Sleep & Delirium in the ICU: What is the Relationship?

Karen J. Bosma, MD, FRCPC
Associate Professor, Department of Medicine, Division of Critical Care Medicine
Disclosures

None relevant to this talk
What we don’t know

What we know
Outline

1. Sleep and Brain Function: Neurobiology
2. Sleep deprivation looks like delirium… but is different
3. Sleep disruption is associated with delirium
   - Does sleep deprivation cause delirium or does the dysfunctional brain not sleep?
4. Can promoting sleep reduce delirium?
Outline

1. Sleep and Brain Function: Neurobiology
2. Sleep deprivation looks like delirium… but is different
3. Sleep disruption is associated with delirium
   • Does sleep deprivation cause delirium or does the dysfunctional brain not sleep?
4. Can promoting sleep reduce delirium?
Why do we sleep?

“Sleep drives metabolite clearance from the adult brain”

- During natural sleep or anesthesia,
  - 60% increase in interstitial space
  - Increased convective exchange of CSF with interstitial fluid
  - Increased rate of β-amyloid clearance during sleep
  - Enhanced removal of potentially neurotoxic waste products that accumulate in the CNS during wakefulness
1) Wakefulness is associated with synaptic potentiation in several cortical circuits
2) Synaptic potentiation is tied to the homeostatic regulation of slow wave activity
3) Slow wave activity is associated with synaptic downscaling
4) Synaptic downscaling is tied to the beneficial effects of sleep on neural function and indirectly on performance
Slow Wave Sleep
Stage N3 (deep sleep)

- minimum of 20% delta waves (0.5–2 Hz), hardest to arouse
- Thought to be important for declarative memory processing (facts and knowledge)

REM Sleep

- Rapid eye movements, low amplitude, mixed frequency EEG
- Accounts for 18-22% of total sleep time
- Elaborate, vivid dreams occur
- Loss of skeletal muscle tone
- Thought to be important for consolidation of procedural memory (learning complex tasks)
Sleep Electrophysiology

Stage N1

- Transition from alpha waves (8–13 Hz) (common in the awake state) to theta waves (4–7 Hz)
- Loss of some muscle tone and most conscious awareness of the external environment; Low arousal threshold

Stage N2

- sleep spindles (11-16 Hz) and K-complexes
- EMG muscular activity decreases
- conscious awareness of the external environment disappears; Harder to arouse
- occupies 45–55% of total sleep in adults
Outline

1. Sleep and Brain Function: Neurobiology
2. Sleep deprivation looks like delirium… but is different
3. Sleep disruption is associated with delirium
   • Does sleep deprivation cause delirium or does the dysfunctional brain not sleep?
4. Can promoting sleep reduce delirium?
Sleep Deprivation Research

• 1896 – First sleep deprivation study in humans
  – 1 assistant professor and 2 instructors kept awake 90 hours
  – Visual hallucinations in 1 subject
  
  Patrick and Gilbert, Psychol Rev 1896;3:469-483

• 1955 – 275 Military
  – 112 hours of total sleep deprivation (TSD)
  – Few instances of behaviour resembling acute schizophrenia
  
  Tyler, Dis Nerv Syst 1955;16:293-299

• Perceptual illusions, transient hallucinations, depersonalization most common symptoms
Case: Randy Gardner

- Stayed awake 11 days, 25 minutes (264.4 hours)
- Dec. 28, 1963 to Jan 8, 1964, San Diego, CA
- Stanford sleep researcher Dr. William C. Dement, Lt. Cmdr John J. Ross attended

Bruce McAllister (left) and Joe Marciano Jr. (right) help Randy Gardner stay awake as he gets a checkup at the naval hospital
Psychiatric and EEG Observations on a Case of Prolonged (264 Hours) Wakefulness

GEORGE GULEVICH, MD; WILLIAM DEMENT, MD; AND LAVERNE JOHNSON, PhD, SAN DIEGO, CALIF

Day 0

Day 3

Day 6

Day 9

Day 11

90 hr: illusion

Irritability, ↑suspiciousness, resentment

“waking dreams”, lapses of memory, ↓awareness of environment

Psychiatric interview

“No delusions, hallucinations, or delirium”
Continuous plots of the EEG stages during the first recovery night, represented by the upper two plots (a table of 14 hours, 40 minutes); and one week postrecovery represented by the bottom plot (about seven hours totally). Stage 1 represents REM sleep. The thick bars above Stage 1 indicate the relatively stable REM periods. Note the instability of the REM periods during the first recovery night, with frequent alternations between REM and awake (A), and between REM and Stage 2.
Lessons: Randy Gardner

TSD 11 d not sufficient to induce psychosis
Co-morbid disposition likely necessary
Further studies examined selective REM deprivation
REM rebound, SWS loss not cumulative

• Complete return to normal after 2 nights sleep

Sleep deprivation record-holder
Randy Gardner on “To Tell the Truth” (May 11, 1964)
Sleep Deprivation

- Inattention
- Delusions
- Hallucinations
- Impaired memory
- Slurred speech
- Discoordination
- Moodiness/ irritability
- Decreased reaction time
- Complete recovery after sleep

Delirium

- Inattention
- Delusions
- Hallucinations
- Fluctuating mental status
- Incoherent thought and speech
- Reduced awareness of environment
- Hyper or hypoactive
- Longterm neurocognitive sequelae in some patients
Sleep deprivation may be just one of “multiple insults” to the brain, thereby amplifying risk of delirium (hypothesis).

**Diagram:**
- **Direct Effect on the Brain:** Medications, Dementia, Sepsis, Head trauma, Advanced age, Alcoholism
- **Stress Response:** Critical illness, Mechanical ventilation, Pain, Sepsis
- **ICU Environment:** Noise, Light/Circadian disruption, Patient care activities, Stress and sensory deprivation

*Weinhouse et al. Critical Care 2009, 13: 234*
Outline

1. Sleep and Brain Function: Neurobiology
2. Sleep deprivation looks like delirium… but is different
3. Sleep disruption is associated with delirium
   - Does sleep deprivation cause delirium or does the dysfunctional brain not sleep?
4. Can promoting sleep reduce delirium?
The correlation between sleep deprivation and the intensive care unit syndrome

- 62 patients
- Mental status exam q8h
- Sum of 3 scores
- 15 min interval blocks
- √ if interruption
- 75 min of uninterrupted time considered 1 potential cycle
- % of normal sleep at home

Disorientation to:
- place (city or type of institution) 1 point
- time (year only) 1 point
- person (self) 2 points

Combativeness
- Hallucinations (auditory or visual) 3 points
- Paranoia (patient states that staff is trying to do him harm) 4 points
- Delusions (patient indicates that he is another person or is performing an inappropriate task) 4 points
Number of patients with mental status changes

- No sleep deprivation: 37
- Moderate <50% sleep deprivation: 8
- Severe >50% sleep deprivation: 7

- No changes
- Some mental status changes
• 29 mechanically ventilated patients in surgical ICU
• Twice daily CAM-ICU
• PSG performed once weaning was initiated
• Strata: REM <6% vs. REM ≥6% of TST
Number of Patients with and without Delirium

- REM <6%: 73%
- REM >=6%: 7%

P<0.05
Risk Factors for REM <6%

- Multivariable analysis:
- Delirium prior to PSG
- Daily dose of lorazepam
• Adult MS-ICU patients
• PSG 10 pm-10 am, sleep physician blinded to delirium score
• Delirium assessment:
  – ICDSC bedside RN q12 h
  – CAM-ICU by research assistant
• Acute Physiology Score <13
• Glasgow Coma Scale >10
• Receiving minimal sedation
• No history of abnormal EEG
• 21 patients with 11 ± 4 hrs of PSG recording
*p<0.05

- **Sleep Efficiency**
  - Non-Delirious: 60%
  - Delirious: 40%

- **Sleep Maintenance Efficiency**
  - Non-Delirious: 70%
  - Delirious: 50%
Figure 5. Characteristic Hypnograms

(a) Delirious, Primarily Wake, No REM; (b) Delirious, Many Awakenings, some REM; (c) Non-delirious, More REM, More SWS; (d) Non-delirious, Consolidated sleep, REM rebound
Associations: Delirium

• Inability to consolidate sleep
• Multiple awakenings, more stage 1 light sleep
• Extended sleep period, equal TST
• Reduced sleep maintenance efficiency
• Limitation: 24 hr PSG would enhance data but was not possible due to daily activities
Outline

1. Sleep and Brain Function: Neurobiology
2. Sleep deprivation looks like delirium… but is different
3. Sleep disruption is associated with delirium
   • Does sleep deprivation cause delirium or does the dysfunctional brain not sleep?
4. Can promoting sleep reduce delirium?
Outline

1. Sleep and Brain Function: Neurobiology
2. Sleep deprivation looks like delirium… but is different
3. Sleep disruption is associated with delirium
   • Does sleep deprivation cause delirium or does the dysfunctional brain not sleep?
4. Can promoting sleep reduce delirium?
Can promoting sleep reduce ICU delirium?

• RCT: Use of ear plugs – improved subjective sleep quality and reduced delirium
  
  Van Rompaey, Crit. Care, 2012

• Pre-post intervention study of multi-factorial sleep promotion bundle... subjective sleep quality unchanged but delirium incidence reduced
  
  Kamdar Crit Care Med 2013; 41:800–809
Can promoting sleep reduce ICU delirium?

• RCT: Nocturnal Dexmedetomidine  
  Skrobik, AJRCCM 2018;197(9):1147-1156

• Associated with a greater proportion of patients who remained delirium-free during the ICU stay  
  – [40/50 (80%)] vs. placebo [27/50 (54%)]; RR 0.44; 95% CI, 0.23–0.82; P= 0.006)

• Leeds Sleep Evaluation Questionnaire score similar  
  – (mean difference, 0.02; 95% CI, 0.42–1.92) between the 34 dexmedetomidine and 30 placebo patients able to provide one or more assessments.
Self-report vs PSG

- Patient perception of sleep quality may be related to time asleep, sleep latency, wake after sleep onset
- Delirium may be associated with micro-arousals/sleep fragmentation/REM/SWS
- How we measure sleep is important:
  - Patient experience and insight important
  - Polysomnography also revealing
Summary

• Human brains need sleep
• Sleep disruption in the critically ill can be severe and is characterized by:
  – Sleep fragmentation
  – Abnormal circadian rhythms
  – Increased light sleep (stage N1 and N2)
  – Decreased deep sleep (stage N3 or “slow wave sleep”) and REM sleep
• Sleep disruption appears to be associated with delirium
• Causal relationship not clearly established; however several interventions to improve sleep have demonstrated reduced delirium... even though improvement in sleep was not measured
• The interplay of medications, critical illness, cerebral perfusion, sleep and delirium is complex, but an important area of current research
THIS IS A BRAIN

THIS IS A BRAIN

WITHOUT SLEEP.

ANY QUESTIONS?