The Effects of Sleep and Sleep Deprivation

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Effects of Sleep Deprivation

- HTN
- Nocturia
- Drowsy Driving
- Insulin Resistance
- Hormonal Changes
- ↓ Vascular Function
- ↑ BMI

- Inflammation
- Adolescent Injuries
- Vaccine Effectiveness
- Cancer
- Memory Problems
- PTSD Improvement
- Delirium
Prevalence of Insufficient Sleep* Among New York Adults by Region

Adults (%) reporting ≥ 14 days of insufficient sleep in past 30 days.

Source: 2008–2009 BRFSS, Centers for Disease Control and Prevention
Adults (%) reporting ≥ 14 days of insufficient sleep in past 30 days.
Prevalence of Insufficient Sleep* Among Massachusetts Adults by County

Note: Respondents from Dukes and Nantucket were combined due to inadequate numbers for individual counties.

Source: 2008–2009 BRFSS, Centers for Disease Control and Prevention

Adults (%) reporting ≥ 14 days of insufficient sleep in past 30 days.
Major Disasters –
Fatigue/Sleep Deprivation

- Exxon Valdez disaster
- Challenger space shuttle explosion
- Three Mile Island nuclear accident
- Chernobyl explosion

Wells et al, Neurodiagn J, 2012
Alzheimer’s Disease

• Sleep problems are common
• B-amyloid – key molecule identified in AD
• Amyloid plaque deposits in preclinical AD
  – associated with poor sleep quality
  – no change in sleep quantity

• Treat with benzodiazepines????

Ju et al, JAMA Neurol, 2013
Dementia - Benzodiazepines

• Subjects:
  – 1063 &
  – mean age 78.2
  – free of dementia

• New use of benzo’s in patients > 65yo increased dementia risk 50%

Hypertension in MEN

• ↓ SWS = ↑ risk of HTN
• With SWS < 4% of TST:
  – Poorer sleep quality
    • Shorter sleep duration
    • More awakenings
  – More severe sleep apnea

Redline et al, Hypertension, 2011
2 Melatonin Receptors

- Deep sleep ↓ BP.
- $\text{MT}_1$ – blocks NREM.
- $\text{MT}_2$ – favors NREM (no $\Delta$ in REM).
- New drug (rats and mice) – UCM765:
  - Binds to $\text{MT}_2$ receptors.

Ochoa-Sanchez et al, J Neurosci, 2011
Resistant HTN

• Poor sleep quality twice as likely to have resistant HTN.
• Patients with HTN, more likely to have sleep problems.

AHA, High Blood Pressure Research Scientific Sessions, 2012
Nocturia

• Common in older individuals with insomnia
• Significantly associated with
  – ↑ nocturnal wakefulness
  – ↓ subjective restedness after sleep

“Sweet” Dreams

• Sniffing flowers while asleep led to more positive dreams.

• Sulfur odor led to more negative dreams.
Pubertal Onset First Active During SWS

• Subjects: 9-15 yo
• Luteinizing hormone (LH)
  – Triggers ovulation
  – Stimulates testosterone production
• Examined pulses of LH secretion in relation to sleep stages.
• Most LH pulses followed SWS.

Shaw et al, J Clin Endocrinol Metab, 2012
Teenager

1. At the onset of puberty, 1.5 hr delay in melatonin release.
2. Sleep Pressure slows.
3. Light
   - Lose some sensitivity to morning light
     • Alertness and awakening worsens
   - More reactive to nighttime light
     • Activity later into the evening
Driving

• 100 drivers – vehicles equipped with instruments
  – 5 video channels
  – Accelerometers
  – Lane-tracking software
  – In-vehicle network sensor
  – Radar units

• Data collected on 132 drivers (others drove vehicle)

DOT, 100-Car Naturalistic Driving Study, 2006
Results

- 10,548 events
  - 82 crashes
  - 761 near crashes
  - 8295 incidents (i.e. braking hard)
  - 1423 non-conflict events (i.e. running a red light w/out traffic present)

DOT, 100-Car Naturalistic Driving Study, 2006
Results

- 20,000 randomly selected 6-second video segments
  - 38 subjects involved in fatigue-related crashes and near-crashes
  - 11 drivers accounting for 58% of all fatigue-related crashes and near-crashes

- Suggests ~12% of all crashes and near-crashes are fatigue related.

- 18-20 yo’s account for more fatigue-related crashes than other groups.

DOT, 100-Car Naturalistic Driving Study, 2006
Low Cost Driver Fatigue Monitoring

EPIC™ Sensor Technology

Plesseysemiconductors.com
Caffeine Use - Long Distance Commercial Motor Vehicle Drivers

- Associated with reduced risk of crashing
- Fatigue management still is a priority, but . . .
- Caffeine can maintain alertness

Optimal Sleep

- 16-18 yo perform better academically w/ 7 hrs of sleep
- 16 yo = 7 hrs
  - NSF: Teens = 8.5-9.25 hrs
- 12 yo = 8-8.5 hrs
- 10 yo = 9-9.5 hrs
  - NSF: 5-12 yo = 10-11 hrs
- Most studies – teens keep sleeping until satisfied

Eide et al, East Econ J, 2012
“The highest obesity rate of any state in 1995 was less than the lowest obesity rate in 2010.”
Fat Cells

• Young, lean, healthy subjects
• Sleep deprivation
  – reduces fat cells’ ability to respond to insulin by 30%.
  – decreases total-body insulin response by ~16%.
• Leads to disruption of energy regulation →
  – weight gain
  – diabetes

Insulin Sensitivity

• Comparable to difference between cells from:
  – obese vs. lean people.
  – diabetics vs. non-diabetics.

Energy Imbalance

- ↓ sleep may disrupt appetite hormone regulation:
  - ↑ ghrelin
  - ↓ leptin
- ↑’d wakefulness may promote food intake.
- “Sufficient sleep” may promote weight loss.

Shlisky et al, J Acad Nutr Diet, 2012
Hormonal Changes

- 27 subjects
  - Normal weight
  - 30-45 yo &
  - Normally sleep 7-9 hrs
- Either 4 or 9 hrs in bed.
- 4-day study period.
- Sleep had no effect on:
  - glucose
  - insulin
  - leptin

St-Onge et al, Sleep, 2012
Short sleep (4 hrs)

- Up’ed ghrelin in , but not in .
- Down’ed glucagon-like peptide-1 (GLP-1) in , but not .
  - GLP-1
    - Up’s insulin sensitivity
    - Down’s food intake by up’ing satiety in the brain

- Overeat during short sleep:
  - Increased appetite
  - Reduced fullness feeling

St-Onge et al, Sleep, 2012
Reduced Sleep in Teens Associated With:

• Insulin resistance (IR)\(^1\)
  – Long sleep not associated with IR.
  – Fragmented sleep not associated with IR, but with ↑ glucose levels.
  – Increasing sleep duration may ↓ diabetes risk.

• ↑’s in BMI (14-18 yo)\(^2\)
  – Extending sleep to 10 hrs could ↓ obesity prevalence.

1. Matthews et al, Sleep, 2012
Sleep deprivation in pupils taking maths and science tests, aged 9-10

Percentage of pupils in class where learning suffers from lack of sleep, according to teachers, out of 50 countries

Source: Boston College
Sounds and Dreams

• Need to be
  – low enough to not wake you.
  – loud enough to perceive them.

• Ocean sounds – beach vacation?
Vascular Function

- Subjects: 20-35yo
- First 2 study nights – slept 8h/night.
- Then, ↓’d sleep length (4 hrs) for 3 consecutive nights.
  - Reduced sleep length (4 hrs) for 1st 2 nights = ↓’d vascular function (cardiovascular disease?)
  - 3rd consecutive sleep deprived night, vascular function returned to baseline
    - adaptive response to acute sleep loss???

Pugh et al, Exp Biol meeting, 2013
Breathing Control

• Reduced sleep length (4 hrs) for 2 consecutive nights = impaired breathing control
  – Subjects exposed to CO₂ – should ↑ TV and f
  – Less sleep = ↓ breathing control (sleep apnea?)

• Subjects slept 10h/night x 5 nights: vascular function and breathing control IMPROVED.

• Preliminary findings (Abstract), NOT Peer Reviewed.

Pugh et al, Exp Biol meeting, 2013
Inflammation

• Higher levels of inflammation
  – Risk factor for heart disease & stroke

• <6 hrs sleep, increased:
  – Fibrinogen
  – IL-6
  – C-reactive protein

Morris, AHA Scientific Sessions, 2010
Cardiovascular Disease

Owens et al, Respir Care, 2010
Heart Failure and Insomnia

• 11 year study
• 54,279 Norwegians
• 20-89 yo
• Those w/ insomnia: 3½ X more likely to develop heart failure.
• Insomnia criteria =
  – Trouble falling sleep AND
  – Problems staying asleep AND
  – Waking without feeling refreshed

Laugsand et al, Eur Heart J, 2013
Insomnia Linked to SA?

• 20 patients with insomnia (primarily maintenance)
• Denied SA (snoring, apneas)
• No previous sleep testing

Krakow et al, Sleep, 2012
Insomnia → SA

• Subjects reported awakenings caused by:
  – Stress
  – Nightmares
  – Bathroom trips
  – Racing thoughts
  – Physical discomfort
  – Anxiety
  – Worries
  – Unknown reasons

Krakow et al, Sleep, 2012
Insomnia → SA

• PSG - 478 of 531 (90%) awakenings followed sleep breathing events
• 10% of awakenings caused by non-breathing factors:
  – Leg jerks
  – Facility interaction
  – Spontaneous

Krakow et al, Sleep, 2012
Insomnia → SA

• 30 awakenings > 5 min.
  – Each followed a breathing event
  – ↑’s likelihood of an insomnia episode

• Subjective vs. Objective

Krakow et al, Sleep, 2012
Adolescent Injury & Sleep

• Higher grade level, greater likelihood of injury.
• Adolescent athletes sleeping ≥ 8 hours, 68% less likely to be injured than athletes sleeping less.

Am Acad Pediatr National Conference and Exhibition, 2012
Vaccines

• Poor sleep can reduce vaccine effectiveness.

• Three-dose hepatitis B vaccine.

• Sleeping < 6 hrs/night (vs. > 7 hrs):
  – far less likely to build up antibody responses.
  – therefore, 11.5x more likely to be unprotected by the vaccine.

• Objective and subjective sleep quality were not predictors of antibody response.

Prather et al, Sleep, 2012
Sleep Disruption ↑’s Risk of:

• Breast cancer.¹
• Prostate cancer.¹
• Nursing home/assisted-living placement (3x more likely).²

Sleep Stability

Subjects generating more sleep spindles during a quiet night of sleep = higher tolerance for noise during a subsequent, noisy night of sleep

Dang-Vu et al, Curr Biol, 2010
SWS

• Memory consolidation
• Slow waves start in the cerebral cortex (cognitive functions)

Stroh et al, Neuron, 2013
Spicy Food and Dreams

• Spicy foods fragment sleep -> more likely to remember your dreams.
Sleep Learning

• As subjects slept, a tone was played, followed by an odor.

• Then, another tone played, followed by an odor at the opposite end of the pleasantness scale.

• Later that night, only exposed to tones.

Weizmann Institute, Nat Neurosci, 2012
Sleep Learning - Results

• While asleep, sniffing after tones as if odor was still present.

• Next day, awake subjects heard tones alone:
  – Tones w/pleasant odor; sniffed deeply
  – Tones w/unpleasant odor; short, shallow sniffs

Weizmann Institute, Nat Neurosci, 2012
2\textsuperscript{nd} Experiment -> Learned Response:

• More pronounced during REM.
• Transfer of association between sleep and waking, evident only during non-REM.

• Suggests:
  – REM = more open to influence from surroundings, but forget into wakefulness.
  – non-REM = memory consolidation.

Weizmann Institute, Nat Neurosci, 2012
Post-Traumatic Stress Disorder (rats)

• Sleep deprivation after trauma exposure, later did not exhibit behavior indicating memory of event.
• Allowed to sleep = did remember.
• Sleep deprivation in the first hours after stress might help prevent PTSD.

Cohen et al, Neuropsychopharmacology, 2004
Sleep Disruption in the ICU

• Associated with:
  – Impaired immune function
  – Decreased inspiratory muscle endurance
  – Extended mechanical ventilation
  – Delirium
  – Severe morbidity

Hu et al, Crit Care, 2010
Earplugs and Eye Masks

• Simulated ICU noise and light

Results:
• More REM
• Shorter REM latency
• Less arousals
• Elevated melatonin levels
• Subjective sleep quality improved

Hu et al, Crit Care, 2010
Delirium in the ICU

• Three interventions introduced in stages:
  1. Environmental checklist
     • Turning off hallway/room lights and TV
     • Consolidating staff visits
     • Reduce overhead paging
     • Minimize unnecessary equipment alarms
  2. Patients offered
     • Eye masks
     • Ear plugs
     • Tranquil music
  3. Discouraged common sleepers
     • Benzos known to cause delirium

Kamdar et al, Crit Care Med, 2013
Delirium in the ICU

• With all interventions, improved
  – Perceived nighttime noise.
  – Incidence of delirium/coma.

Kamdar et al, Crit Care Med, 2013
Extending Sleep (10 hrs)

• In mildly sleepy, healthy adults:
  – ↑’s daytime alertness.
  – ↓’s pain sensitivity.

• Importance of adequate sleep in:
  – Chronic pain conditions
  – Elective surgical procedure preparation

Roehrs et al, Sleep, 2012
Hypersomnia Antidote?

• 7 pts remained sleepy despite:
  – above-ordinary sleep amounts.
  – stimulant tx.

• flumazenil:
  – restored alertness.
  – counteracted mysterious somnogen in CSF.

• Release parking brake – block GABA.

Position and Dreams

Prone position increases likelihood of sexual dreams.
Treatment
Cognitive Refocusing Therapy

- Eliminates bedtime ruminations
  - Identify personally engaging, but non-arousing thoughts:
    - song lyrics
    - TV program plots
    - recipes
  - Used to go to sleep or to go BACK to sleep.

Gellis et al, Behav Ther, 2012
Intensive Sleep Retraining

- Restrict bed period to 5 hrs the night prior to treatment
- Arrival to lab at 9:00 pm
- Set-up and explanation
- Tx begins at 10:30 pm, ends at 11:00 pm on night #2
- 50 half-hour sleep onset opportunities

Harris et al, Sleep, 2012
ISR

- Sleep onset limited to 20 min.
- If sleep onset, 3 consecutive minutes of sleep.
- In bedside chair between opportunities
  - quiet alertness
  - reading
  - watching movie
- Detailed treatment feedback given
- Home by taxi

Harris et al, Sleep, 2012
Color TV and Dreams

If you grew up (3-10 yo) before color TV, you might be more likely to dream in black and white.
Beta-Blockers and Melatonin

• U.S. - ~22 million people take BB
• BB suppress endogenous nighttime melatonin secretion.
• May explain side effect of insomnia.
• Results after 3 weeks of nightly melatonin supplementation (2.5 mg):
  – improved sleep quality (TST, sleep efficiency)
  – No apparent tolerance
  – No rebound sleep disturbance (positive carryover)

Scheer et al, Sleep, 2012
Insomnia Medication

• Piromelatine
  – Tx of primary and co-morbid insomnia
  – Phase II clinical study
  – Safe and well tolerated
  – Improved
    • WASO
    • Sleep efficiency
    • TST
    • Total time awake
    • Time in NREM
DORA-22

- Dual orexin receptor antagonist (DORA)
  - Lateral hypothalamus
- Study done on rats and monkeys
- Induces sleep without effects on:
  - Attention
  - Memory

Zolpidem – ED Visits

- ED visits involving adverse reactions to zolpidem ↑’d ~220% from 2005 to 2010.
- ≥ 45 yo represented ~¾ of all ED zolpidem-related visits.
- ≥ 65 yo represented ~⅓ of all ED zolpidem-related visits.
- In 2010, accounted for 68% of all ED zolpidem-related visits.

Sleeping Pills – Benzo’s

- 2% of UK and US population (10% elderly) have taken bz’s for 12 months or more.
- Linked to an ↑ risk of infections and death from sepsis in critically ill patients.
- Associated with a 54% increase in risk to contract PN.
  - Similar risk associated with zopiclone

Obiora et al, Thorax, 2012
Sleeping Pills – Benzo’s

• Risk of dying w/in 30 days of being dx’d with PN, 22% higher.
  – 32% higher w/in 3 years of dx.

• Results do not prove cause and effect.

• Further investigation needed.

Obiora et al, Thorax, 2012
Space Station

• 2001 – ~50% of astronauts take sleeping medication.

• Avoid insomnia in U.S. section of Space Station:
  – Replace fluorescent lights with LEDs that dim and Δ hues
    • Blue, white, and red lights
    • Mimic time of day on Earth
    • Will be tested in 2016 – ~$11 million
Postprandial Somnolence

• Parasympathetic activation
• Hypocretin ↓
• Insulin-induced hypokalemia
• Insulin/tryptophan
Postprandial Somnolence

- Alerting effects of light to *retinal* cells = suppresses melatonin (maximally sensitive to short-wavelength light)
- Long-wavelength red (630 nm) and short-wavelength blue (470 nm) light delivered to the *corneas*.
- Compared to darkness, red or blue light in the middle of the afternoon reduces power in the following ranges:
  - Alpha (blue, not significant)
  - Alpha theta (blue, not significant)
  - Theta (red ONLY)
- Red light increases alertness during “post-lunch dip”.

Sahin et al, Physiol Behav, 2013
Sleep Tight, Tada!

- Stimulants
- Loud
- ETOH
- Exercise
- Pillows and Bed

- Technology
- Ingest
- Go to sleep and wake at the same time
- Hot tub
- Tobacco
Tada!

- Temperature (car windows?)
- Allergies
- Darkness and light
- Associate bedroom with sleep