"Sleeping with the Enemy" Link to Cognitive and Cardiovascular Disease
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Division of Pulmonary
Sleep Medicine
Don’t ever go to sleep, Too many people die there”

Mark Twain
The Temporal Lobe mainly revolves around hearing and selective listening.

It receives sensory information such as sounds and speech from the ears.

It is also key to being able to comprehend, or understand meaningful speech.

This lobe is special because it makes sense of the all the different sounds and pitches (different types of sound) being transmitted from the sensory receptors of the ears.
Engage
OUR Mission is:
Sleep function, regulation and dysfunction

Review Cognition: executive function/performance and sleep issues

Correlate the complex bidirectional relationships of Sleep Disorders and Cardiovascular Disease

Offered Insight for Clinical Practice
What is Sleep

• a periodic, rapidly reversible neuro-behavioral state
What is Sleep

• characterized by almost simultaneous changes in activity patterns and mode of firing of central nervous system neurons and circuits
- Homeostatic
- Circadian
- Central factors

Sleep Drive

Sleep Tendency

CNS and Physiological Arousal

Level of Arousal

- Medications
- Environment
- Time

- Medications
- Environment
Biochemical Pharmacology of Sleep

- Dopamine
- Norepinephrine
- Histamine
- Acetylcholine
- Serotonin
- Interleukin-1
- Adenosine
- Prostaglandins
- Melatonin
- Neuropeptides
- GABA

- Acetylcholine Receptors
- Muscarinic Receptors
- Nicotinic Receptors
- Adrenergic Receptors
- Orexin Receptors
- Serotonergic Receptors
Sleep Flip/Flop Switch

• A periodic, rapidly reversible neuro-behavioral state
• Brain circuitry & neurotransmitter
• Key is in hypothalamus shuts off arousal
• Hypothalamic stabilize the switch
• Ventrolateral preoptic nucleus
• Serotonin, dopamine, noradrenaline, orexin, GABA
Sleep System
Sleep – Wake Regulation

Nighttime sleep

• First part of night- sleep because we have been awake all day (homeostatic drive high)
• Second part of night- sleep because circadian alertness is low

• Daytime wakefulness

• First part of day- awake because We slept at night (homeostatic drive low)
• Second part of day/evening- awake because circadian alertness is high (although sleep drive is building)
**REM vs. nREM Sleep?**

<table>
<thead>
<tr>
<th>Physiologic Variable</th>
<th>NREM</th>
<th>REM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>Regular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>Regular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Regular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Skeletal muscle tone</td>
<td>Preserved</td>
<td>Variable</td>
</tr>
<tr>
<td>Brain 02 consumption</td>
<td>Reduced</td>
<td>Absent</td>
</tr>
<tr>
<td>Ventilatory response</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>Temperature</td>
<td>Normal</td>
<td>Reduced</td>
</tr>
<tr>
<td>Sexual changes</td>
<td>Rare</td>
<td>Poikilothermic</td>
</tr>
</tbody>
</table>

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Meet Your Brain Waves
Beta

• With normal waking consciousness, alertness, logic, critical reasoning
• Majority of adults operate on it

Alpha

• In deep relaxation with eyes closed
• Heightens imagination, visualization, memory learning, concentration
• Gateway to your subconscious
Theta

- In light sleep
- Realm of subconsciousness
- Brief as one drifts to Alpha and awake from Delta
- Vivid visualization and creativity

Delta

- In deep sleep with eyes closed
- Awareness is fully detached
- Process information from unconscious
- Deep healing and regeneration
Sleep the Great Regulator of the Body
What are Sleep Functions

- Regulates Organ functions
- synchronizes hormonal regulation
- Orchestrates repairs
- Maintains cognition executive functions
- Decreases: metabolic rate, sympathetic nervous activity, blood pressure, heart rate
- Increase in cardiac vagal tone
- Growth, detox and repair
Presenting Symptoms that would suggest need for a deeper probe investigation

- **Related to sleep**
  - Unrefreshing or restorative sleep
  - Disturbing snoring
  - Breathing pauses
  - Restless sleep
  - Nocturia
  - Nocturnal sweating
  - Gasping sound
  - Wake suffocating

- **Related to wakefulness**
  - Tiredness
  - Lack of energy
  - Sleepiness
  - Memory impairment
  - Depression
  - Lost interest
  - Sexual dysfunction
  - Headaches
Sleep complaints tee up a clinical evaluation

- Sleep Questionnaire
- Sleep Log or Sleep Diary
- Drug and Alcohol History
- Psychiatric History
- Medical, Cardiac and Neurologic History
- History of Illnesses (admissions)
- Family History
- Psychical Examination
- Medical Test (echo, heart cath)
- Sleep Testing
Sleep dysfunction conditions and issues

1. Insomnia.
2. Sleep Disorders Breathing. (SDB)
3. Hypersomnia.
4. Sleep related movement disorders
5. Parasomnias.
6. Circadian Rhythm Sleep Disorder
### Possible causes of insomnia

<table>
<thead>
<tr>
<th>Headache</th>
<th>Abdominal pains</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bad or vivid dreams</td>
<td>Fever/night sweats</td>
</tr>
<tr>
<td>Problems of breathing</td>
<td>Leg cramps</td>
</tr>
<tr>
<td>Chest pain/heartburn</td>
<td>Fear/anxiety</td>
</tr>
<tr>
<td>Need to pass urine or move bowels</td>
<td>Depression</td>
</tr>
</tbody>
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Sleep Disorder Breathing

• Umbrella term:
  – partial or complete cessation of breathing occurs throughout the night resulting in:
    1. daytime sleepiness or
    2. Fatigue
    3. snoring, pauses in breathing described by bed partners, and disturbed sleep
Signs and Symptoms of Sleep Disorder Breathing (SDB)

- DEPRESSION
- EXCESSIVE DAYTIME SLEEPINESS
- GASPING, CHOKING DURING SLEEP
- IMPAIRED CONCENTRATION
- IRRITABILITY
- MEMORY LOSS/DETERIORATION
- MORNING HEADACHE OR HEADACHE DISORDERS

- NIGHTTIME CHEST PAIN
- FREQUENT NIGHT TIME URINATION
- OBESITY
- POOR JUDGMENT
- RESTLESS SLEEP
- SEXUAL DYSFUNCTION,
- LOW DRIVE OR INTEREST
- SNORING, APNEA
- DIFFICULT TO CONTROL BLOOD SUGAR
Sleep Disorder Breathing (SDB):

The clinical conditions includes:

• obstructive apnea
• obstructed hypopnea
• central sleep apnea
• complex sleep apnea
• upper airway resistance syndrome
• nocturnal hypoventilation syndrome
Sleep related movement disorders

1. Restless Leg Syndrome
2. Periodic Limb Movement Disorder
3. Sleep Related Leg Cramps
4. Sleep Related Bruxism
5. PD, MS, ALS, Seizure
Other possible causes of Sleep Fragmentation

Cough
COPD
Obesity
CVA
CHF
A Fib
Wife or Husband
Pets
Next we will review cognition, executive function/ performance.

And the impact on it by sleep issues
Cognition is: What makes us Human

• It is memory and executive function
Cognition is: **What make us Human**

- Interwoven layers of knowledge allow us to:
  - recognize similarities,
  - see new and old patterns,
  - different perspectives,
  - resolve problems
  - become empathetic
Cognition Changes

• As we age the brain (mind) literally acts differently

• We think differently

• Our brain dries
The Brain needs Neurogenesis - Plasticity

<table>
<thead>
<tr>
<th>1. Improve rapid visual processing</th>
<th>1. Correct executive problems</th>
</tr>
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<tbody>
<tr>
<td>2. Enhanced learning</td>
<td>2. Arrest memory decline</td>
</tr>
<tr>
<td>3. Regain spatial recognition</td>
<td>3. De spam the brain</td>
</tr>
<tr>
<td>4. Cognitive energy</td>
<td></td>
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</tbody>
</table>
What are the types of Memory?

- **Episodic:** specific past events involve the person
- **Implicit:** un-conscious part of memory uses past experience to shape current behavior (loss of inhibition)
What are the types of Memory?

- **Semantic:**
  - store of facts and general knowledge

- **Executive function:**
  - goal directed behavior
Why is Executive Function Important?

- Behavioral inhibition
- Set shifting
- Self regulation & arousal
- Perseveration
- Analysis synthesis

- Working memory
- Abstract thinking
- Conceptualization
- Attention
- Mental flexibility
- Problem solving
- ID Fake News
What happens with Loss Cognition? (ability to reason and remember)

1. MCI:
   - Altered brain speed
   - Altered Neurogenesis (Potholes)
   - Altered hormone regulation

• Memory disorder
• Dementia
• Alzheimer
What does Sleep Dysfunction do to the Brain?

- Fragmentation alters metabolism
- Fatigue alters brain speed and reasoning
- Arousals disrupt brain waves
- Alters neurogenesis and energy
- Cognitive memory impairment
- Increase risk for cerebral microvascular disease
- Alters Toxin removal
Hormonal Regulation with Sleep
Do Sleep Disruptions alter Hormonal Regulation?

- Insomnia.
- Sleep Disorders Breathing. (SDB)
- Hypersomnia.

- Sleep related movement disorders
- Parasomnias.
- Circadian Rhythm Sleep Disorder
Altered Hormonal Regulation

- Central neurotransmitter
- HPA
- Peripheral endocrine gland
- Renin
- Hypothyroidism
- Adrenocorticotrophic
- Corticosteroids
- Aldosterone
- Vasopressin
- Leptin (Satiety +)
- Growth hormone deficiency (sws)
Altered Hormonal Regulation

Leptin (Satiety +)
- powerful respiratory stimulant,
- Elevated with SDB: adaptive mech, leads to resistance
- Hunger
- OBESITY, CHD
- Insulin resistance
- Impaired fibrinolysis

Growth hormone deficiency (sws)
- Pulse secreted mostly in sleep in slow wave,
- Low IGF has vascular endothelial cell receptors,
- Dec nitric oxide = dec vasodilatation
- Impede vascular smooth muscle cell growth
So if sleep impact so much, how about Cardiovascular Diseases. Is there a Bidirectional Relationship between sleep disorders and CVD?
Does SDB predispose, **those at risk** for HTN, CAD, stroke and or HF?

Does CVD and Stroke promote or exacerbate lethal SDB (CSA, CSR)?

Does Tx of both reduce mortality and morbidity?
Some Common Cardiovascular Dysregulations

- Hypertension
- Arrhythmias, A fib
- CAD
- Autonomic dysregulation
- Oxidative stress, endothelial dysfunction
- Pulmonary hypertension
- Congestive heart failure
- Platelet activation, hypercoag, Stroke, TIA
<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Diseases</th>
</tr>
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<tbody>
<tr>
<td>Hypertension</td>
<td>Arrhythmias</td>
</tr>
<tr>
<td>Obesity</td>
<td>A fib</td>
</tr>
<tr>
<td>Diabetes</td>
<td>CAD/MI</td>
</tr>
<tr>
<td>Depression</td>
<td>CHF :</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>• Systolic</td>
</tr>
<tr>
<td>Sleep Disorder Breathing</td>
<td>• Diastolic</td>
</tr>
<tr>
<td></td>
<td>• Sudden death</td>
</tr>
</tbody>
</table>
Sleep Heart Health Study
Sleep disorder breathing and CVD

• Elevated RDI = inc triglyceride + dec HDL

• HTN (diastolic dysfunction)
  – nocturnal HTN more resistant to Tx

• In CHF: 37% with diastolic have OSA
• 30% with systolic have OSA
FIGURE 1. Graph of ambulatory 24-hour blood pressure readings, with nocturnal dip.
Circulation 2012/Wisconsin Sleep Cohort
CVD and Sleep Apnea

In primary HTN: 35%
In CAD: 30%
In HF up to: 58%
With Stroke: 42% (risk post CVA high for 6 months)

Mortality risk: 3.8 x all cause, CV x 5.2 Higher
What are some Vascular effects of OSA

• Intermittent hypoxia • O2 free radical • activation of inflammatory pathways • impaired endothelial fx & inc • BP independent of sympathetic activation

• Hypercoagulability from inc expression of adhesion molecules & vascular smooth muscle proliferation
Figure 1. Pathophysiological effects of OSA on the cardiovascular system.
Pathophysiological effects of OSA on the cardiovascular system.

Obstructive apneas increase left ventricular (LV) transmural pressure (ie, afterload) through the generation of negative intrathoracic pressure (Pit) and elevations in systemic blood pressure (BP) secondary to hypoxia, arousals from sleep, and increased sympathetic nervous system activity (SNA).

Apnea also suppresses the sympathetic inhibitory effects of lung stretch receptors, further enhancing SNA.

The combination of increased LV afterload and increased heart rate (HR) secondary to increased SNA increases myocardial O$_2$ demand in the face of a reduced myocardial O$_2$ supply.

These conditions predispose a patient acutely to cardiac ischemia and arrhythmias, and chronically could contribute to LV hypertrophy and, ultimately, failure. The resultant fall in stroke volume will further augment SNA.
Does CVD and Stroke promote or exacerbate lethal SDB (CSA, CSR)?
Does CVD and Stroke promote or exacerbate lethal SDB (CSA, CSR)?

• Yes they are bidirectional insults
• Chances of having sleep apnea post CVA is 42% for next 6 months
Pathophysiology of central sleep apnea in heart failure (HF).
Pathophysiology of central sleep apnea in heart failure (HF).

HF leads to increased left ventricular (LV) filling pressure. The resulting pulmonary congestion activates lung vagal irritant receptors, which stimulate hyperventilation and hypocapnia.

Superimposed arousals cause further abrupt increases in ventilation and drive PaCO2 below the threshold for ventilation, triggering a central apnea. Central sleep apneas are sustained by recurrent arousals resulting from apnea-induced hypoxia and the increased effort to breathe during the ventilatory phase because of pulmonary congestion and reduced lung compliance.

Although central apneas have a different pathophysiology than obstructive apneas and are not associated with the generation of exaggerated negative intrathoracic pressure, they both increase sympathetic nervous system activity (SNA).

The consequent increases in blood pressure (BP) and heart rate (HR) increase myocardial O2 demand in the face of reduced supply. This chain of events contributes to a pathophysiological vicious cycle.
Figure 3. Schematic representation of the potential bidirectional relationship between obstructive and central sleep apnea sleep (OSA and CSA, respectively), and heart failure (HF). For example, various combinations of intermittent hypoxia, elevated sympathetic nervous system activity (↑SNA), and reduced intrathoracic pressure (↓PIT) could lead to the development or progression of HF, whereas sodium and fluid retention arising from HF could lead to overnight rostral fluid shift into peripharyngeal structures or the lungs and facilitate the development or worsening of OSA and CSA, respectively.
Why worsening nocturnal dyspnea?

Figure 1. Fluid retention in the legs and its rostral shift. Similar to fluid movement from the bottom of the bottle while upright into the neck when horizontal, dependent fluid accumulated in the legs while upright during the day shifts rostrally and could redistribute into the neck or the lungs when recumbent during sleep in response to gravity.
Four Question to Frame Your Assessment of?

Does the patient have HTN, DM, A Fib, Heart Failure
Nocturia, Worsening obesity
And or are which may be resistant to TX

Is there an elevate Stop Bang or Epworth Score
HX of snoring ,hypersomnia
Pending surgery + any combination of any on this page

• Do family members report restless sleep, snore, apnea, irregular breathing
• Personality changes

• Is there a ? of stroke, TIA, MCI, Dementia
• Neurodegenerative disorder, mood disorder (depression, bipolar, or anxiety issues)
**Four Question to Frame Your Assessment of ?**

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This looks like a case for Sleep Guys on deck 3
This looks like he may need a consult/sleep test.

Possible in lab or home study. Right!
Evaluating These Patients is Challenging

Occurrence is high as is risks
Reluctance to admit issues

On the one hand...
Evaluating These Patients is Challenging

Testing in now easier
Better Tx and Outcomes

On the one hand...

...On the other
Patients are often willing to come face to face with the facts
Sleeping with the enemy or sleeping with a friend
Summary: What does this all mean for your practice?

1. Patient with HTN (resistant on more than 2 drug), CHF, A fib + poor control + poor sleep and nocturia

2. Is there a ? of stroke, TIA, MCI, Dementia + snore, apnea

3. Neurodegenerative disorder, mood disorder (depression, bipolar, or anxiety issues) + insomnia or hypersomnia

• Should have a brief sleep review with you or others
THE EPWORTH SLEEPINESS SCALE

STOP-BANG Screening Questionnaire for Sleep Apnea
Testing has never been easier

Treatments are at Star Trek levels
Quality of changed lives never been higher

Thanks for your time
Any Questions?

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