



Sleep and Parkinson's Disease

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Musculoskeletal Symptoms and Non-REM Sleep Disturbance in Patients with “Fibrositis Syndrome” and Healthy subjects. *Psychosomatic Medicine* 1976;37:341-351.

- discovered alpha wave intrusion in their deep, slow wave (stage III/IV) sleep
- also found alpha intrusion in patients with chronic fatigue syndrome, rheumatoid arthritis and chronic pain
- reproduced symptoms of fatigue, sore/tender tissues, and dysphoria in healthy subjects after 3 nights of no slow wave sleep
- symptoms resolved after 2 nights of recovery sleep


Health requires a balance between wake and sleep



Hormones of Wake

Primarily Catabolic Hormones:


- Adrenalin
- Noradrenalin
- Cortisol



Hormones of Sleep

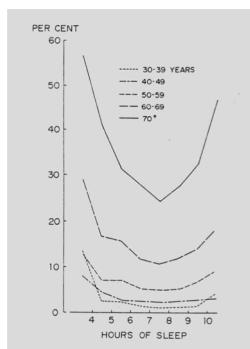
Primarily Anabolic Hormones:

- Growth hormone
- Testosterone
- Erythropoietin
- Leptin





### Insomnia and Mortality-Men



Kripke et al. *Arch Gen Psychiatry* 1979; 36:103-116

### Insomnia and Mortality

- Men who reported usually sleeping less than 4 hours/night were 2.8 times as likely to have died within six years as men who reported 7.0 to 7.9 hours of sleep.
- Reduced sleep is a greater mortality risk than smoking, hypertension, or cardiac disease.

Kripke et al, *Arch Gen Psychiatry* 1979; 36:103-116

### Beta Amyloid

- Beta-amyloid is a type of protein “waste” that increases in the neurons of the brain when you are awake and decreases when you sleep.
- Lack of sleep has been shown to result in increased levels in the brain.
- This protein is found in abnormally large quantities in the brain of patients with Alzheimer’s disease. It is thought that this protein may “clog up” the neurons and interfere with their function.
- It has also been found that patients with Alzheimer’s are more likely to suffer from sleep disorders such as obstructive sleep apnea than other people of similar age.

### Hormone changes as we age

- Are the changes we see in our bodies as we age the inevitable result of aging or the consequence of our lifelong lifestyles catching up with us?

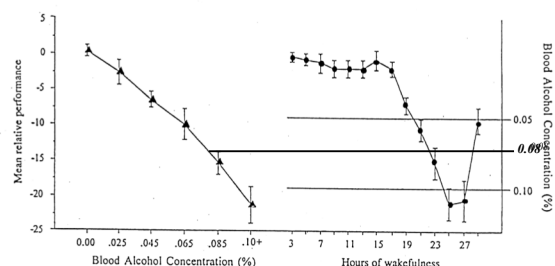
### Sleep in Parkinson’s Disease

- Insomnia 60%
  - Restless Legs Syndrome
  - Pain
  - Dopamine dysregulation
  - Nocturnal akinesia
  - Hallucinations/confusion
- REM Behaviour Disorder (RBD) 15 – 59%
  - reduced Parkinson symptoms during parasomnia
- Excessive Daytime Sleepiness 30%
  - Obstructive Sleep Apnea
  - Atypical Narcolepsy (degeneration of hypocretin neurons)
  - Sleep Attacks from anti-Parkinson medication
- Morning Sleep Benefit 10 – 15% (average 84 minutes)

### Fatigue vs Alcohol

#### Response Latency

(Lamond & Dawson, 1999)



### Sleep Deprivation is Cumulative

- 22 hours awake results in a reduction in performance = 0.08 blood alcohol.
- 4 hrs. sleep/night for 2 weeks results in a reduction in performance equivalent to no sleep for 3 days.
- People do not accurately predict when they will fall asleep.



### National Sleep Foundation Omnibus Sleep In America Poll (OSAP 2000)

- 58% of the general population suffer from sleep disorders at least 3 days per week
- 66% get less than 8 hours sleep
- 33% get less than 6.5 hours sleep
- 20% find sleepiness interferes with daily activities a few days/week
- 51% drowsy while driving in past year
- 17% dozed off while driving in past year

### Sleep in Primary Care

- Up to 69% of primary care patients suffer from sleep disorders.<sup>1</sup>
- Primary care physicians may identify as few as 0.15%.<sup>2</sup>
- Doctors trained in sleep disorders are 6x's more likely to ask patients about sleep.<sup>3</sup>

1. Shochat et al. *SLEEP* 1999; 22:S359-65

2. Rosen. *Sleep Medicine* 2001; 2:47-55

3. Haponik. *J Gen Intern Med* 1996; 11:759-62



### Impact of sleep debt on metabolic and endocrine function

4 hours of sleep loss/night for 6 days:

- 40% reduction in rate of glucose clearance
- 30% reduction in insulin response to glucose
- Decreased thyroid hormone
- Increased evening cortisol
- Increased sympathetic nervous system activity (similar changes to that seen in obesity & aging)

Spiegel K, Leproult R, Van Cauter E. *Lancet* 1999; 354:1435-9

### Impact of Short Sleep Duration on Sleepiness, Performance, Mood and Glucose Metabolism

Chronically short sleepers (306 vs 486 min/nt)

- Secreted 65% more insulin
- Insulin sensitivity 40% less than normal
- Significantly decreased reaction times
- Lower scores on the Global Affect scale

Colecchia EF, Spiegel K, Kim R, et al. *SLEEP* 2000; 23:A253

### Sleep in Type II Diabetes

- Weekday self reported sleep 6.1 hours
- Prefer to get 1.83 more hours of sleep
- 71% report poor sleep quality (>5 on PSQI)
- ↑ HbA1c with sleep debt and worsening sleep quality

Ryden AM, Knutsin KL, Mander BA, Van Cauter E. *SLEEP* 2002; 25:A105-6

### Acute Sleep Loss Increases Hunger

After restriction to 4 hours in bed/night for two nights:

- 18% less leptin
- 28% more ghrelin
- 24% higher hunger ratings
- 23% higher global appetite ratings (33% for high fat, high carbohydrate foods)

Spiegel et al. *Ann Intern Med* 2004; 141:846-50

### Chronically Short Sleepers Have Increased BMI

Study of 1024 subjects with chronic sleep restriction showed an association with reduced leptin, increased ghrelin and elevated BMI.

Taheri S, et al. *SLEEP* 2004; 27:A146-7

### Sleep Deprivation Causes Obesity

- ↓ lean muscle mass from : ↓ growth hormone
  - ↓ testosterone
  - ↓ leptins and ↑ leptin resistance
  - ↑ ghrelin
  - ↑ insulin resistance
  - ↑ evening cortisol
  - ↑ sympathetic activity
  - ↑ fatigue contributes to ↓ exercise
- (Similar to changes seen in aging!)



### Sleep Deprivation & Hypertension

- Acutely causes increased sympathetic tone, heart rate, blood pressure and salt retention
- Chronic sleep restriction <5 hours/night leads to 2 fold increase incidence in hypertension

Gangwisch JE, et al. *Hypertension* 2006; 47:833-839

### Increasing Sleep Duration Lowers BP

- 22 subjects with prehypertension<sup>1</sup> or stage 1 hypertension<sup>2</sup> on no or stable medication, habitually sleeping less than 7 hours per night increased their sleep time an average of 35 minutes (actigraphy) over a 6 week intervention study.
  - Subjects with an AHI > 15 and PLM index of > 10 events per hour based on PSG were excluded
  - Systolic BP dropped 14 mmHg
  - Diastolic BP dropped 7 mmHg
1. Prehypertension – SBP 120-139 & DBP 80-89 mmHg,
  2. Hypertension type 1 – SBP 140-159 & DBP 90-99 mmHg

Haack M et al. *J Sleep Res.* 2013; 22:295-304

### Increasing Sleep Duration Lowers BP

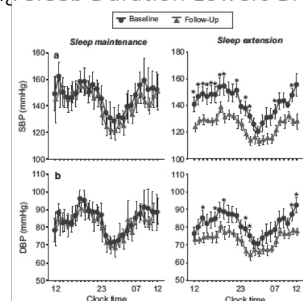


Figure 3. Systolic blood pressure (SBP, a) and diastolic blood pressure (DBP, b) across the 24-h baseline (circles) and follow-up (triangles) period in the sleep maintenance group (N = 9) and sleep extension group (N = 13). \*P < 0.05 compared with follow-up measures.

Haack M et al. *J Sleep Res.* 2013; 22:295-304

### Sleep Deprivation & Stroke

- 10 year follow-up of 7844 adults in the NHANES
- Compared to those sleeping 8 or more hours per night, risk of stroke increased:
  - 50% in those sleeping 6 – 8 hours
  - 90% in those sleeping 6 – 8 hours who also had daytime sleepiness.

Qureshi A et al. *Neurology* 1997; 48:904-10

### Sleep Deprivation & Myocardial Infarction

- Chronic sleep restriction <5 hours/night associated with a 45 – 300% increase risk of myocardial infarction in women

Ayas N, et al. *Arch Intern Med* 2003;163:205-9

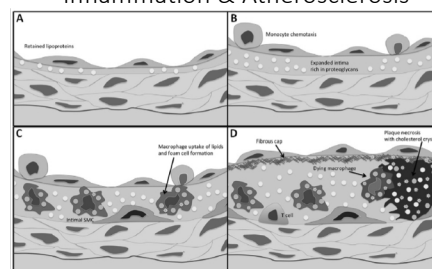
Meisinger C, et al. *SLEEP* 2007;30:1121-7

### Sleep, Inflammation & Pain

- Chronic sleep restriction to 4 hours/night for 10 days associated with elevated IL-6 levels and increased pain ratings

Haack M, Sanchez E, Mullington M. *SLEEP* 2007;30:1145-52

### Inflammation & Atherosclerosis



**Figure 3.** Progression of atherosclerosis and plaque formation. (A) The subendothelial retention of lipoproteins is an early initiating factor in atherogenesis. (B) This initiating process results in monocyte chemotaxis in response to trapped low-density lipoprotein particles. As well, the intimal layer expands, coupled with changes in extracellular matrix composition, including glycosaminoglycan-rich proteoglycans which have high affinity for apolipoprotein B. (C) Lipoprotein uptake by macrophages results in foam cell formation, further advancing the atherosclerotic lesion. Even minimally modified low-density lipoprotein can lead to cholesterol crystal formation, leading to Toll-like receptor (TLR) inflammation priming and macrophage activation. (D) Cholesterol crystals can be found not only within the lipid-rich necrotic core, but also in subendothelial areas both intra- and extracellularly. Resident macrophage and foam cell death may result directly because of cholesterol crystals, leading to release of intracellular contents including lipoproteins, further expanding the necrotic core. Cholesterol crystals can also further activate Toll-like receptor (TLR) inflammasomes, maintaining the pathological inflammatory response within the atherosclerotic lesion. SMC, smooth muscle cell.

Wong BW et al. *Canadian Journal of Cardiology* 2012; 28:631-641

### Insomnia as a Risk Factor for Psychiatric Disorders

For people with insomnia longer than 1 year:

- 40 times increased risk for developing major depression.
- 25 times increased risk for developing new-onset phobia, obsessive compulsive disorder or panic disorder.

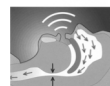
Ford et al, *JAMA* 262:1479-84, 1989

### Sleep Disorders:

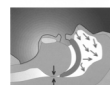
- are very commonly associated with psychiatric disorders
- increase the risk of developing psychiatric disorders.
- reduce the effectiveness of psychiatric disorder treatment
- may prevent the remission of psychiatric disorder
- increase the risk of relapse
- increase the risk of suicide

[illegible]

### Normal breathing



## Snoring



## Sleep Apnea

- 25-30% of Hypertensives have OSA<sup>1</sup>
- 35% of Coronary Artery Disease patients<sup>2</sup>
- 16 - 38% of Myocardial Infarction patients<sup>3</sup>
- 30-50% of Stroke victims have OSA<sup>4</sup>

1. Silverberg and Oksenberg *Sleep* 1997; 20:794-806
2. Koehler and Schafer *Sleep* 1996
3. Alihanka et al. *Sleep Res.* 1983; 12:272
4. Bassetti and Chervin *Principles and Practice of Sleep Medicine*, 3<sup>rd</sup> ed. p1075, 2000

- 80% of type 2 diabetics are overweight and in particular have central obesity
- Central obesity increases the risk of OSA
- 12% of type 2 diabetics had moderate to severe OSA
- 70% of moderately obese diabetics who snored or were sleepy had OSA

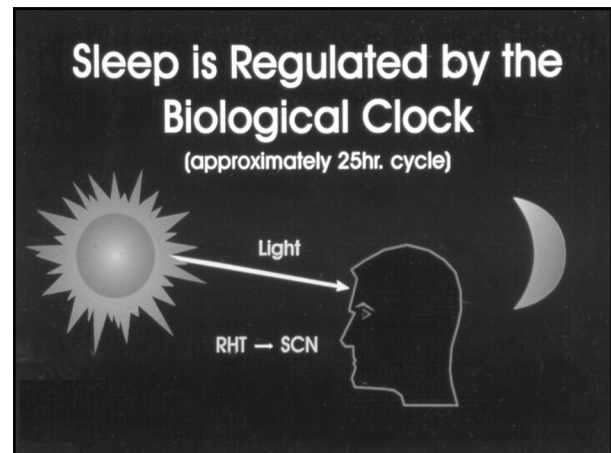
Brooks, B et al. *Journal of Clinical Endocrinology & Metabolism*  
1994;79:1681-5

- Do you snore?
- Do you wake up refreshed?
- Has anyone told you that you stop breathing in your sleep?

- Trouble getting legs comfortable or keeping them still when inactive or in evening
- “Creepy-crawly” sensations
- History of sciatica or paresthesias
- History of iron deficiency, diabetes, or chronic renal failure

### Periodic Limb Movement Disorder

- Witnessed repetitive leg or body twitching, kicking or flailing
- Waking with a jerk
- Restless sleep, messed up bed
- History of restless legs



### Delayed Sleep Phase Syndrome

- Habit of going to bed late and sleeping in
- Feels rested if allowed to go to bed when sleepy and wake up on own

### Tx Delayed Sleep Phase Syndrome

- Sleep Program
- 30-45 min. bright light within first hour of normal wake up time.
- May advance alarm and subsequent bedtime 30-60 every 1-3 days.
- Maintain regular sleep schedule. Do not sleep in later than one hour!

### Advanced Sleep Phase Syndrome

- Habit of going to bed early and waking up early.
- Feels rested if allowed to go to bed when sleepy and wake up on own but ends up out of sync with the rest of society.

### Tx Advanced Sleep Phase Syndrome

- Sleep Program
- Delay bed time one hour per night until at preferred bed time.
- May use bright light from 2 hours prior to bedtime to help delay biological clock.
- Must use an alarm. Set it for current approximate wake time.
- Once waking with alarm for at least 2 nights, delay alarm 30 minutes at a time until waking at preferred time.
- Do not expose eyes to bright light before alarm or else biological clock will advance again.

### REM Behaviour Disorder (RBD)

- Normally your muscles are paralyzed in REM so you don't act out your dreams
- In RBD you may lose the REM paralysis
- Caused by a neurodegenerative process in the part of the brain that controls REM paralysis
- 30% of people with RBD will develop PD in 7 years
- 15 – 60% of PD have RBD

### Psychophysiological Insomnia

- Habit of thinking, worrying, planning or problem solving in bed
- Watching the clock, and having anxious, frustrating or angry thoughts about inability to sleep
- Feel nervous or tense in bed
- Light sleeper hearing every little noise

### Improving Sleep Hygiene

- Avoid caffeine within 6 hours of bedtime
- Avoid heavy exercise within 4 hours of bedtime
- Avoid heavy meals within 3 hours of bedtime
- Avoid TV and computer within 1 hour of bedtime
- Maintain a regular bedtime and wake time
- Do not get up to eat or smoke
- Use bed primarily for sleep or sex
- Get up if you can't sleep within 20 minutes

### The Good Sleep Triad

**Conditioning:** bed primarily for sleep or sex  
cool, dark and quiet  
regular bed time & wake time  
turn clock away

get up if you can't sleep  
**Wind-down:** hot bath,  
relaxing activities  
no screens  
light carbohydrate snack  
“worry time”

**When You Go To Bed:**  
set alarm, relaxation technique



Remember...



...sleep is the key to health and healing.