The Relationship & Importance of Sleepiness and OSA

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Conflict of Interest Disclosures

1. I do not have any potential conflicts of interest to disclose, OR

2. I wish to disclose the following potential conflicts of interest:

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Details of Potential Conflict</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td>J.B Hunt Sleep Apnea Research Project</td>
</tr>
<tr>
<td>Consultant</td>
<td>UCB Pharma</td>
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<tr>
<td>Speakers’ Bureaus</td>
<td></td>
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<tr>
<td>Financial Support</td>
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<tr>
<td>Other</td>
<td>Chief Medical Officer, Fusion Health</td>
</tr>
</tbody>
</table>

3. The material presented in this lecture has no relationship with any of these potential conflicts, OR

4. This talk presents material that is related to one or more of these potential conflicts, and the following objective references are provided as support for this lecture:

1. 

2. 
Sleepiness ≠ Fatigue

- **Fatigue**: weariness from bodily or mental exertion

- **Sleepiness**: a readiness or inclination to sleep
Sleepiness

• Sleepiness: leads to falling asleep or……
  • Micro-sleeps
  • Errors of Commission
  • Errors of Omission

• Sleep Deprivation: is 1 cause of Sleepiness
  • Poor Executive Function … planning, sequencing
  • Erratic Emotional Function … anger, rage, down
  • Problems with Memory … retrieval, multi-task
When Your Brain Gets Sleepy

Normal Activity & Preserved Performance

Loss of Activity & Loss of Performance

(Adapted from, Drummond et al., NeuroReport, 1999)
When a Driver Gets Sleepy

- Motor vehicle crashes are leading cause of injury, morbidity, and mortality

- In US, more than 40,000 deaths and 6 million injuries occur from motor vehicle accidents every year\(^1\)

- Sleep-related accidents comprise 15-20% of all motor vehicle crashes\(^2\)

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When Any Operator Gets Sleepy

Planes (Buffalo 2009)

Trains (Boston 2009)

Buses (Oakland, TX 2009)

Ships (1989)

Oil Rigs (2010)
Remember: Sleepiness is a Symptom
Causes of Sleepiness

- Quantity of Sleep
- Quality of Sleep
- Disorder of Wakefulness
Causes of Sleepiness

- **Quantity of Sleep**
  - Inadequate sleep hygiene
  - Circadian timing of sleep
  - Sleep delays related to primary sleep disorders

- **Quality of Sleep**

- **Disorder of Wakefulness**
Quantity of Sleep

Map depicts age-adjusted percentage of adults who reported 30 days of insufficient rest or sleep during the preceding 30 days.

- Behavioral Risk Factor Surveillance System, United States 2008, CDC
Age-adjusted prevalence of adults aged ≥20 years reporting sleep-related difficulty carrying out selected activities, by usual sleep duration

- *National Health and Nutrition Examination Survey, United States, 2005—2008, CDC*
Causes of Sleepiness

- **Quantity of Sleep**
  - Inadequate sleep hygiene
  - Circadian timing of sleep
  - Sleep delays related to primary sleep disorders

- **Quality of Sleep**
  - Sleep-disordered breathing (Sleep Apnea)
  - Restless Legs Syndrome/Periodic Limb Movements
  - Sleep Fragmentation (sleep, medical & psychiatric disorders)

- **Disorder of Wakefulness**
Quality of Sleep

Brain Arousal
Brain Arousal = Fight or Flight

Releases “Stress” Hormones

Elevated Blood Pressure & Heart Rate

Sympathetic Over-activity = Cardiovascular Disease

HYPERTENSION & HEART DISEASE
Brain Arousal = Fight or Flight

Glucose Released Into Bloodstream

↓ ↓ ↓ ↓ ↓

Weight Gain & Obesity

Sympathetic Over-activity = Unregulated Insulin Response

DIABETES

OBESITY
Obesity Epidemic in the US

Source: Centers for Disease Control and Prevention; www.cdc.gov
Sleepiness Epidemic in the US

Map depicts age-adjusted percentage of adults who reported 30 days of insufficient rest or sleep during the preceding 30 days.

- Behavioral Risk Factor Surveillance System, United States 2008, CDC
Causes of Sleepiness

- **Quantity of Sleep**
  - Inadequate sleep hygiene
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- **Quality of Sleep**
  - Sleep-disordered breathing (Sleep Apnea)
  - Restless Legs Syndrome/Periodic Limb Movements
  - Sleep Fragmentation (sleep, medical & psychiatric disorders)

- **Disorder of Wakefulness**
  - Narcolepsy
  - Neurological diseases/injury
  - Idiopathic hypersomnolence
Detecting Sleepiness

- Subjective Tests
- Objective Tests
Detecting Sleepiness

- **Subjective Tests**
  - Epworth Sleepiness Scale
  - Stanford Sleepiness Scale
  - Pictorial Sleepiness Scale
  - Others

- **Objective Tests**
# Epworth Sleepiness Scale

<table>
<thead>
<tr>
<th>Situation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Watching TV</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Sitting inactive in a public place</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Passenger in a car for an hour without a break</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Lying down to rest in the afternoon when circumstances permit</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>Sitting quietly after a lunch without alcohol</td>
<td>0 1 2 3</td>
</tr>
<tr>
<td>In a car, while stopped for a few minutes in traffic</td>
<td>0 1 2 3</td>
</tr>
</tbody>
</table>

- **(0-10)**
- **(10-15)**
- **(>15)**

Stanford Sleepiness Scale

Using the scale below, indicate the single number that best describes your level of alertness or sleepiness at each time:

1 = Feeling active, vital, alert, or wide awake
2 = Functioning at high levels, but not at peak; able to concentrate
3 = Relaxed, awake but not fully alert; responsive
4 = A little foggy
5 = Foggy, beginning to lose track; having difficulty staying awake
6 = Sleepy, woozy, fighting sleep; prefer to lie down
7 = Cannot stay awake, sleep onset appears imminent

Pictorial Sleepiness Scale

(Maldonado et al, Sleep 2004;27(3):541-8)
### PEDIATRIC DAYTIME SLEEPINESS SCALE

If you are in school, please answer the following questions as honestly as you can by circling one answer only:

<table>
<thead>
<tr>
<th>Question</th>
<th>4</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>How often do you fall asleep or get drowsy during class periods?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
| Always                                                                   |    |    |    |    | Never
| Frequently                                                               |    |    |    |    | Never
| Sometime                                                                 |    |    |    |    | Never
| Not often                                                               |    |    |    |    | Never
| Never                                                                   |    |    |    |    | Never
| How often do you get sleepy or drowsy while doing homework?              | 4  | 3  | 2  | 1  | 0 |
| Always                                                                   |    |    |    |    | Never
| Frequently                                                               |    |    |    |    | Never
| Sometime                                                                 |    |    |    |    | Never
| Not often                                                               |    |    |    |    | Never
| Never                                                                   |    |    |    |    | Never
| Are you usually alert most of the day?                                  | 4  | 3  | 2  | 1  | 0 |
| Always                                                                   |    |    |    |    | Never
| Frequently                                                               |    |    |    |    | Never
| Sometime                                                                 |    |    |    |    | Never
| Not often                                                               |    |    |    |    | Never
| Never                                                                   |    |    |    |    | Never
| How often are you ever tired and grumpy during the day?                  | 4  | 3  | 2  | 1  | 0 |
| Always                                                                   |    |    |    |    | Never
| Frequently                                                               |    |    |    |    | Never
| Sometime                                                                 |    |    |    |    | Never
| Not often                                                               |    |    |    |    | Never
| Never                                                                   |    |    |    |    | Never
| How often do you have trouble getting out of bed in the morning?         | 4  | 3  | 2  | 1  | 0 |
| Always                                                                   |    |    |    |    | Never
| Frequently                                                               |    |    |    |    | Never
| Sometime                                                                 |    |    |    |    | Never
| Not often                                                               |    |    |    |    | Never
| Never                                                                   |    |    |    |    | Never
| How often do you fall back to sleep after being awakened in the morning? | 4  | 3  | 2  | 1  | 0 |
| Always                                                                   |    |    |    |    | Never
| Frequently                                                               |    |    |    |    | Never
| Sometime                                                                 |    |    |    |    | Never
| Not often                                                               |    |    |    |    | Never
| Never                                                                   |    |    |    |    | Never
| How often do you need someone to awaken you in the morning?              | 4  | 3  | 2  | 1  | 0 |
| Always                                                                   |    |    |    |    | Never
| Frequently                                                               |    |    |    |    | Never
| Sometime                                                                 |    |    |    |    | Never
| Not often                                                               |    |    |    |    | Never
| Never                                                                   |    |    |    |    | Never
| How often do you think you need more sleep?                              | 4  | 3  | 2  | 1  | 0 |
| Always                                                                   |    |    |    |    | Never
| Frequently                                                               |    |    |    |    | Never
| Sometime                                                                 |    |    |    |    | Never
| Not often                                                               |    |    |    |    | Never
| Never                                                                   |    |    |    |    | Never

**Total score**

### Karolinska Sleepiness Scale

1 = extremely alert  
2 = very alert  
3 = alert  
4 = rather alert  
5 = neither alert nor sleepy  
6 = some signs of sleepiness  
7 = sleepy, but no effort to keep awake  
8 = sleepy, some effort to keep awake  
9 = very sleepy, great effort to keep awake  
10 = extremely sleepy, falls asleep all the time
For Comparison: Fatigue Scales

### Table 2. Fatigue Severity Scale (FSS)

<table>
<thead>
<tr>
<th>Statement</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. My motivation is lower when I am fatigued.</td>
<td></td>
</tr>
<tr>
<td>2. Exercise brings on my fatigue.</td>
<td></td>
</tr>
<tr>
<td>3. I am easily fatigued.</td>
<td></td>
</tr>
<tr>
<td>4. Fatigue interferes with my physical functioning.</td>
<td></td>
</tr>
<tr>
<td>5. Fatigue causes frequent problems for me.</td>
<td></td>
</tr>
<tr>
<td>6. My fatigue prevents sustained physical functioning.</td>
<td></td>
</tr>
<tr>
<td>7. Fatigue interferes with carrying out certain duties and responsibilities.</td>
<td></td>
</tr>
<tr>
<td>8. Fatigue is among my three most disabling symptoms.</td>
<td></td>
</tr>
<tr>
<td>9. Fatigue interferes with my work, family, or social life.</td>
<td></td>
</tr>
</tbody>
</table>

*Patients are instructed to choose a number from 1 to 7 that indicates their degree of agreement with each statement, where 1 indicates strongly disagree and 7, strongly agree.

(Krupp et al., Arch Neurol. 1989;46:1121-23)
Detecting Sleepiness

• **Subjective Tests**
  • Epworth Sleepiness Scale
  • Stanford Sleepiness Scale
  • Pictorial Sleepiness Scale
  • Others

• **Objective Tests**
  • Multiple Sleep Latency Test
  • Maintenance of Wakefulness Test
  • Psychomotor Vigilance Task
  • Driving Simulation
Multiple Sleep Latency Test

Daytime PSG test:

- Five 20 min. naps
- Try to sleep
- 2 hours between naps
- Mean sleep latency
- REM sleep

\[
<5 \text{ min} \quad \text{pathological} \quad 5-8 \text{ min} \quad \text{abnormal} \quad >8 \text{ min} \quad \text{normal}
\]
MSLT: 10 yr Crash Prevalence

Figure 2—Crash prevalence in each MSLT-based sleepiness group for the primary study endpoint—police-verified motor vehicle crashes during the 10-year study assessment period. Cochran-Armitage trend test, P < 0.05

(Drake et al., Sleep, 2010;33(6):745-52)
MSLT: 10 yr Crash Severity

Figure 3—Crash prevalence in each MSLT-defined sleepiness group for single occupant motor vehicle crashes during the 10-year study assessment period. Cochran-Armitage trend test, P < 0.05; *Post hoc χ², P < 0.05; Severe injury accidents were those which “prevent normal activities and require hospitalization.”

(Drake et al., Sleep, 2010;33(6):745-52)
Maintenance of Wakefulness Test

Daytime PSG test:
- Four 20/40 min. tests
- Try to stay awake
- 2 hours between naps
- Mean sleep latency
- REM sleep

19.4 - 26.1 minutes (lower limit of normal)

MWT: Motivation for License

40 min: 75% no sleep

20 min: 90.7% no sleep

Psychomotor Vigilance Test

Test of Alertness:
- 10 minute standard
- PVT-B (3 min version)
- Lab validated tool
- Errors of commission
- Errors of omission
- Response times

(Astronaut Richard Arnold)

Psychomotor Vigilance Test

(Basner & Dinges, Sleep, 2011;34(5):581-91)
Figure 1—Example of the driving performance of a fully alert (upper part) and a sleepy (lower part) patients with obstructive sleep apnea syndrome, showing lane position and crashes (C) over time. The tracings run from left to right and represent the amount of oscillation from the midline of the simulated road over the period of 30 minutes (1800s). Note the overall worse performance of the sleepy patient with a clear deterioration over time of the steering performance associated with crash occurrence.

(Pizza et al., Sleep, 2009;32(3):382-91)
Sleepiness, OSA and Driving

- Sleepiness and OSA
- Sleepiness, OSA and CPAP
Sleepiness, OSA and Driving

- Sleepiness and OSA
  - Causal relationship
  - Association with crashes
- Sleepiness, OSA and CPAP
Sleepiness in OSA: AHI and MSLT

- Sleepiness in OSA is directly associated with overall severity (total AHI) and non-REM severity (non-REM AHI).

AHI Quartiles

<table>
<thead>
<tr>
<th>Category</th>
<th>AHI Quartiles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(8.3 - 29.2)</td>
</tr>
<tr>
<td></td>
<td>(29.3 - 59.8)</td>
</tr>
<tr>
<td></td>
<td>(≥59.9)</td>
</tr>
</tbody>
</table>

- Predictor Variable
  - REM time², minutes: II (1.33 (1.17 - 1.52)), III (1.21 (1.07 - 1.37)), IV (1.28 (1.12 - 1.46))
  - NREM time², minutes: II (1.31 (1.17 - 1.47)), III (1.21 (1.11 - 1.32)), IV (1.30 (1.20 - 1.41))
  - NREM-AHI, events/hr: II (1.21 (1.01 - 1.46)), III (1.20 (1.05 - 1.37)), IV (1.10 (1.04 - 1.16))
  - REM-AHI, events/hr: II (1.01 (0.96 - 1.06)), III (1.02 (0.97 - 1.07)), IV (1.01 (0.96 - 1.05))

(Punjabi N. et al., Sleep, 2002;25(3):307-14)

(Chervin & Aldrich, Sleep, 1998;21(8):799-806)
Sleepiness in OSA: Driving & MWT

• Sleepiness in OSA (severe) vs controls
• PSG; 40 min MWT; 90 min Drive Simulation
• 4 MWT categories (3 OSA; 1 control):
  • 0-19 min (Very Sleepy)
  • 20-33 min (Sleepy)
  • 34-40 min (Alert)
  • Controls
• # of inappropriate lane crossings
  • Significantly more in Very Sleepy and Sleepy vs Controls and Alert

(Phillip et al., Ann Neurol, 2008;64(4):410-6)
Sleepiness in OSA: Crashes

Figure 1—Example of the driving performance of a fully alert (upper part) and a sleepy (lower part) patients with obstructive sleep apnea syndrome, showing lane position and crashes (C) over time. The tracings run from left to right and represent the amount of oscillation from the midline of the simulated road over the period of 30 minutes (1800s). Note the overall worse performance of the sleepy patient with a clear deterioration over time of the steering performance associated with crash occurrence.

(Pizza et al., Sleep, 2009;32(3):382-91)
Sleepiness, OSA and Driving

- **Sleepiness and OSA**
  - Causal relationship
  - Association with crashes

- **Sleepiness, OSA and CPAP**
  - Effect of treatment
  - Effect of missed treatment
OSA Treatment and Driving Accidents

- Over 3 yrs CPAP reduces driving accidents in OSA patients (from 1.7 to 0.6 accidents/yr)

*Figure 2  Mean (SD) accident rates for (A) patients with OSA during the 3 years before and after treatment with CPAP and (B) control subjects during the same time frame.*

*(George CFP, Thorax, 2001;56:508-12)*
OSA Treatment and Driving Accidents

Figure 3: Distribution of accidents in patients with OSA (A) during the 3 years before and (B) during the 3 years after treatment with CPAP, and in controls during the same time frame (C, D).

66% no accident

85% no accident

(George CFP, Thorax, 2001;56:508-12)
OSA Treatment and Crash Risk

• Meta-analysis of all studies (9) comparing pre-post-OSA treatment for crash risk prior to 2010

• CPAP results in significant improvement in daytime sleepiness *after only 1 night*

![Figure 1—Random-effects meta-analysis of pre-post CPAP crash risk ratio data](image)

(Tregear S et al., Sleep, 2010;33(10):1373-1380)
Missed OSA Treatment and Sleepiness

- Effects of being taken off CPAP for 1 night in patients with OSA
- Assessed sleepiness with PVT, MSLT, SSS before and after withdrawal of CPAP
- Stable CPAP treatment ranged from 30-237 days
- Reversal of benefits demonstrated in objective tests: PVT and MSLT

(Kribbs NB et al., Am J Respir Crit Care Med, 1993;147(5):1162-8)
Missed OSA Treatment and Crash Risk

- Long-term CPAP treated men (50-75 yrs old) tested in driving simulator, KSS and EEG before and after taken off CPAP for 1 night
- Significant increase in driving incidents and both subjective and objective sleepiness
In Summary

Sleepiness has multiple Causes

- **Quantity of Sleep**
  - Eating, TV, Radio, Texting, Phones, Lights
  - Schedule Shifting, Individual Biology of Circadian Rhythms
  - Insomnia – Medical, Psychological, Somnological

- **Quality of Sleep**
  - Sleep Apnea
  - Restless Legs Syndrome/Periodic Limb Movements
  - Sleep Fragmentation (Medical, Psychological, Somnological)

- **Disorder of Wakefulness**
  - Narcolepsy (rare and incompatible with DOT license)
  - Neurological diseases/injury
  - Idiopathic hypersomnolence
In Summary

Sleepiness has multiple Consequences

- **Health**
  - Diabetes/Obesity
  - Mental Stress/Physiological Stress
  - Accidents and Injuries

- **Safety**
  - Errors in Reaction
  - Errors in Judgment
  - Fall Asleep Accidents

- **Expense**
  - Burden on Employers is Rising from ALL angles
  - Sleepiness is Preventable and Treatment Generates ROI
In Summary

Sleepiness has multiple Treatments

• Quantity of Sleep
  • Sleep Hygiene, Light Therapy
  • Maintain Operators on their Best Biological Schedule
  • Treat the Multiple causes of Insomnia

• Quality of Sleep
  • Sleep Apnea must be treated EVERY NIGHT
  • RLS/PLMs must be identified to be treated EVERY NIGHT
  • Sleep Fragmentation is Health Fragmentation

• Disorder of Wakefulness
  • Medical therapies aside from Caffeine are available to treat Sleepiness and can be very effective
Sleep Apnea is Just the Tip of the Iceberg
Thank you

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Light Therapy

Full Spectrum

Blue Wavelength

[Graph showing wavelength distribution]