

NMAFP 59th Annual Family Medicine Seminar Taos, New Mexico GET DOWN TONIGHT SOLVING THE MYSTERY OF NOCTURNAL DIPPING

FRANK M. RALLS, M.D.

ASSOCIATE PROFESSOR: UNIVERSITY OF NEW MEXICO

PROGRAM DIRECTOR: UNM SLEEP MEDICINE FELLOWSHIP

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NONE

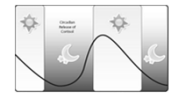
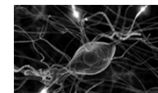
Type of Potential Conflict	Details of Potential Conflict
Grant/Research Support	
Consultant	
Speakers' Bureaus	
Financial support	
Other	Any remaining typos in this presentation are the responsibility of the editor

GET DOWN TONIGHT Get the Respect You Deserve!



Objectives:

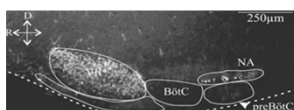
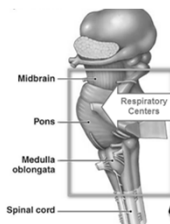
Understand the Importance of "Getting Down Tonight"!



Sleep: "natural" anti-inflammation

GET DOWN TONIGHT

Starting the anti-inflammatory Process
Breathing During NREM Sleep is Controlled by CO₂



GET DOWN TONIGHT Myth: Less Sleep is Not Important

- Adequate Sleep causes a DECREASE in :
 - Neuronal excitability
 - α B amyloid protein
 - INFLAMMATION

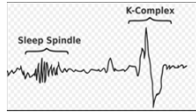


Tabuchi et. al., Curr Biol 2015, Ju, Nat Rev Neurol. 2014, Rothman, Brain Res. 2013

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Length of Sleep Time, NOT SUBJECTIVE FEELINGS, Predicts Memories

- Reduction of Stress
- Consolidating Memories
- Learning



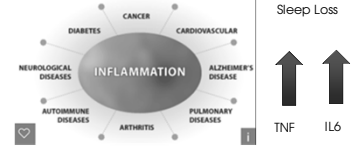
Meco et al., Neurobiol Aging 2014, Kadoya et al., Plos 2016



GET DOWN TONIGHT

Sleep The Natural anti-inflammatory

- First 1/2 of the night
- Slow-wave sleep inhibits cortisol secretion
- Lowest in a 24 hour period
- Lowers cortisol throughout the day



Chrousos et al., Endotext 2016

GET DOWN TONIGHT

Diagnostic Criteria for AD

Dementia Syndrome

- Objective cognitive or behavioral impairment in ≥ 2 of the following:
 - Memory;
 - Language functions;
 - Personality, behavior or comportment;

Probable Alzheimer Dementia

- Initial symptoms:
 - Amnesic
 - Non-amnesic (language, executive)

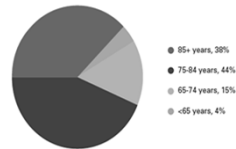


REF: McKhann GM et al, Alzheimer Dement
www.alzheimersanddementia.com

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Sleep Loss -Inflammation -AD

- Most common cause of dementia



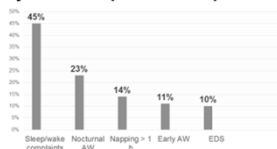
- 11% age ≥ 65 have AD;
- 32% (1:3) by age 85 have AD

Source:
http://www.alz.org/downloads/Facts_Figures_2014.pdf

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Shortened Sleep Times Accelerates Cognitive Impairment

Subjective Sleep/Wake Complaints in AD



REF's: 1) Piatzchi M et al. Neurol Sci 2014;35(12):1955-62. 2) Cipriani G, et al. Psychogeriatrics. 2015;15(1):65-74. 3) Vitello MV et al. CNS Drugs. 2001;15(10):777-96.

GET DOWN TONIGHT

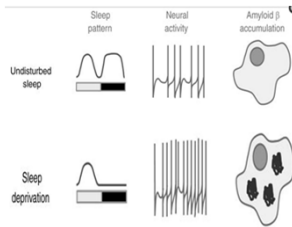
Risk factor for Alzheimer's Disease ¹	Relative risk (RR)
Depression	1.90
Physical inactivity	1.82
Midlife untreated hypertension	1.61
Midlife obesity (BMI ≥ 30)	1.60
Tobacco	1.59
Diabetes mellitus type 2 (DM2)	1.39
POOR SLEEP	1.8-2.8

- Mounting evidence that poor quality of sleep and daytime somnolence increases risk for developing AD.

1) Barnes D and Yaffe K. Lancet Neurology 2011;10:9:819-28; 2) Guarnieri B et al. Eur Neurol. 2015;74(1-2):43-8; 3) Benedict C et al. Alzheimers Dement 2015;11(9):1090-7; 4) Ju YE et al. JAMA Neurol 2013;70(5):587-93; 5) Lim AS et al. Sleep 2013;36(7):1027-32; 6) Tronah GJ et al. Ann Neurol 2011;70(3):722-32. 7) Tsapanou A et al. Int J Geriatr Psychiatry. Epub 2015 Jun 1; 8) Spira AP et al. Curr Opin Psychiatry. 2014;27(6):478-4.

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Length of Sleep Time and Neural Excitability



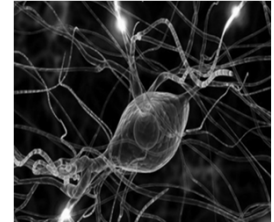
- Increase in amyloid production
- Neuronal mitochondrial damage
- Neuronal apoptosis in the hippocampus
- All behavioral and neuropathological changes were irreversible

Qui et. al., J Alzheimers Dis 2015, Keene and Inlner, Curr Biol 2015

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Length of Sleep Time Predicts Memories

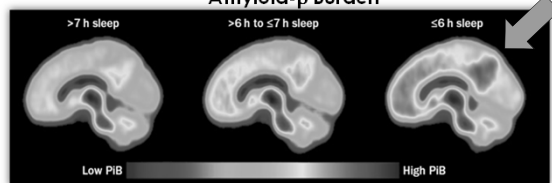
- Sleep loss accelerates the accumulation of the $\alpha\beta$ amyloid protein



Meco et. al., Neurobiol Aging 2014, Kadoya et. al., Plos1 2016

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Short Sleep Duration (≤ 6 h) in 70 Elders Associated with Higher Amyloid- β Burden



PIB-PET Study in 70 older community-dwelling adults with mean age 76 y. REF: Spira AP et al. JAMA Neurol 2013;70:1537-43.

GET DOWN TONIGHT

Alzheimer's Disease Pathology in Brain

Sleep Loss from OSA with Intermittent Hypoxia

Upregulates $A\beta$ and Tau pathology

Neuronal degeneration and axonal dysfunction

Worsening of Alzheimer's Disease and Pathology

REFs: 1) Kadotani H et al. JAMA 2001;285:2888-90. 2) Ancoli-Israel S et al. J Geriatr Soc 2008;56:2075-81. 3) Bliviese DL. J Psychosom Res 2002;53:539-46.

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Length of Sleep Time and Weight

► Ghrelin

- Sleep loss increased calories by 328
- Higher consumption of calories from sweets
- Lower magnitude of weight loss in obese women participating in a weight loss intervention



Broussard et. al., Obesity, 2016, Sawamoto, Nutr Diabetes 2014

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Length of Sleep Time and Falls

- Sleeping < 5 hours doubles the risk of falling
- Sleep Deprivation:
 - Degraded Binocular Coordination
 - Decreased balance X 7



Stone et. al., J Am Geriatr Soc 2014, Kim et. al., Medicine 2016, Tong, Front Neuro, 2016

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Length of Sleep Time:

29,203 healthy Men and Women

Sleep Time	< 5 hours	> 6 hours	> 7 hours	> 8 hours	> 9 hours
Number of Individuals	4564	11,819	9,416	2,869	535
Depression	5.2%	2.3%	1.8%	2.3%	4.3%
Hypertension	18%	16%	15%	15%	21%
Diabetes	6.1%	5.7%	5.1%	4.9%	8.8%

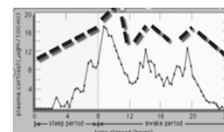
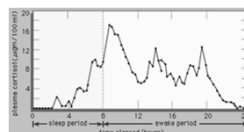
Kim et. Al., Arterioscler Throb Vasc Biol., 2015

GET DOWN TONIGHT

Length of Sleep Time and Cortisol

Slow-wave sleep inhibits cortisol secretion

Lowers cortisol throughout the day



Ly, Jinshia, Psychoneuroendocrinology 2015

GET DOWN TONIGHT

Length of Sleep Time and HRV

- Increased Cortisol Increases Heart Rate
- Sleep loss causes a decrease in HEART RATE VARIABILITY
- NORMAL: Blood Pressure drops 10%
- 5% decrease in BP = 20% increase in cardiovascular mortality

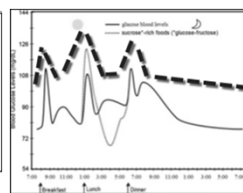
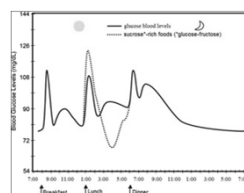


Virtanen, Sleep Med 2015

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LENGTH OF SLEEP TIME

EFFECT ON GLUCOSE



Increased Cortisol Increases Blood Glucose

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Length of Sleep Time and Pain



- 7% more pain for each hour of sleep loss.
- Narcotics and Sleep

Ly, Jinshia, Psychoneuroendocrinology 2015

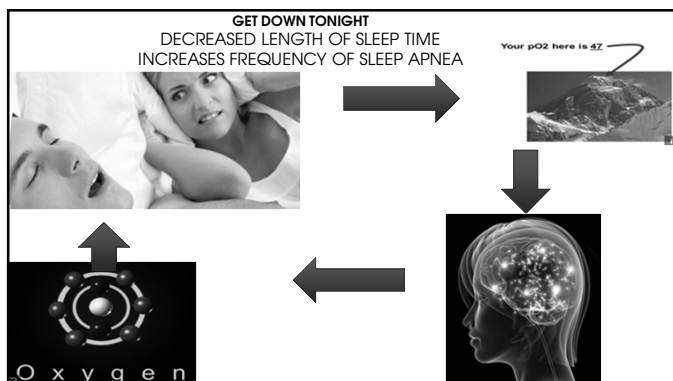
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Length of Sleep Time and CAD

- 89,329 post menopausal women
- Women's health initiative
- 10.3 years
- Sleep < 5 hours or > 10 hours :
- 25% increase in heart disease

Weingarten et.al., Sleep 2016,
Sand-Lincoln et.al., J of Women's Health 2013





GET DOWN TONIGHT
DECREASED SLEEP TIME
+ SLEEP APNEA

- ▶ Chronic intermittent hypoxia
- ▶ Endothelial dysfunction
- ▶ Hypercoagulability due to decreased nitric oxide levels and impaired vasodilations leads to: hypertension, arrhythmia, stroke, coronary artery disease
- ▶ **SLEEP APNEA:**
- ▶ **HEART ATTACKS OCCUR BETWEEN 12-6 AM**
- ▶ Normal 6 AM-12 PM

Updates on Common Medications to Help “Get Down Tonight”:

- ▶ Benzodiazepines (Restoril-temazepam)
- ▶ Non-Benzodiazepines (Ambien – zolpidem)
- ▶ Silenor (doxepin)
- ▶ Belsomra (suvorexant)
- ▶ Rozerem (ramelteon)
- ▶ Anti-Histamines:
 - ▶ Diphenhydramine (Benadryl)
 - ▶ Doxylamine (Unisom)
 - ▶ Quetiapine (Seroquel)
 - ▶ Trazodone (and $\alpha 1$ blocker)
 - ▶ Mirtazapine ($\alpha 2$ blocker)

Updates on Common Medications to Help “Get Down Tonight”:

- ▶ Benzodiazepines (Restoril-temazepam) 8 hours
- ▶ Non-Benzodiazepines
 - ▶ (Sonata –Zaleplon) 1
 - ▶ (Ambien – zolpidem) 3
 - ▶ Lunesta-eszopiclone) 6
- ▶ Silenor (doxepin) 15
- ▶ Belsomra (suvorexant) 12
- ▶ Rozerem (ramelteon) 2
- ▶ Anti-Histamines:
 - ▶ Diphenhydramine (Benadryl)
 - ▶ Doxylamine (Unisom)
 - ▶ Quetiapine (Seroquel)
 - ▶ Trazodone (and $\alpha 1$ blocker)
 - ▶ Mirtazapine (and $\alpha 2$ blocker)

Updates on Common Medications to Help “Get Down Tonight”:
BNZO and Non-BNZO

- ▶ Zolpidem $\alpha 1$
 - ▶ (Sonata)
- ▶ Zaleplon $\alpha 1$
 - ▶ (Ambien)
- ▶ Eszopiclone $\alpha 1 \alpha 2 \alpha 3 \alpha 5$
 - ▶ (Lunesta)
- ▶ Benzodiazepines $\alpha 1 \alpha 2 \alpha 3 \alpha 5$ and BZD

Get Down Tonight
Listen

Updates on Common Medications to Help “Get Down Tonight:

- ▶ Suvorexant (Belsomra)
 - ▶ Hypocretin antagonist
 - ▶ Site of cataplexy
-
- ▶ Doxepin (Silenor)



Conclusion: “Get Down Tonight” Stating the Obvious

- ▶ Sleep Longer and live longer
- ▶ Sleep: The natural anti-inflammatory
- ▶ Reduction in :
 - ◆ Cortisol
 - ◆ Blood Pressure
 - ◆ Lower Heart Rate
 - ◆ Lower blood glucose
 - ◆ Appetite
 - ◆ Pain
 - ◆ Sleep apnea

I am no cook. But I can follow the directions. Which said to let the bird chill in the sink for a few hours.

