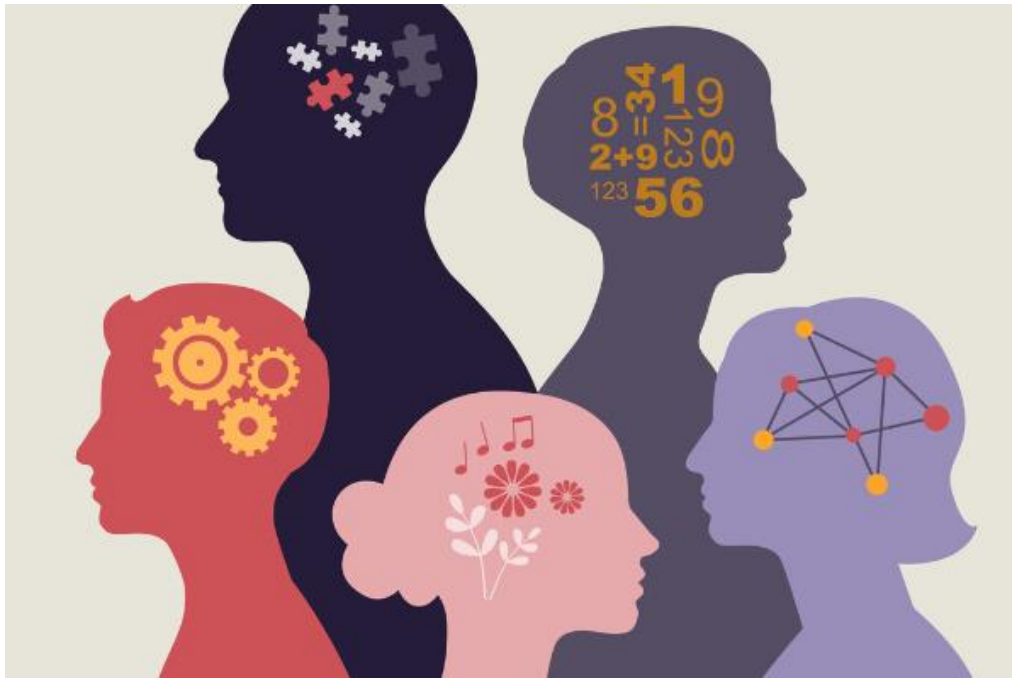
Quantifying Sleep is Challenging



- **Polysomnography** – Invasive, questionable ecological validity, noisy data
- **Wearables** – mostly wrist worn (why?) although some emerging for EEG and leg movements – more on this
- **Sleep Diaries** – one of the gold standards for sleep assessment especially in clinical trials because of its subjective nature, but questionable construct validity - we are looking at an impression of a phenomenon

Regardless, we have endpoints to meet

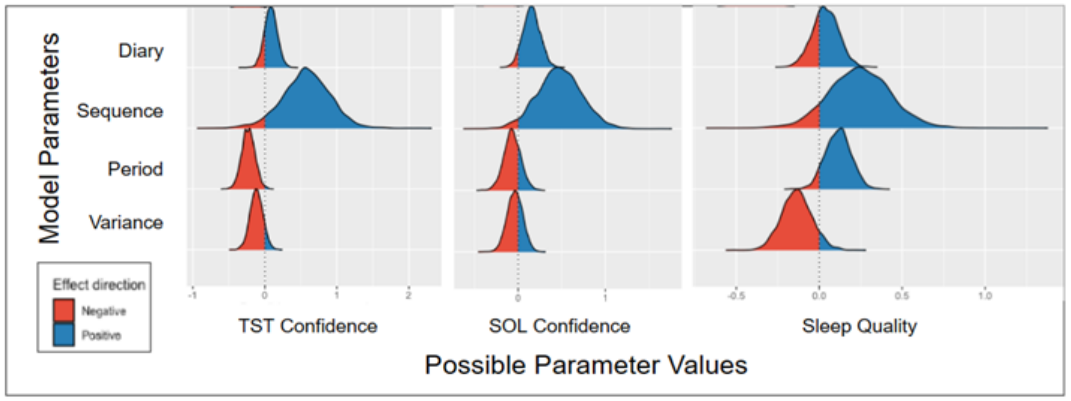
- As currently done, PSG is often prohibitively expensive and not practical for pivotal trials
- Outside the lab, especially in neurodiverse populations, sleep assessment can be enormously challenging
  - Irregular sleeping schedules, non-traditional sleeping arrangements – SMS example
  - Tactile sensitivity/variable ability to report



Consideration 1 – Signal Averaging

- In signal processing, it is mathematically guaranteed that averaging two signals in the time domain that have uncorrelated sources of noise will lead to a better underlying estimate
- In terms of sleep we can think about the human and device as two ‘sensors’ of sleep
- By combining them we can have a better estimate of the underlying ‘true’ value

$$\sigma_{n,avg}{}^2 = \frac{1}{M^2}\sum_{j=1}^{M}\sum_{j=1}^{M} E\left(n_j(p)n_j(p)\right) = \frac{1}{M^2}M\sigma_n{}^2 = \frac{\sigma_n{}^2}{M}$$



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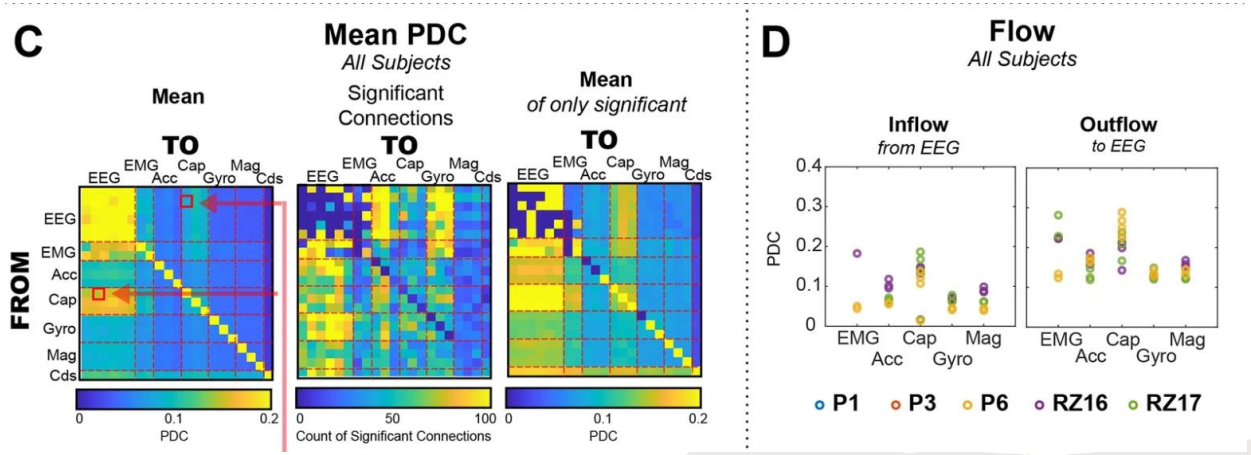
Consideration 2: Move beyond convention

- Wearable devices offer the opportunity to gather lots of sensor-based data
- However, they must be used properly and should make sense physiologically
- In our studies, using a leg monitor to assess sleep has been useful in pediatric and Alzheimer's patients where out of sight = out mind
- Beyond this, it makes sense physiologically, as leg movements and not arm movements are more closely tied to sleep mechanisms



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Call to Action

- Sleep is presents an enigma to therapeutic developers because there are limited options to get quality, reliable, and valid measures that will be accepted by FDA – especially true in neurodiverse populations
- For now, consider using multiple sources of sleep assessment and combining them in an intelligent way – e.g. combinations of wearables, PSG, data
- Consider the neurophysiology of sleep and take a hard look at the devices and assessment tools you consider using
- As a field, it's time that we look at Drug Development Tool Pathway and others to crystallize an approach to its assessment.