Sleep Apnea and Restricted Sleep Patterns: Impact on Cardiometabolic Health

Virend K. Somers, MD, PhD
Professor of Medicine
Mayo Clinic
Consultant in Cardiovascular Diseases
Mayo Clinic and Mayo Foundation
Rochester, Minnesota

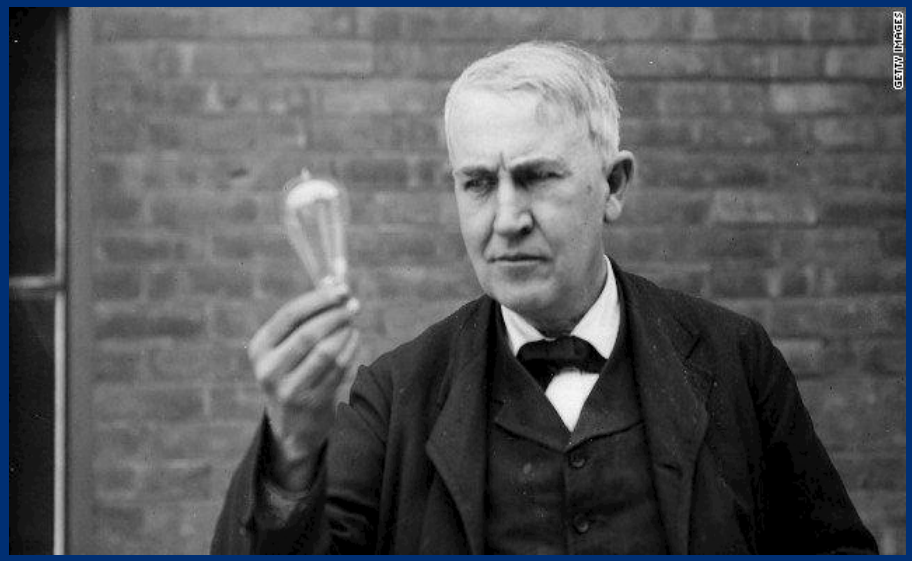
Blessings on him who first invented sleep.

It covers a man all over, thoughts and all, like a cloak.

It is meat for the hungry, drink for the thirsty, heat for the cold and cold for the hot.

It makes the shepherd equal to the monarch, and the fool to the wise.

from *Don Quixote* by de Cervantes

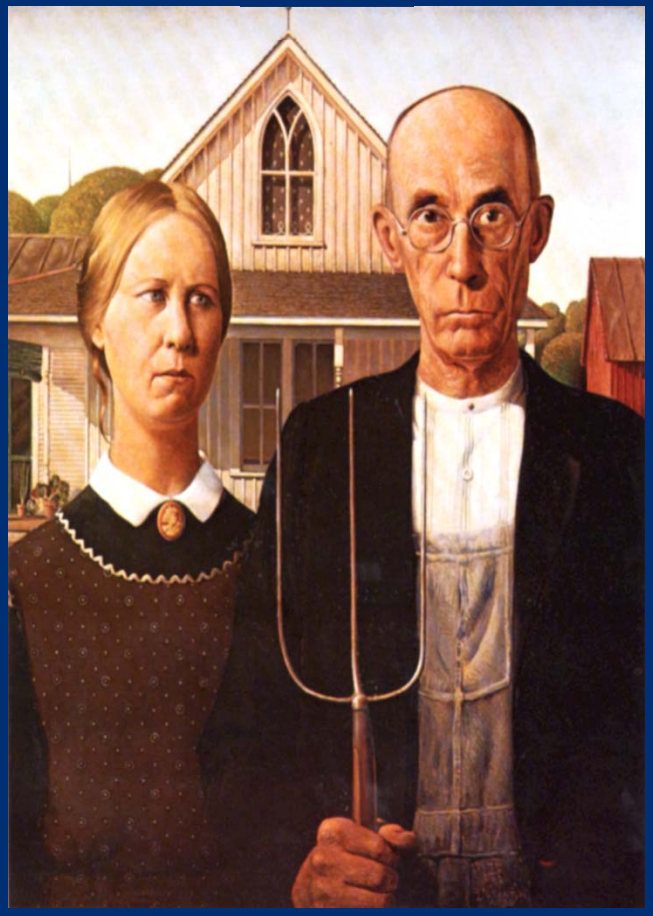


Pretest questions:

Who are these innovators who have transformed society? What, if anything, do they have to do with the obesity epidemic?

The Rise of Obesity in the 20th Century

1930

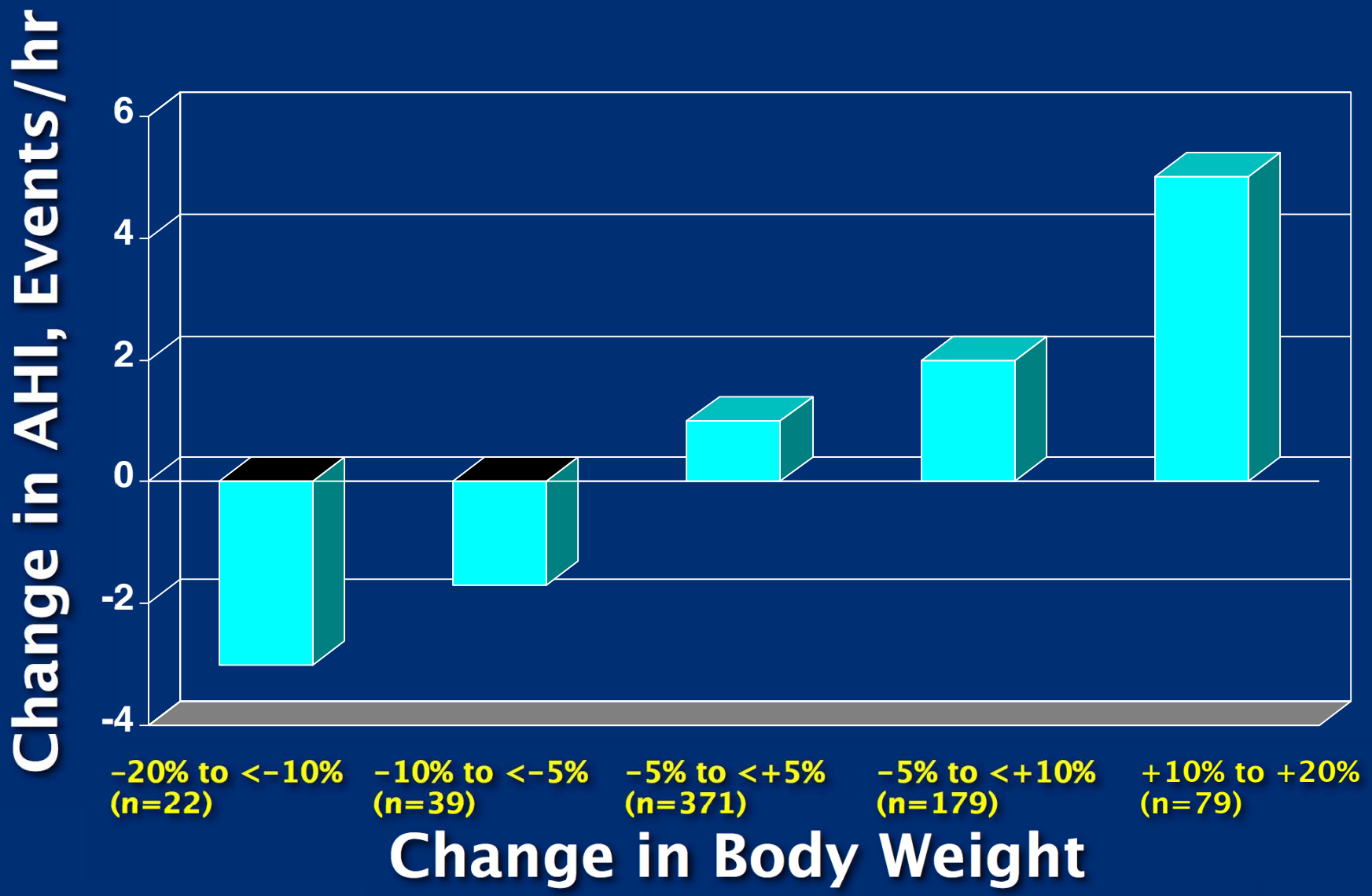


American Gothic
Grant Wood

1996

A Family
Fernando Botero

Effects of Weight Change on OSA



OSA=obstructive sleep apnea; AHI=apnea-hypopnea index

Peppard et al. JAMA. 2000;284:3015-21.

Shift Work Type Disorder

- 15.5 million American adults are affected by shiftwork
  - ü 5% work in the evening
  - ü 4% on permanent night shift
  - ü 4% on rotating shifts
- Shiftwork is hazardous!
  - ü Increased health risk
  - ü Increased accident risk
  - ü Increased social/family problems

Sleep Apnea and Sleep Duration – Implications for…

- CV risk
- Obesity
- Hypertension
- Insulin resistance
- Metabolic syndrome

ORIGINAL INVESTIGATION

A Prospective Study of Sleep Duration and Coronary Heart Disease in Women

Najib T. Ayas, MD; David P. White, MD; JoAnn E. Manson, MD, DrPH; Meir J. Stampfer, MD, DrPH; Frank E. Speizer, MD; Atul Malhotra, MD; Frank B. Hu, MD, PhD

Background: Long-term sleep deprivation is common in today's society. Recent experiments have demonstrated that short-term sleep deprivation in healthy subjects results in adverse physiologic changes, including a decreased glucose tolerance and an increased blood pressure. However, the long-term health consequences of long-term sleep deprivation are unclear. The objective of this study was to determine whether decreased sleep duration (from self-reports) is associated with an increased risk of coronary events.

Methods: We studied a cohort of 71 617 US female health professionals (aged 45-65 years), without reported coronary heart disease (CHD) at baseline, who were enrolled in the Nurses' Health Study. Subjects were mailed a questionnaire in 1986 asking about daily sleep duration. Subjects were followed up until June 30, 1996, for the occurrence of CHD-related events. We assessed the relationship between self-reported sleep duration and incident CHD.

Results: A total of 934 coronary events were documented (271 fatal and 663 nonfatal) during the 10 years of follow up. Age-adjusted relative risks (95% confidence intervals) of CHD (with 8 hours of daily sleep being considered the reference group) for individuals reporting 5 or fewer, 6, and 7 hours of sleep were 1.82 (1.34-2.41), 1.30 (1.08-1.57), and 1.06 (0.89-1.26), respectively. The relative risk (95% confidence interval) for 9 or more hours of sleep was 1.57 (1.18-2.11). After adjusting for various potential confounders, including snoring, body mass index, and smoking, the relative risks of CHD (95% confidence intervals) for individuals reporting 5 or fewer, 6, and 7 hours of sleep were 1.45 (1.10-1.92), 1.18 (0.98-1.42), and 1.09 (0.91-1.30), respectively. The relative risk (95% confidence interval) for 9 or more hours of sleep was 1.38 (1.03-1.86).

Conclusion: Short and long self-reported sleep durations are independently associated with a modestly increased risk of coronary events.

Arch Intern Med. 2003;163:205-209

Nurses Health Study

71617 women 45-65 years

10 year follow-up of Incident CHD

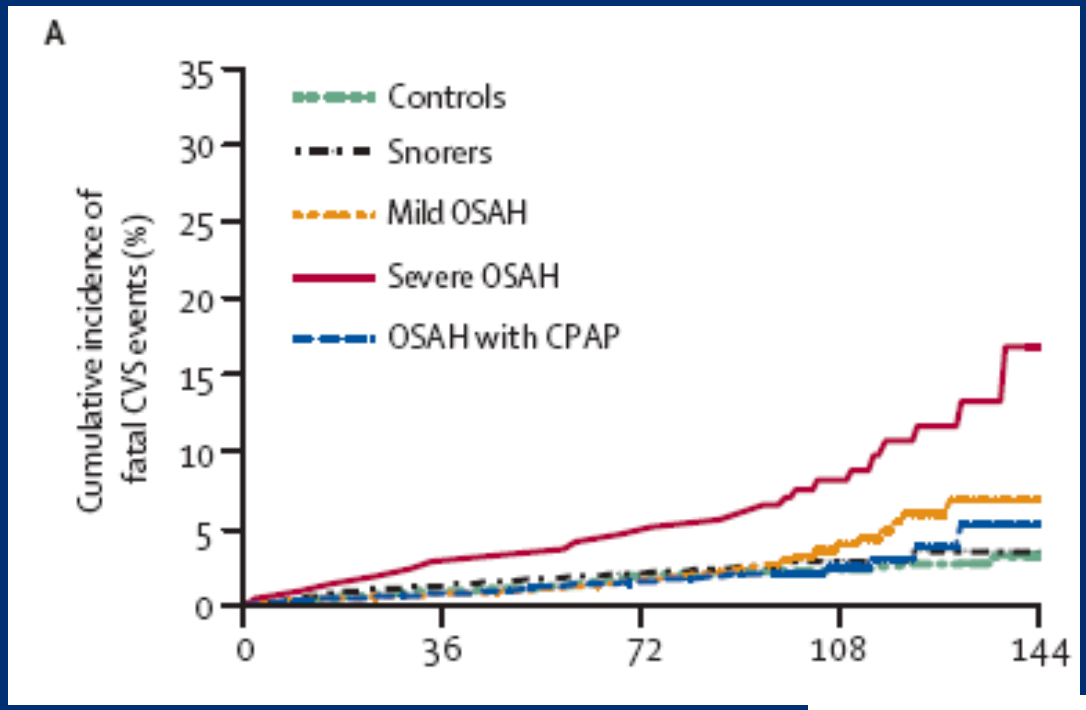
(Ayas et al)

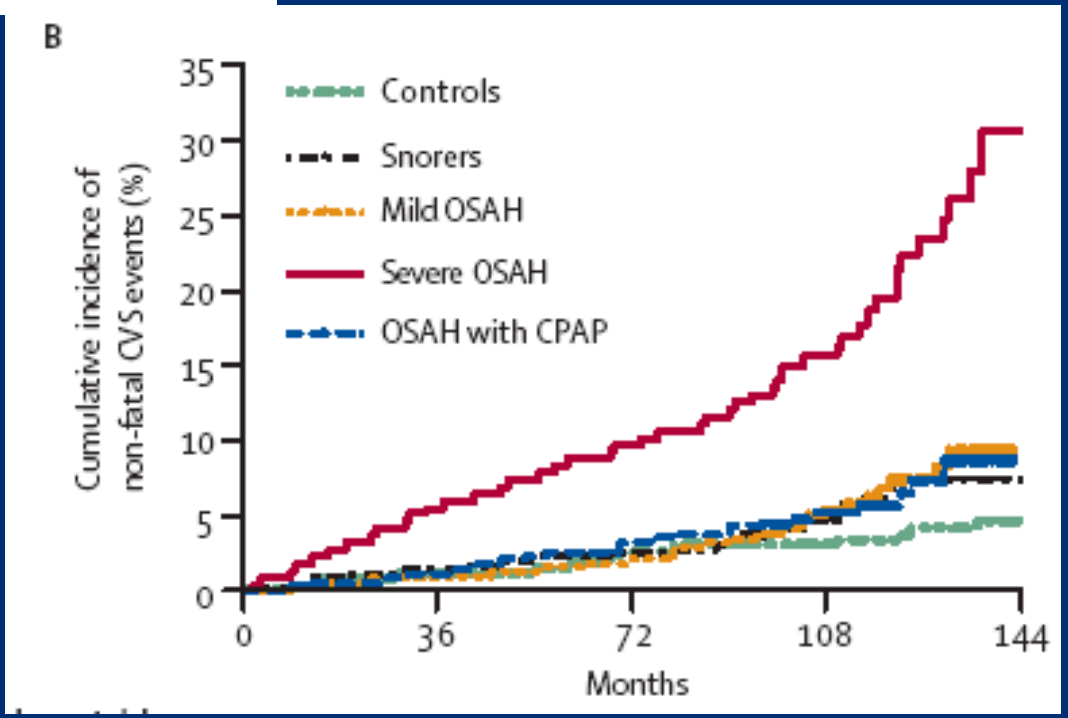
Sleep Duration	Relative Risk	Confidence Interval
5 hours	1.82	1.34 – 2.41
6 hours	1.30	1.08 – 1.57
7 hours	1.06	0.89-1.26
8 hours	1	1

Cardiovascular Diseases Associated with OSA

- Hypertension
- Heart failure
- Stroke
- Cardiac ischemia
- Atrial fibrillation

Cumulative Percentage of Individuals With New Fatal (A) and Non-fatal (B) Cardiovascular Events in Each of the Five Groups Studied





Marin et al. Lancet. 2005;365:1046-53

Sleep Apnea and Sleep Duration – Implications for…

- CV risk
- Obesity
- Hypertension
- Insulin resistance
- Metabolic syndrome

ORIGINAL INVESTIGATION

Overweight and Obese Patients in a Primary Care Population Report Less Sleep Than Patients With a Normal Body Mass Index

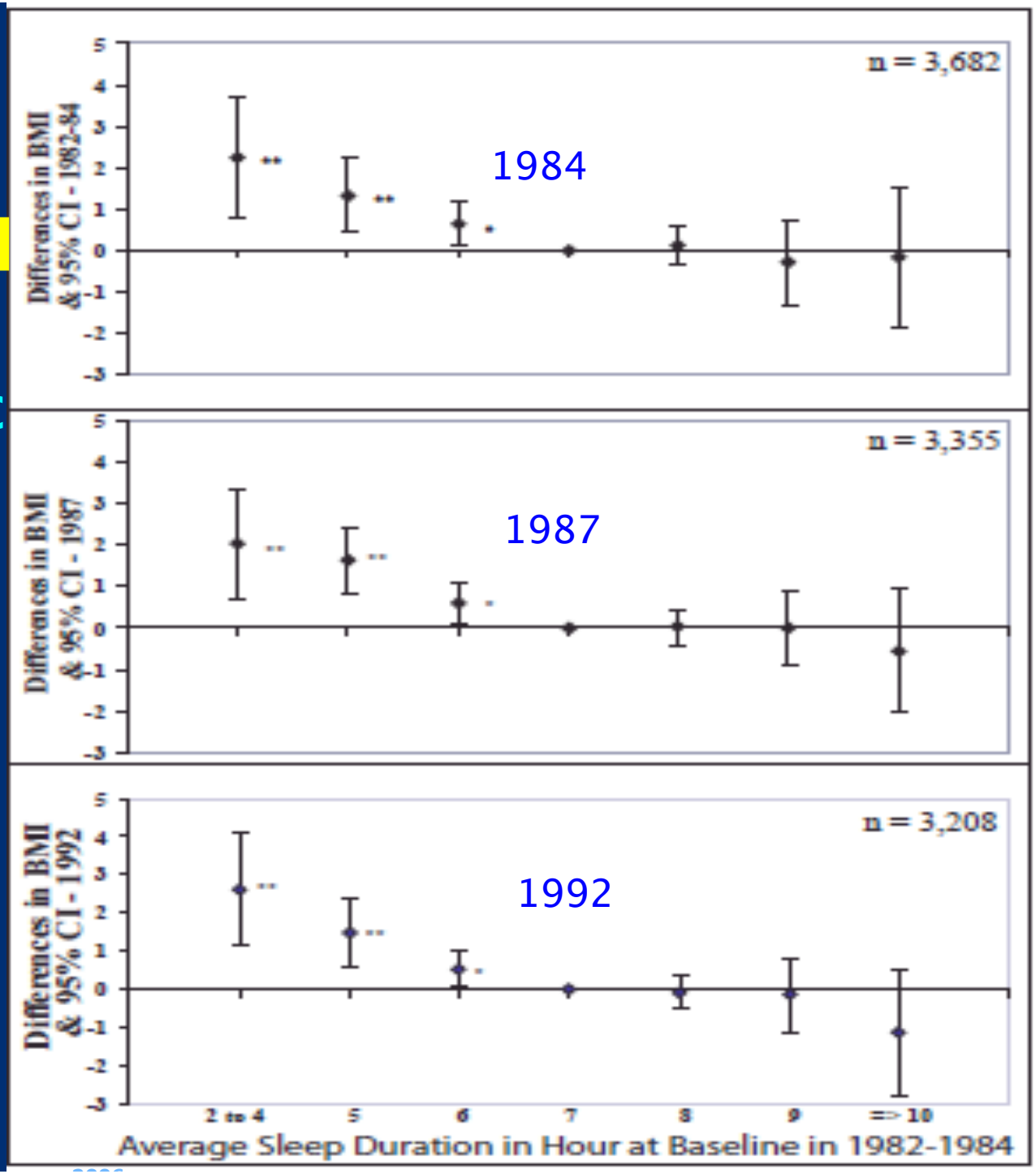
Robert D. Vorona, MD; Maria P. Winn, MSN, FNP; Teresa W. Babineau, MD; Benjamin P. Eng, MD; Howard R. Feldman, MD; J. Catesby Ware, PhD

Arch Intern Med. 2005;165:25-30

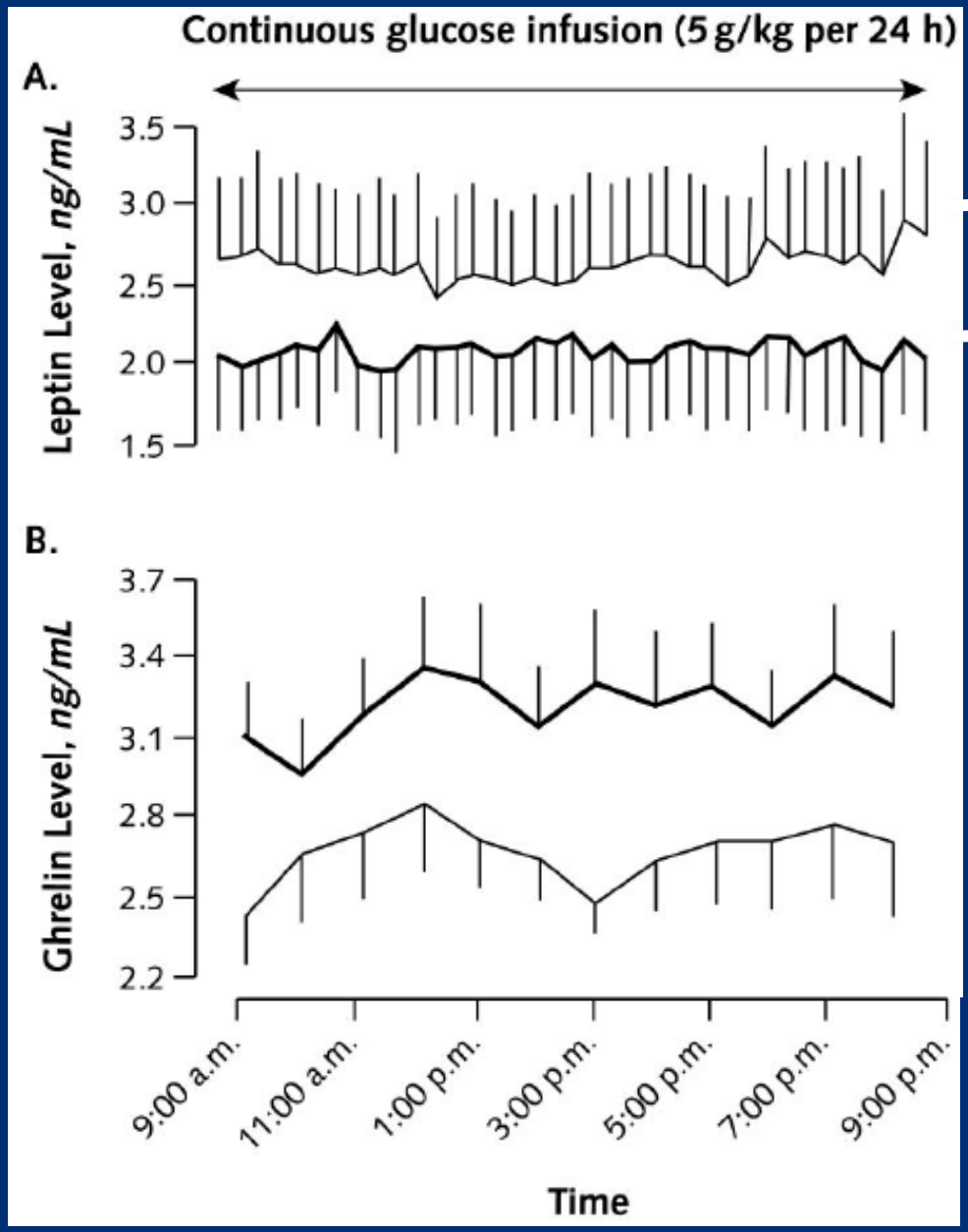
Short sleep duration and obesity

Epidemiologic evidence

NHANES I



Gangswisch et al. Sleep 2005;28:1289-96.
Patel. Am J Epidemiology

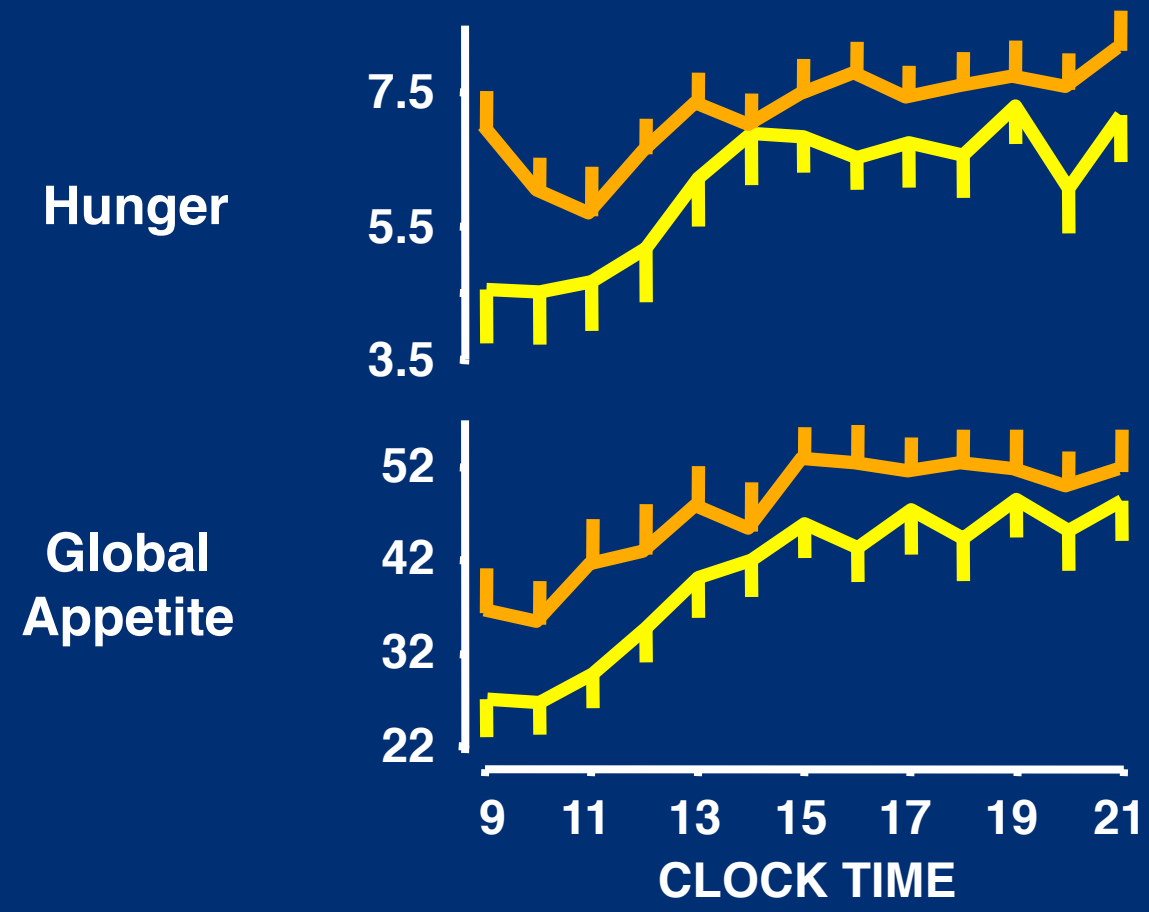


After 2 d of 10-h sleep time

After 2 d of 4-h sleep time

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

Ratings Of Hunger And Appetite



After 2 Days of 4-H Bedtime

After 2 Days of 10-H Bedtime

			p level	% change
Hunger (cms)	6.0 ± 0.5	7.2 ± 0.4	<0.01	+24%
Global Appetite (cms)	39.7 ± 3.0	47.7 ± 3.4	0.010	+23%

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

Sleep Deprivation and Energy Balance

Design

SCREEN 1 d/1 n	1 week home actigraphy	ACCLIMATION 3 d/3n	EXPERIMENTAL 8 d/8 n	RECOVERY 4 d/3 n

- Simple randomization stratified by gender to sleeping *ad lib* or reduction in time in bed by $^1/_3$
- Subjects awoken every day at 6 am but bedtime based on randomization

Typical time in bed: 10:00 pm – 6:00 am = 8 h
Deprived time in bed: 12:40 am – 6:00 am = 5.3 h

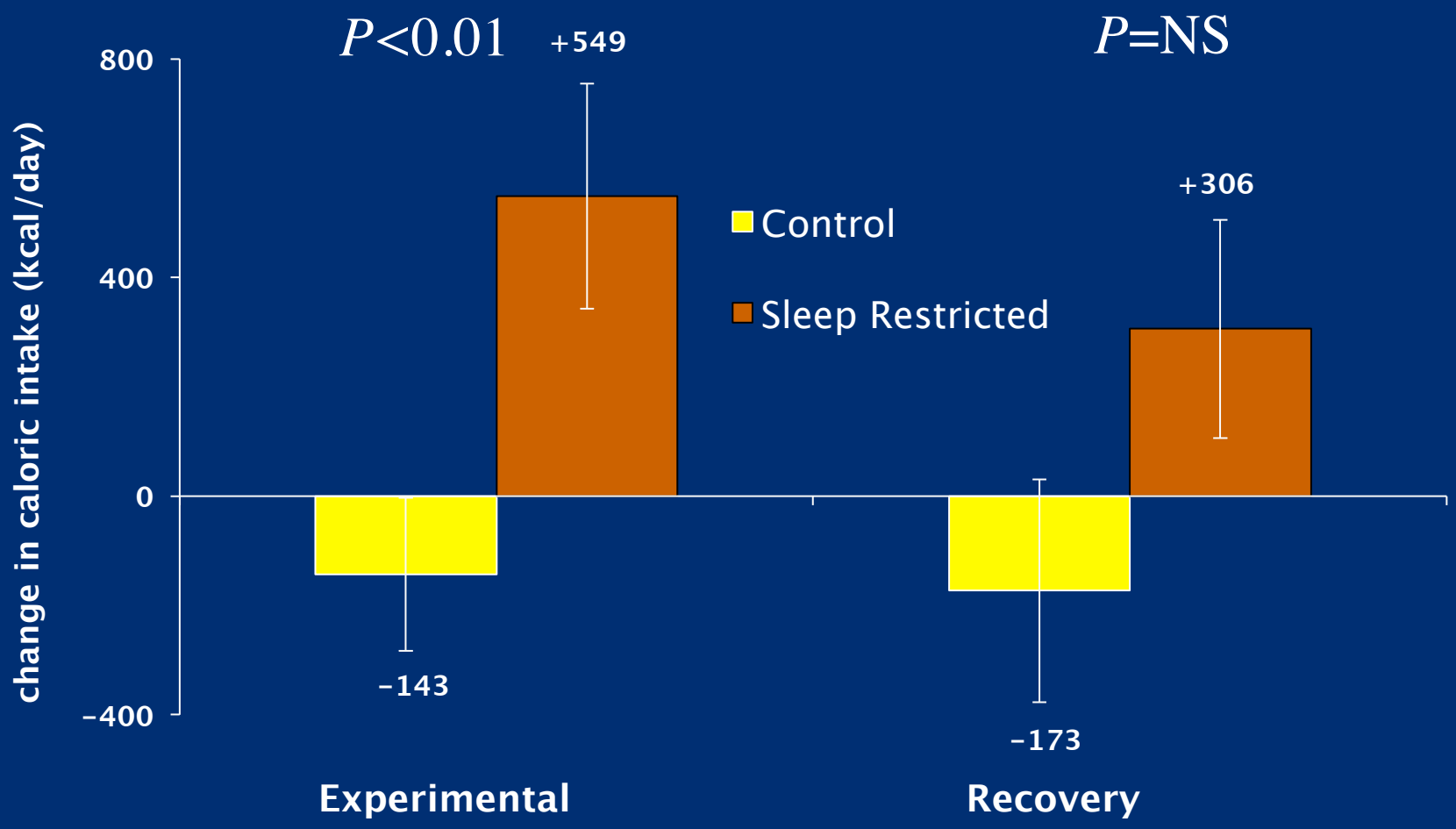
Sleep Deprivation and Energy Balance

Mayo Sleep Monitoring System (MSMS)

- Custom-modified sleep/wake monitoring system based on Compumedics Siesta 802
- 64 channels, 512 Hz, 16 bit resolution
  - Electroencephalogram (EEG)
  - Electro-oculogram (EOG)
  - Electromyogram (EMG)
  - Electrocardiogram (ECG)
  - Extensible, allows addition of more channels
- Specialized electrode placement to allow safe, 23 hour/day monitoring
- Telemetry allowing real-time monitoring
- <1 kg, wearable, unobtrusive

Sleep Deprivation and Energy Balance

Results – caloric intake

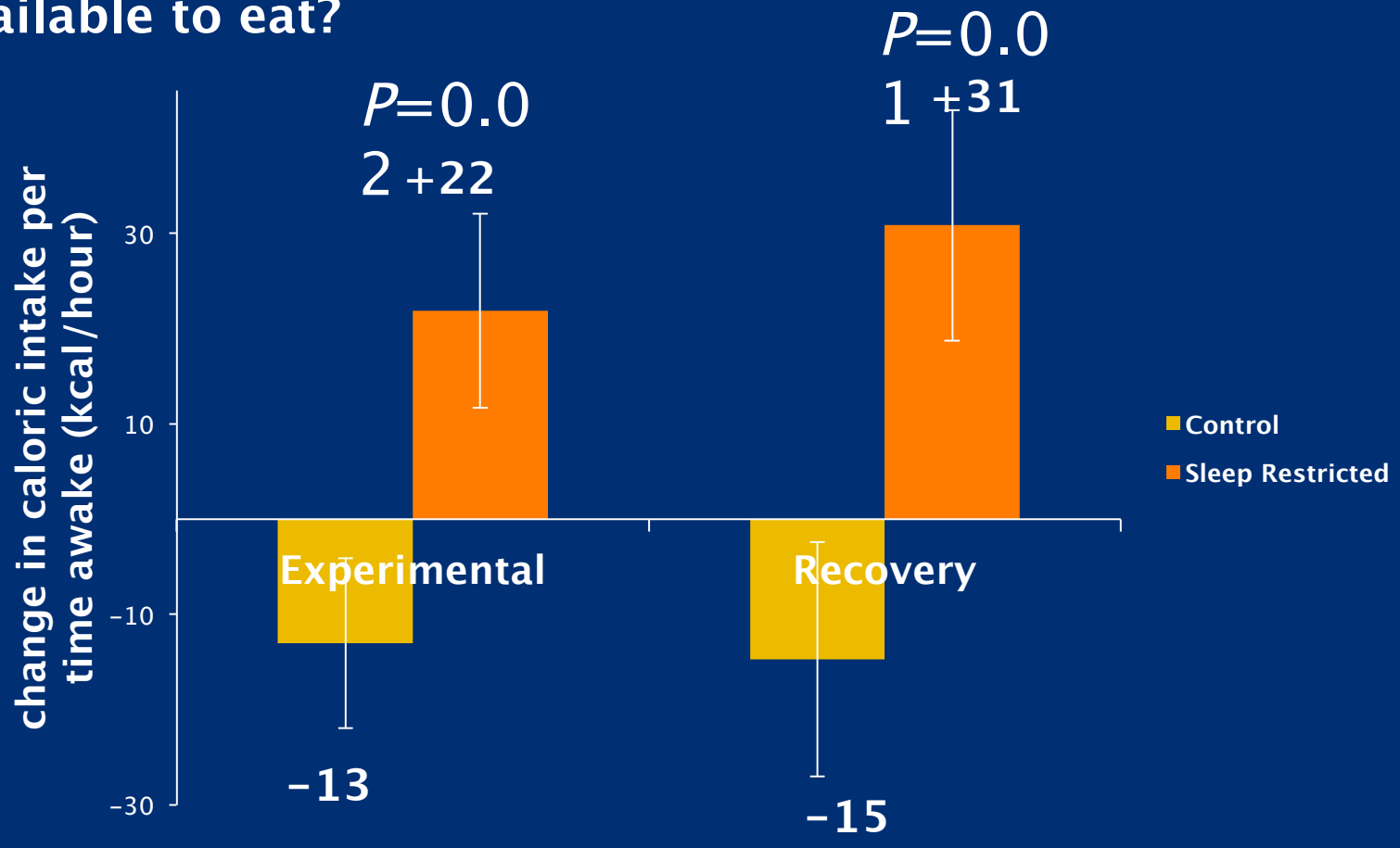


Calvin et al. Chest 2013;144:79-86.

Sleep Deprivation and Energy Balance

Results – caloric intake per hour

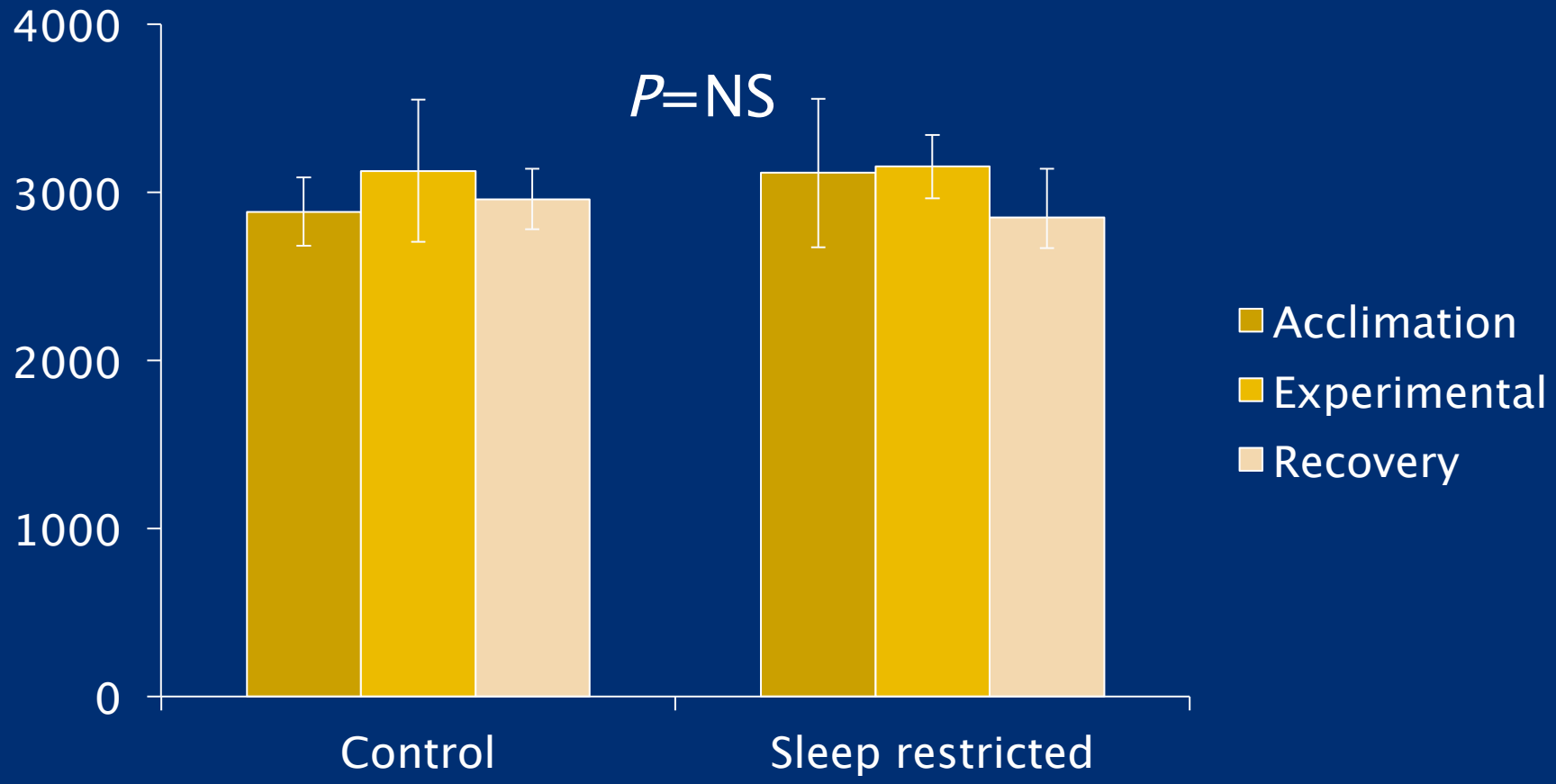
Was the increased caloric intake due to more time available to eat?



Calvin et al. Chest 2013;144:79–86.

Sleep Deprivation and Energy Balance

Results – energy expenditure



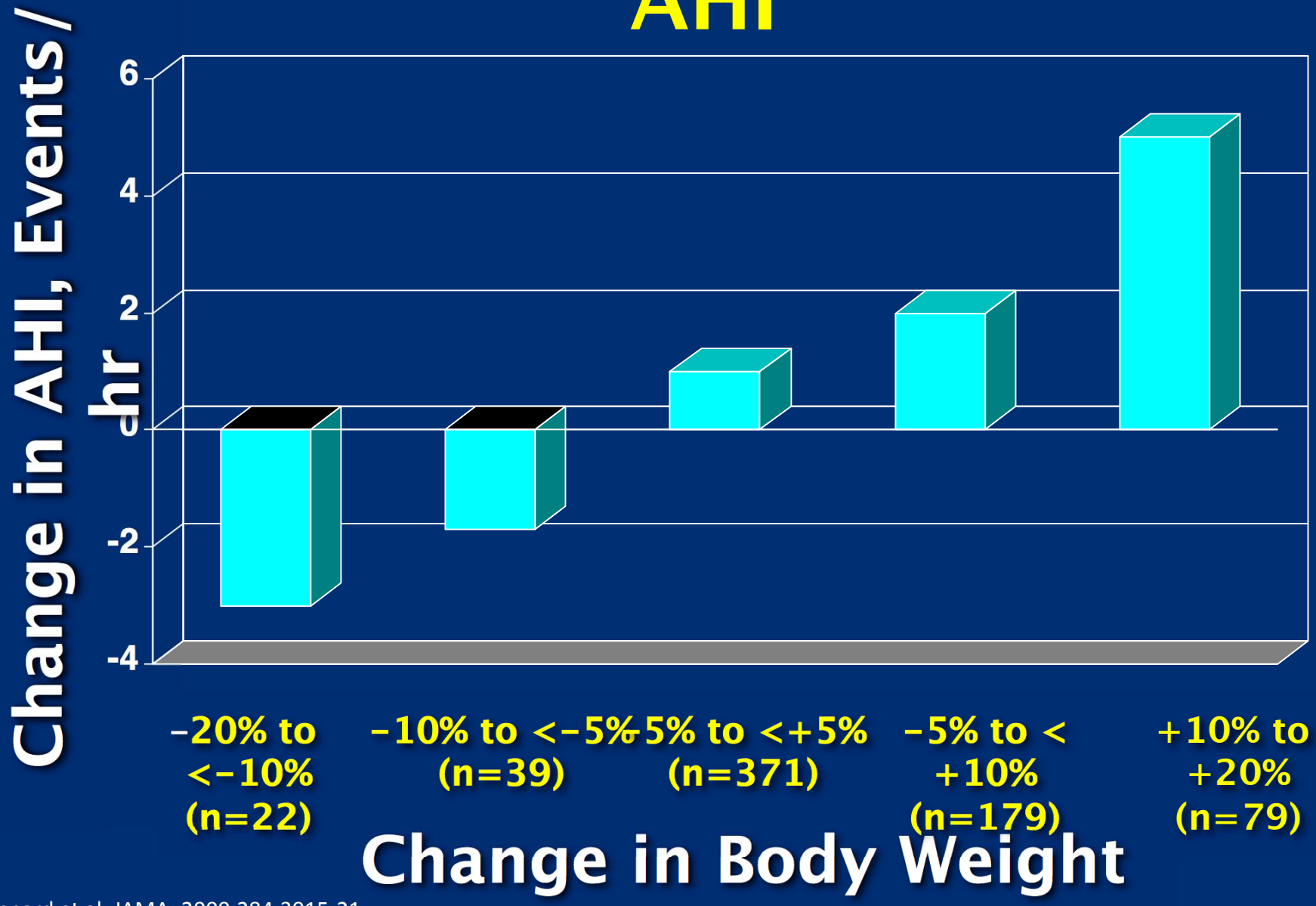
Estimated maximal (95%) energy change <50 kcal/day

Calvin et al. Chest 2013;144:79–86.

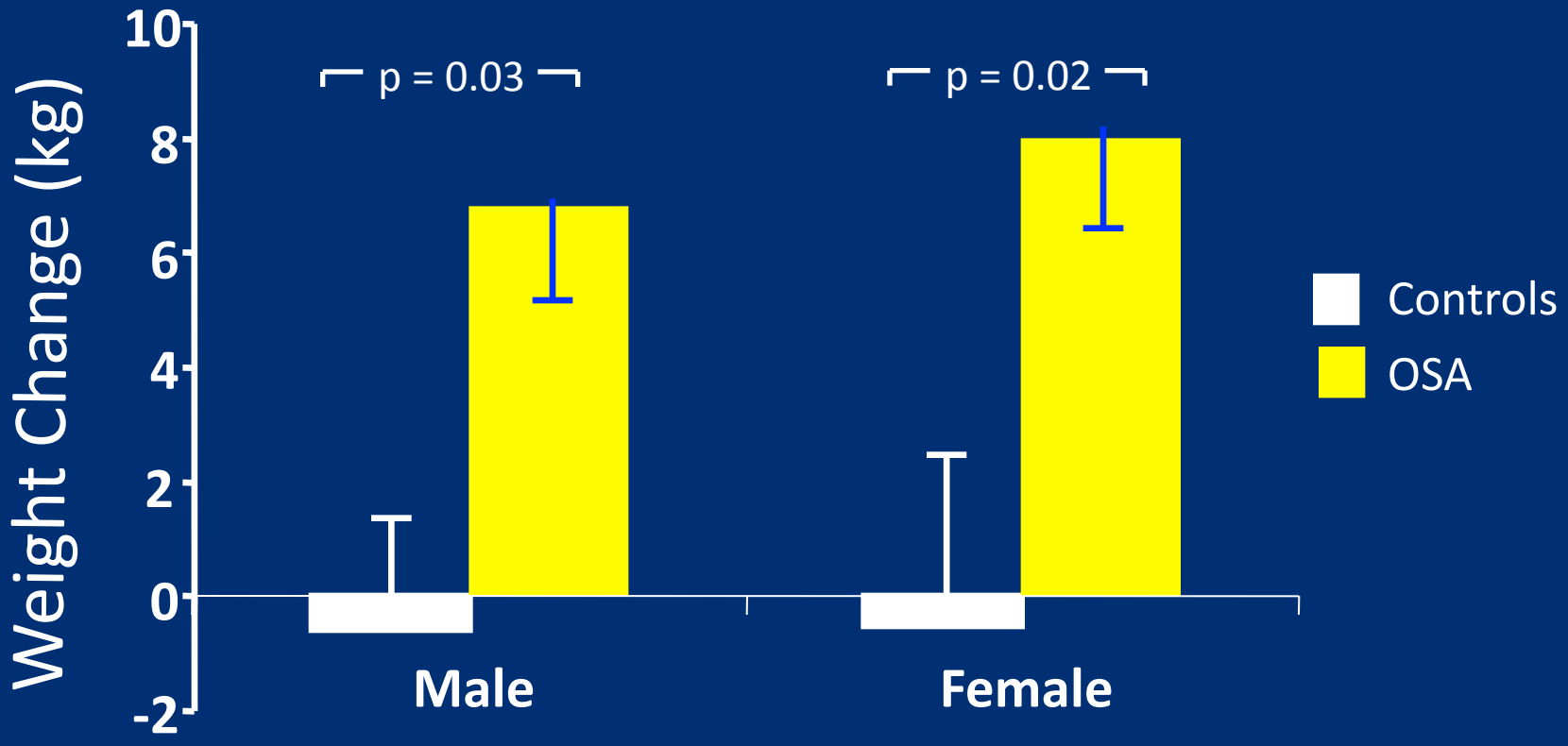
Sleep Deprivation and Energy Balance
Conclusions

- Modest sleep restriction increased caloric intake by 549 kcal/day
- Activity energy expenditure did not change, total energy expenditure likely changes minimally

Effects of Weight Change on AHI



Peppard et al. JAMA. 2000;284:3015-21.



Weight History and OSA

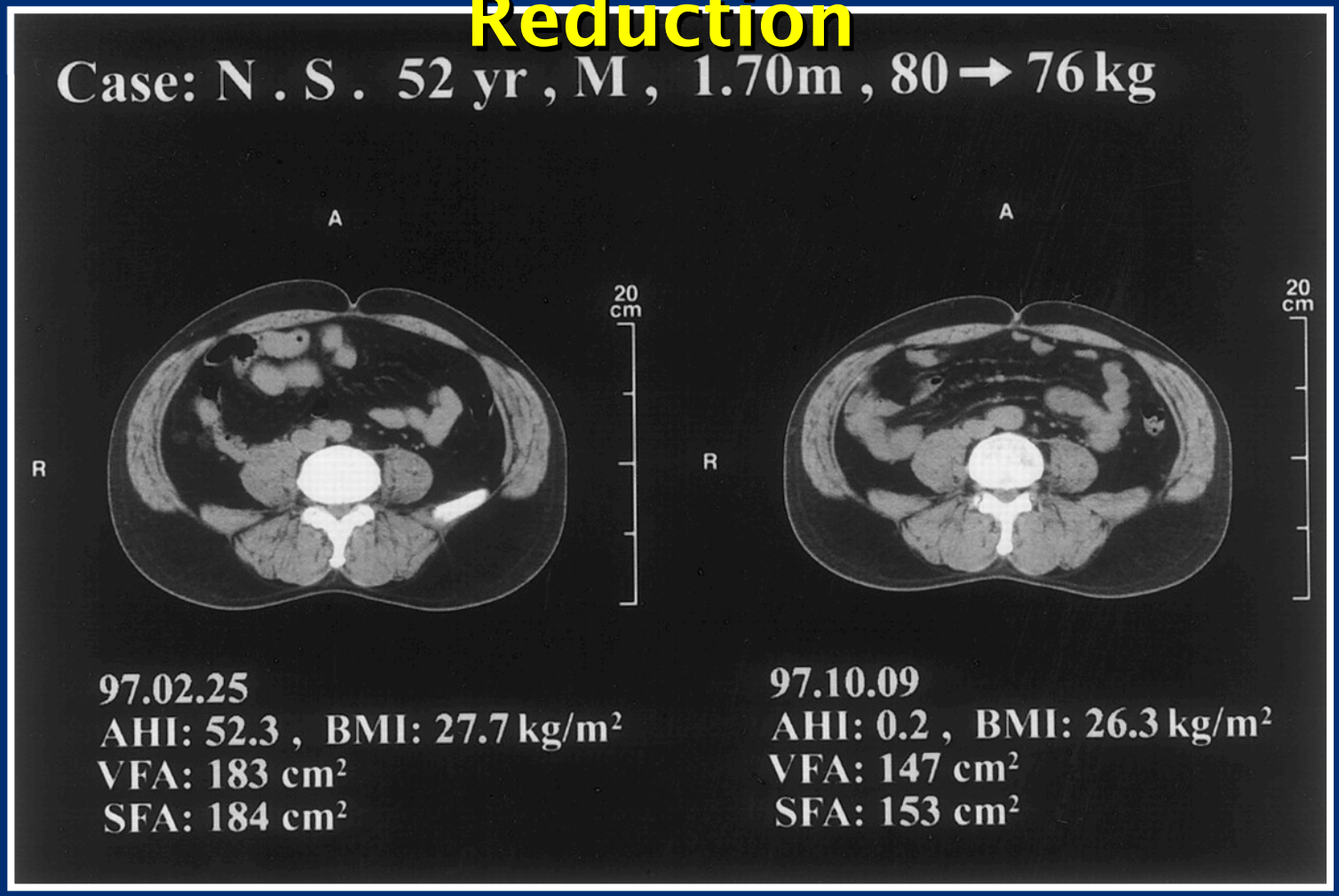
Phillips et al. J Hypertens 1999:17;1297-1300

Changes in Intra-Abdominal Visceral Fat and Serum Leptin Levels in Patients With Obstructive Sleep Apnea Syndrome Following Nasal Continuous Positive Airway Pressure Therapy

Kazuo Chin, MD, PhD; Kouichi Shimizu, MD; Takaya Nakamura, MD; Noboru Narai, RT; Hiroaki Masuzaki, MD, PhD; Yoshihiro Ogawa, MD, PhD; Michiaki Mishima, MD, PhD; Takashi Nakamura, MD, PhD; Kazuwa Nakao, MD, PhD; Motoharu Ohi, MD, PhD

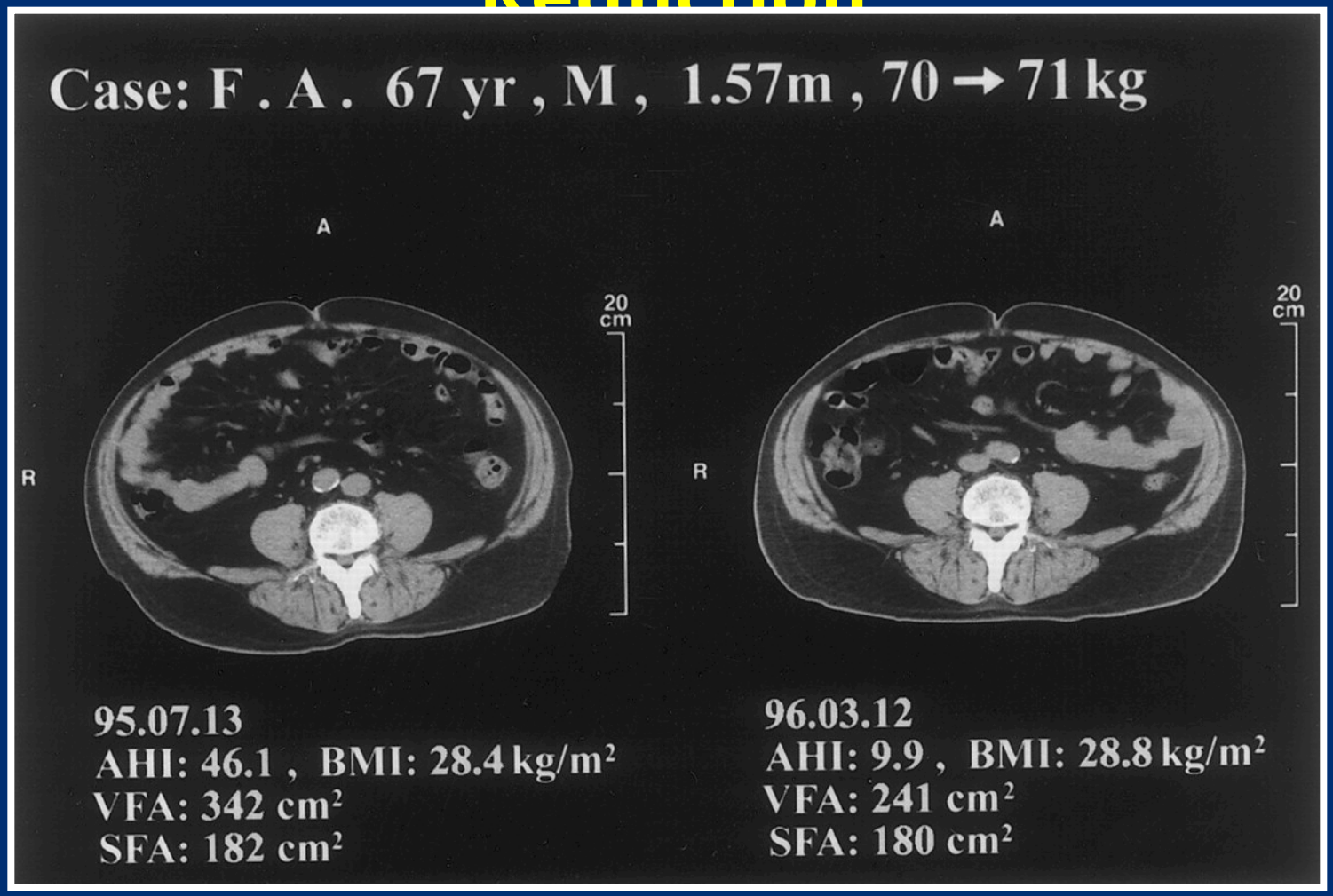
Circulation. 1999;100:706-12

CT Scan at the Umbilicus Level After 6 Months NCPAP With Body Weight Reduction



NCPAP=nasal continuous positive airway pressure
Chin et al. Circulation 1999;100:706-12.

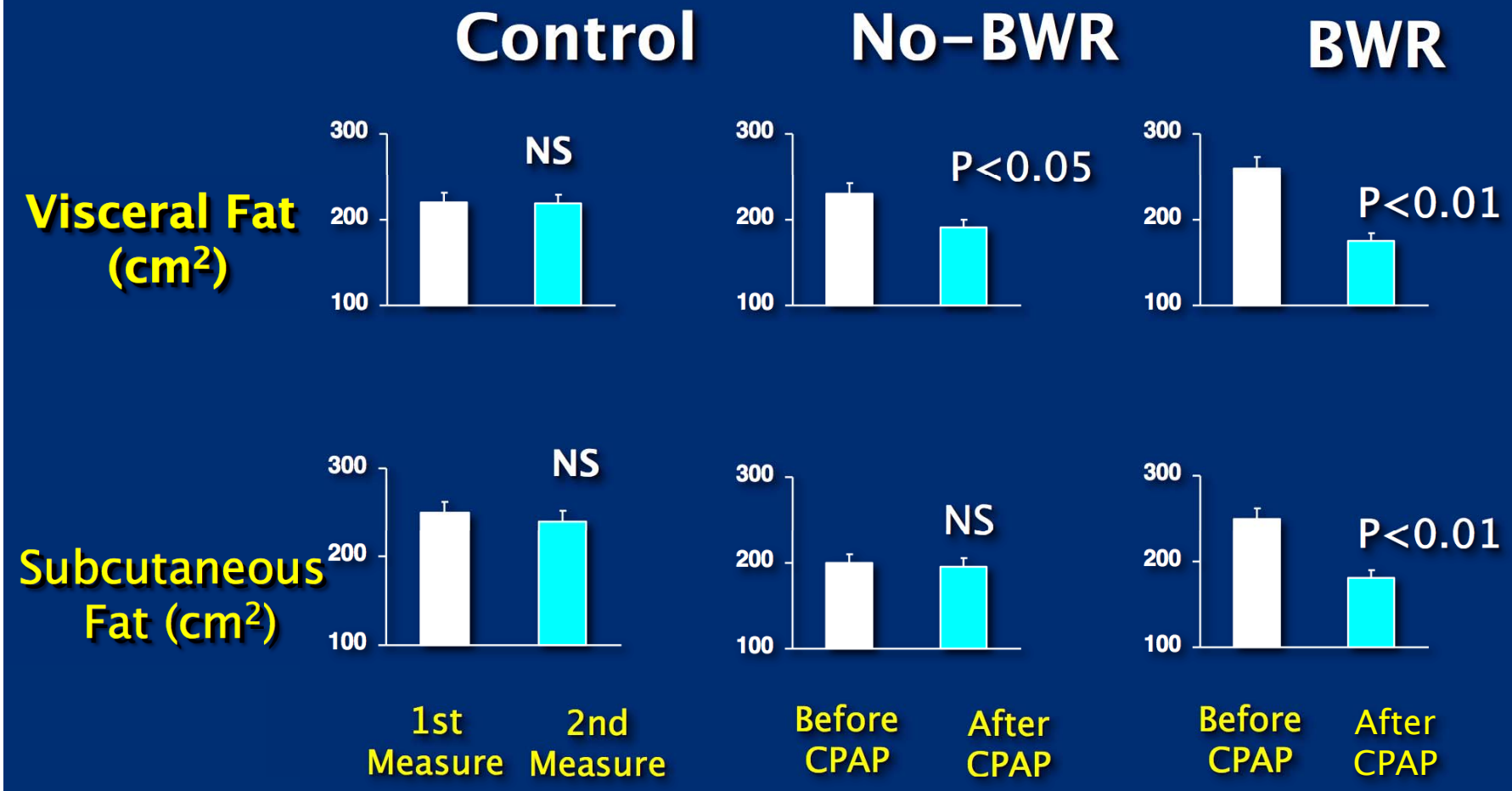
CT Scan at Umbilicus Level After 6 Months NCPAP With No Body Weight Reduction



NCPAP=nasal continuous positive airway pressure

Chin et al. Circulation 1999;100:706-12.

Changes in Body Fat After 6 Months NCPAP



NCPAP=nasal continuous positive airway pressure
Chin et al. Circulation 1999;100:706-12.

Sleep Apnea and Sleep Duration – Implications for…

- CV risk
- Obesity
- Hypertension
- Insulin resistance
- Metabolic syndrome

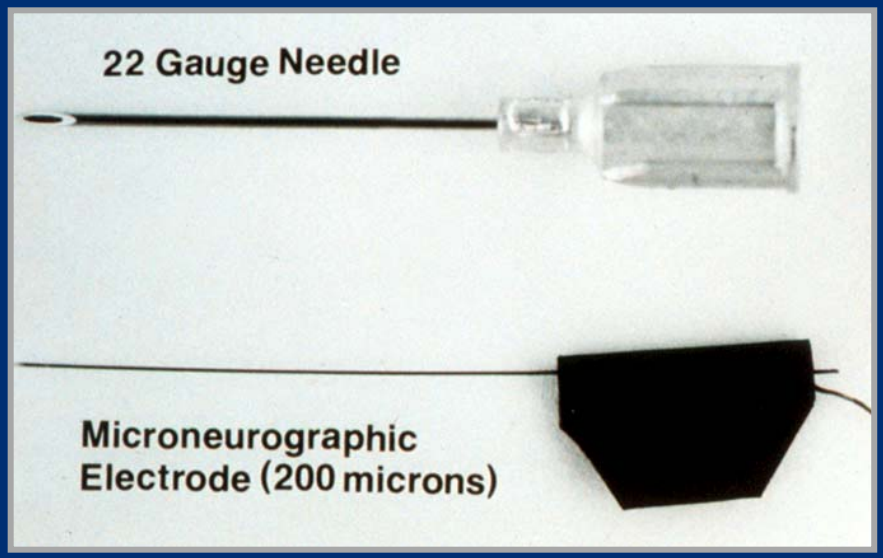
Original Articles

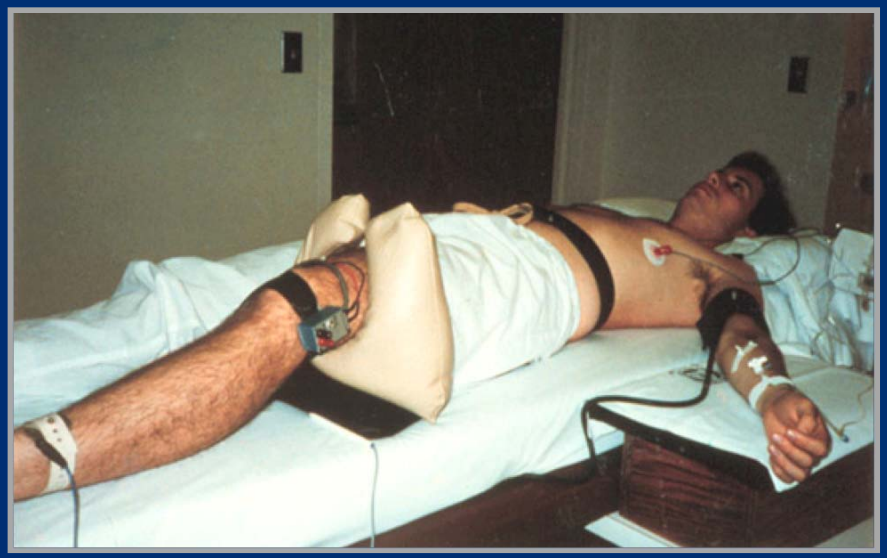
Short Sleep Duration as a Risk Factor for Hypertension

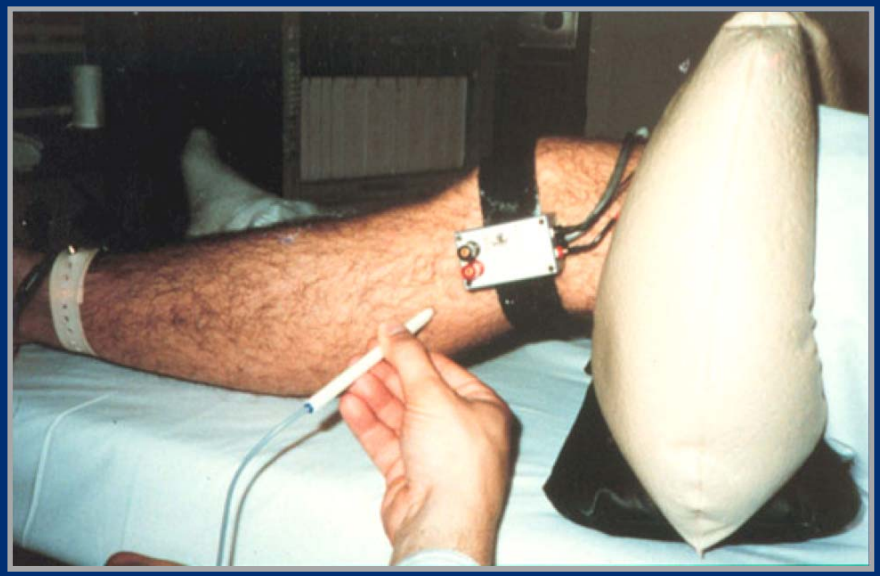
Analyses of the First National Health and Nutrition Examination Survey

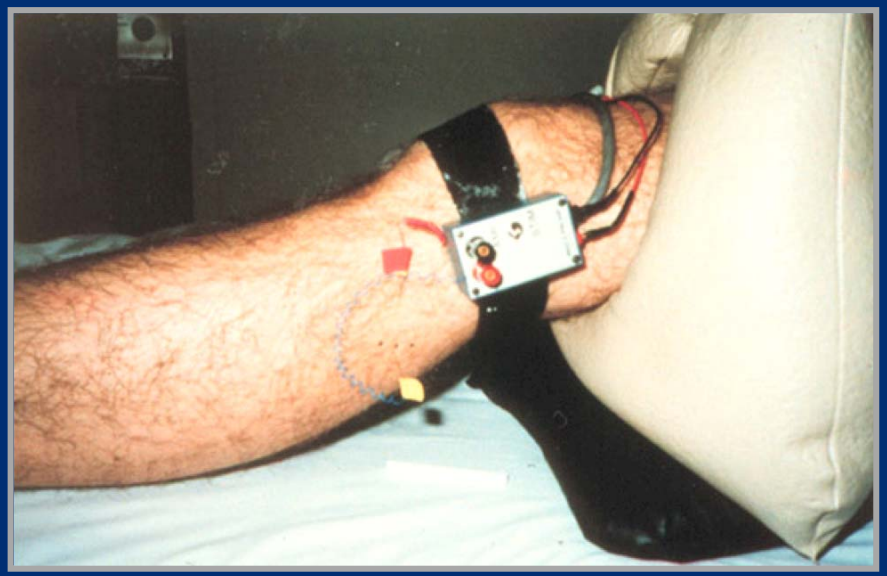
James E. Gangwisch, Steven B. Heymsfield, Bernadette Boden-Albala, Ruud M. Buijs, Felix Kreier, Thomas G. Pickering, Andrew G. Rundle, Gary K. Zammit, Dolores Malaspina

(*Hypertension*. 2006;47:833-839.)

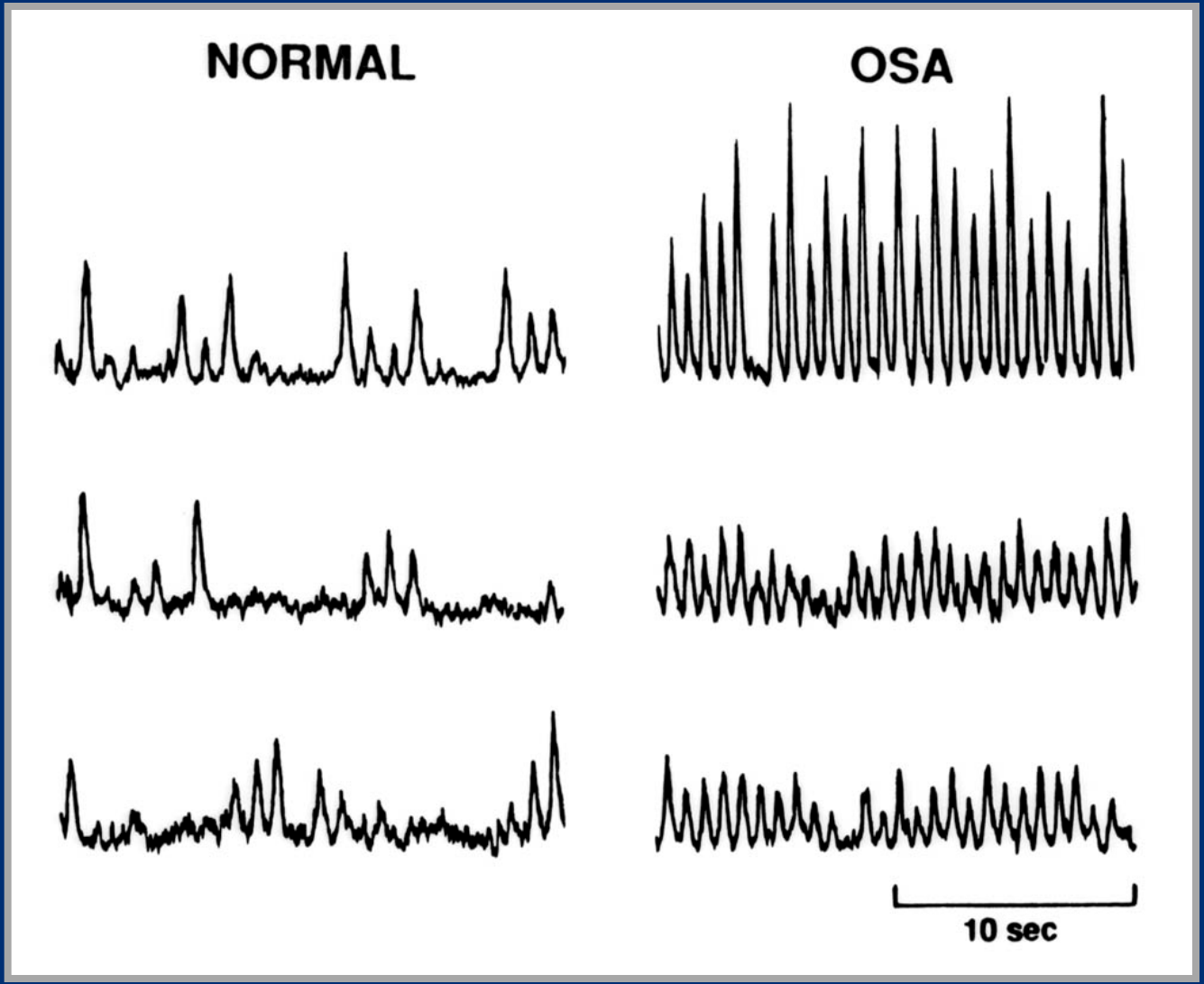

22 Gauge Needle
Microneurographic
Electrode (200 microns)



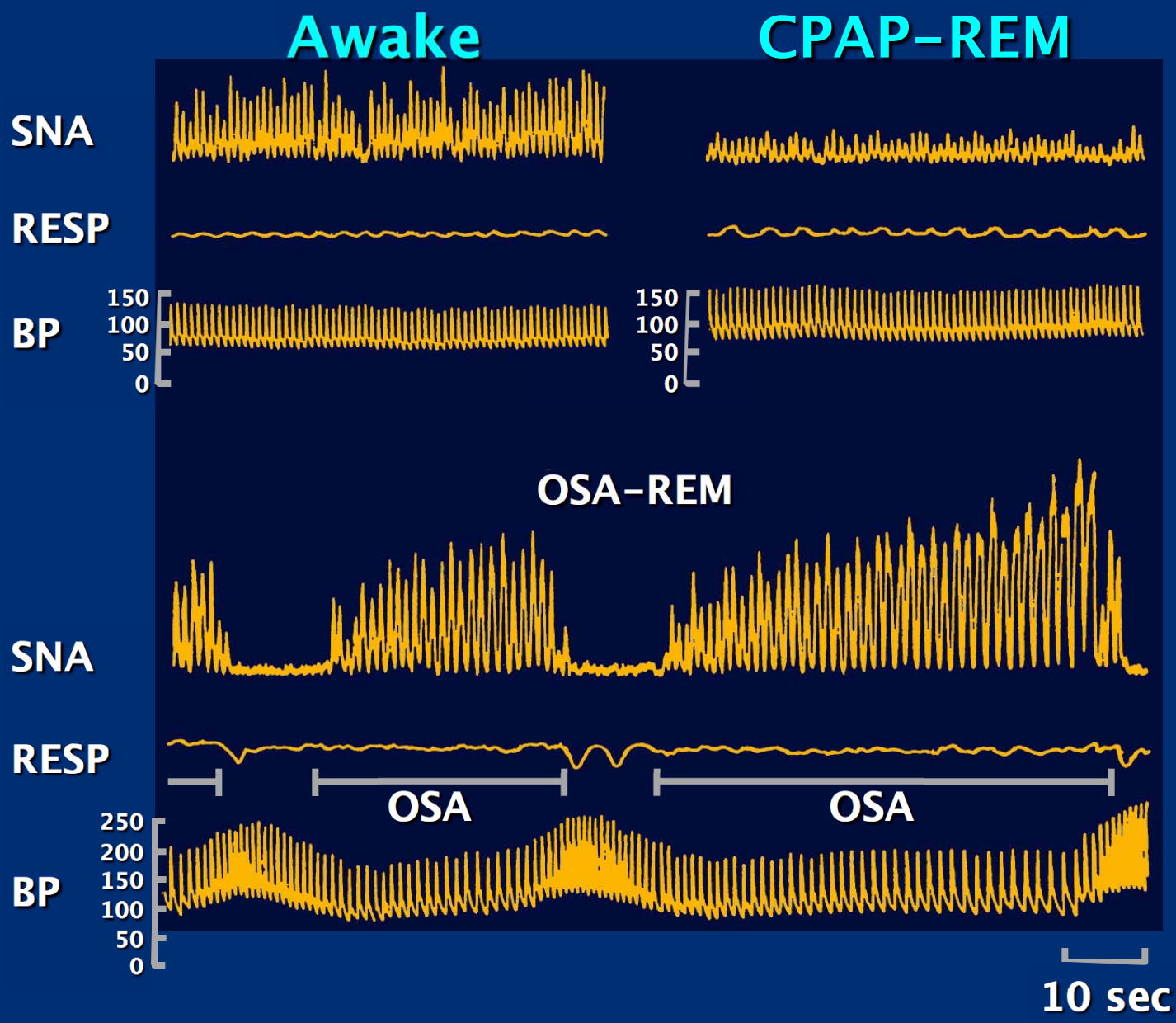




Awake



Somers et al, JCI. 1995;96:1897-904.



Somers et al, JCI. 1995;96:1897-904.

CP1029084-10

SLEEP COHORT STUDY

UNIVERSITY OF WISCONSIN–MADISON

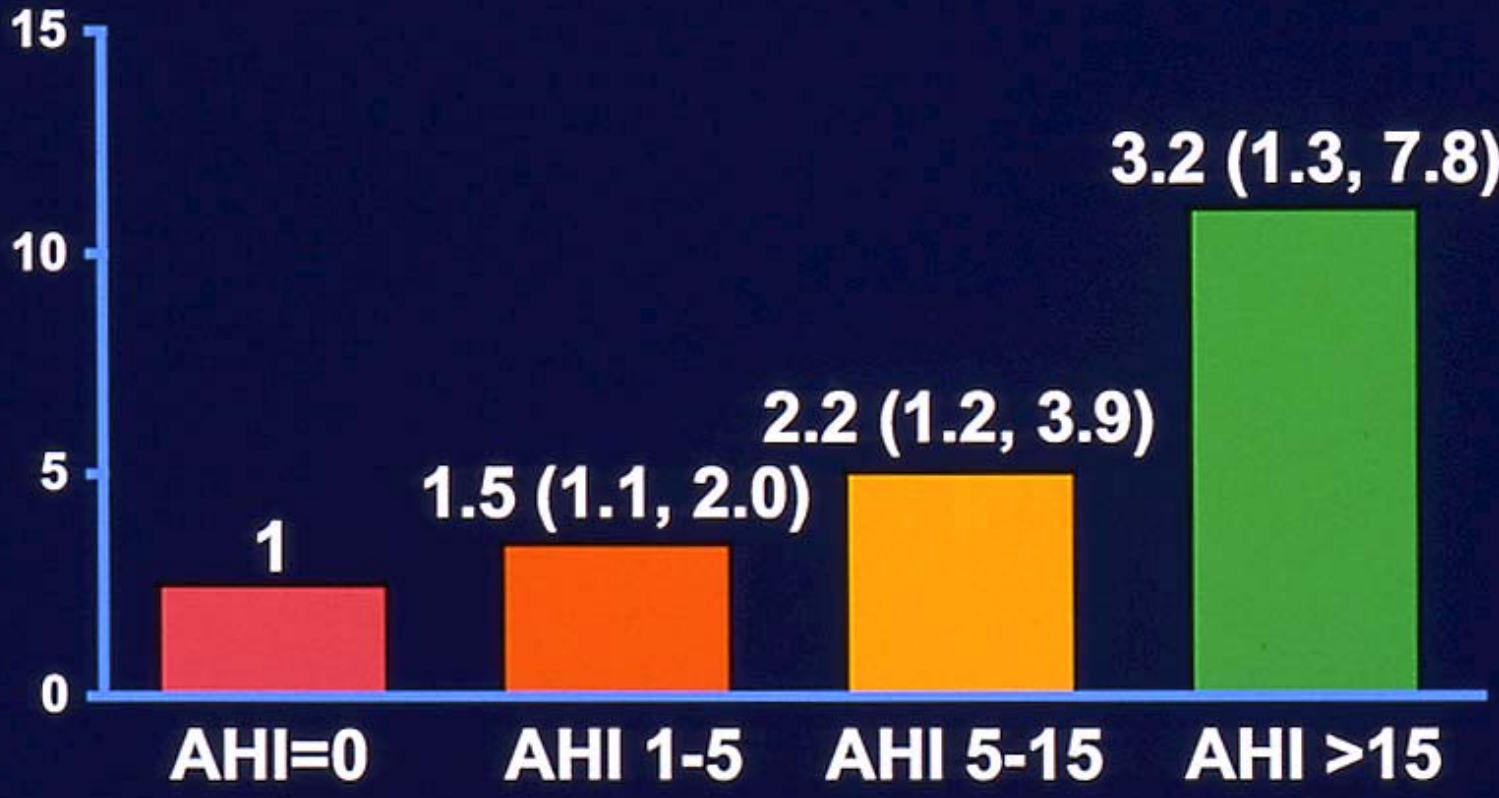
A population study of sleep patterns and problems

T Young, J Dempsey, S Badr, J Skatrud,

M Palta, S Weber, P Peppard, and L Finn

Odds Ratios* for Incident Hypertension at 4-Year F-U with Baseline AHI >0

Wisconsin Sleep Cohort Study



*Adjusted for age, sex, smoking, ALC, BMI, neck girth

Peppard et al: NEJM 2000

CP1029084-5

Sleep Apnea and Sleep Duration – Implications for…

- CV risk
- Obesity
- Hypertension
- Insulin resistance
- Metabolic syndrome

Invited Review

J Appl Physiol 99: 2008–2019, 2005;
doi:10.1152/japplphysiol.00660.2005.

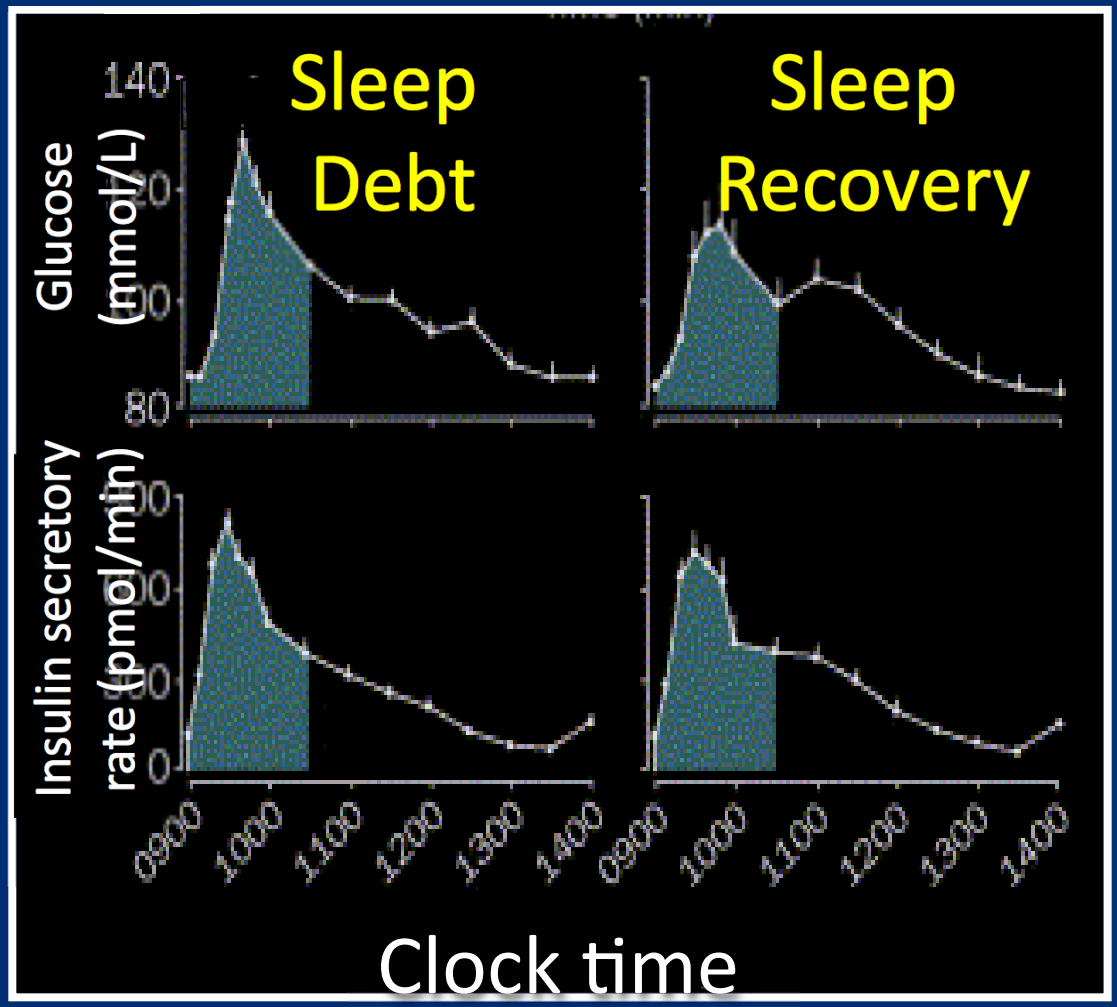
HIGHLIGHTED TOPIC | *Physiology and Pathophysiology of Sleep Apnea*

Sleep loss: a novel risk factor for insulin resistance and Type 2 diabetes

Karine Spiegel,[1] Kristen Knutson,[2] Rachel Leproult,[2] Esra Tasali,[2] and Eve Van Cauter[2]

[1]*Laboratoire de Physiologie, Centre d'Etude des Rythmes Biologiques (CERB), Université Libre de Bruxelles, Belgium; and* [2]*Department of Medicine, University of Chicago, Chicago, Illinois*

Glucose and Insulin Responses to Breakfast



Spiegel et al. Lancet 1999

Glucose Tolerance

Kg Derived From Glucose Disappearance Curve During IVGTT

CLINICAL SIGNIFICANCE

	18-27 yr old subjects in sleep debt	18-27 yr old subjects fully rested
Kg (% per min)	1.45 ± 0.31	2.40 ± 0.41

	61-80 yr old adults with impaired glucose tolerance (1)	21-30 yr old fit subjects (2)
Kg (% per min)	Range: 1.30 - 2.10	Range: 2.20 - 2.90

(1) from Garcia et al. J Am Geriatr Soc. 1997; 45: 813-7.
(2) from Prigeon et al, Metabolism. 1995; 44: 1259-63.

OSA and Insulin Resistance

- Experimental sleep deprivation induces insulin resistance
- Severity of OSA is associated with fasting insulin levels, HOMA
- High prevalence of OSA in type 2 DM
- CPAP is followed by improvement in diabetes

HOMA=homeostatic model assessment

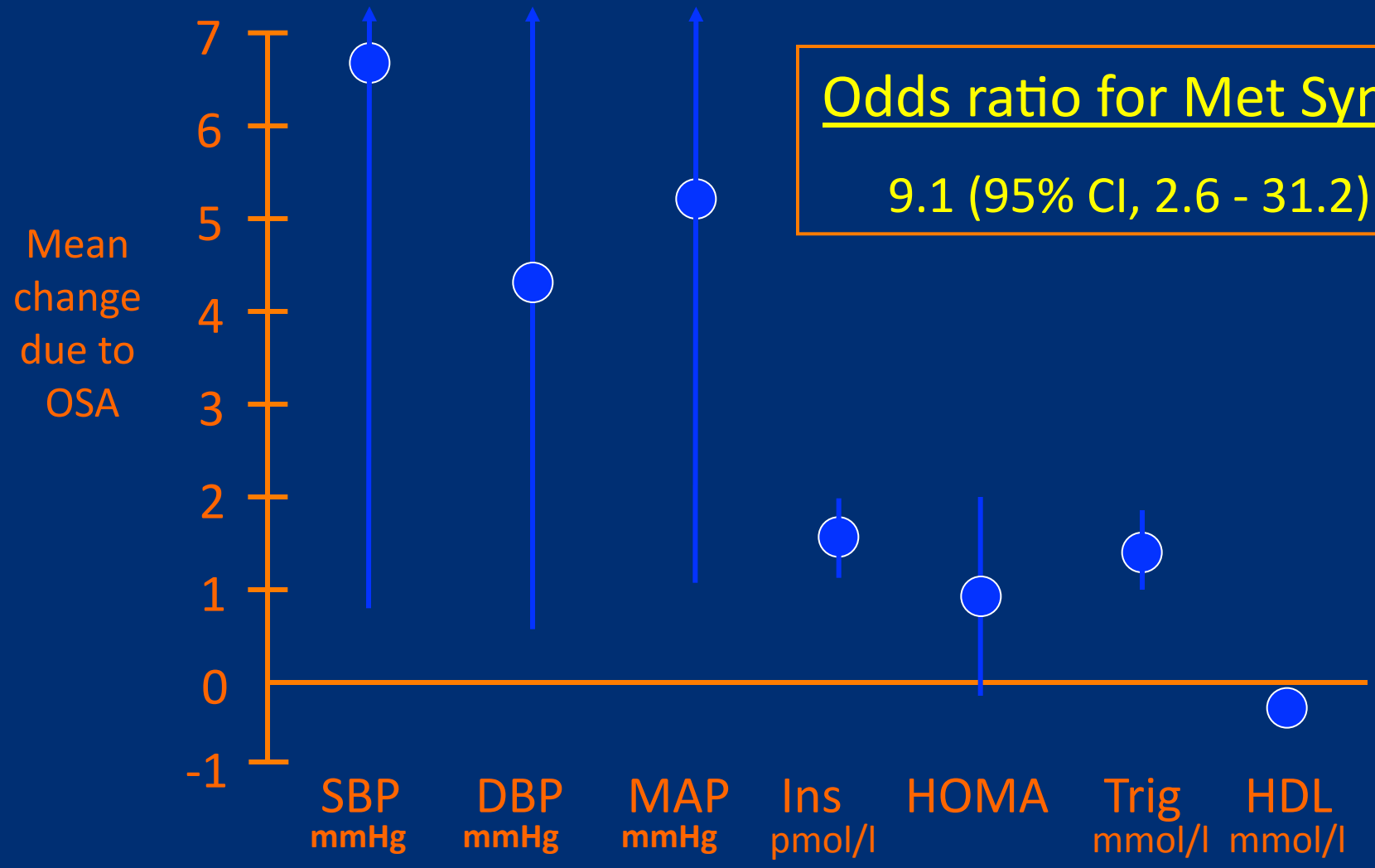
Sleep Apnea and Sleep Duration – Implications for…

- CV risk
- Obesity
- Hypertension
- Insulin resistance
- Metabolic syndrome

	OSA	Met Syn
Hypertension	+++	++
Central obesity	++	+++
Insulin resistance	++	+++
Sympathetic activation	+++	+
Endothelial dysfunction	++	++
Inflammation	++	++

Syndrome X + OSA = Syndrome Z

OSA & Metabolic Syndrome



Odds ratio for Met Synd:

9.1 (95% CI, 2.6 - 31.2)

Coughlin et al. Eur Heart J, 2004;25:735-41.

Metabolic Syndrome and Risk for Total and CV Mortality

Longitudinal studies with 172,573 individuals

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doi:10.1016/j.jacc.2006.09.032

REVIEW AND META-ANALYSIS

Metabolic Syndrome and Risk of Incident Cardiovascular Events and Death

A Systematic Review and Meta-Analysis of Longitudinal Studies

Apoor S. Gami, MD,*† Brandi J. Witt, MD,*† Daniel E. Howard, MD,† Patricia J. Erwin, MLS,‡
Lisa A. Gami, RN,*† Virend K. Somers, MD, PHD, FACC,*†§ Victor M. Montori, MD, MSC†‖¶
Rochester, Minnesota

Metabolic Syndrome and Outcomes

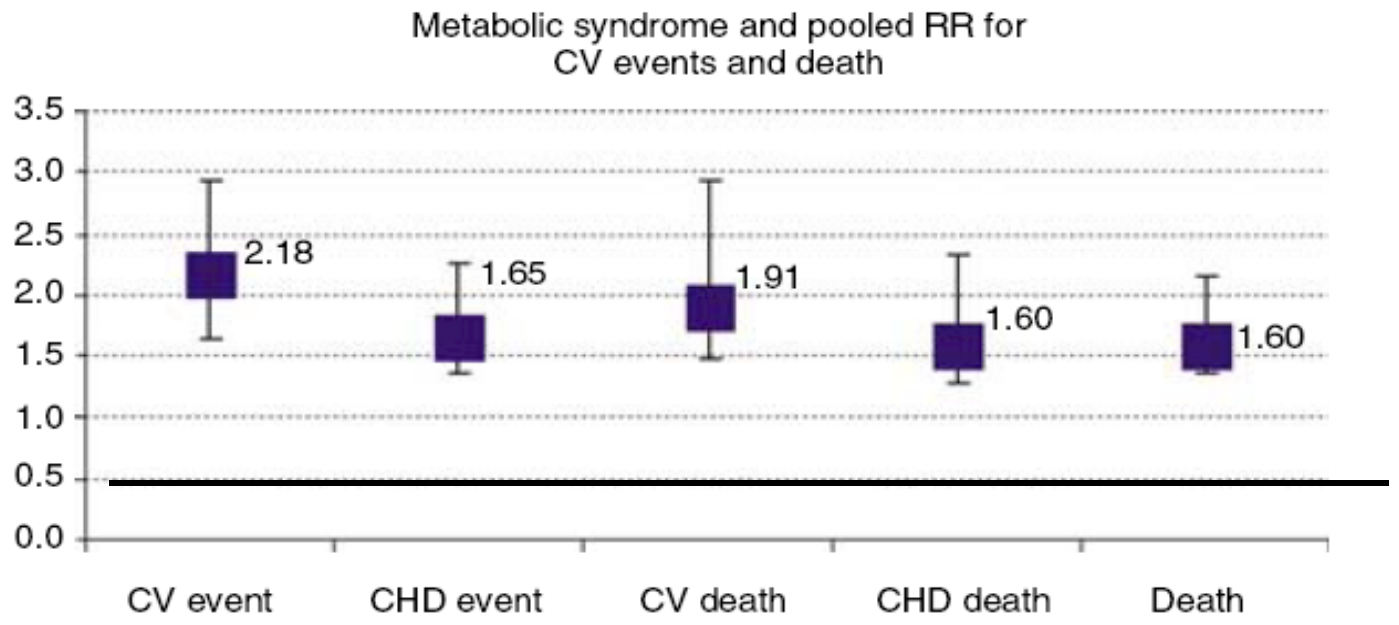
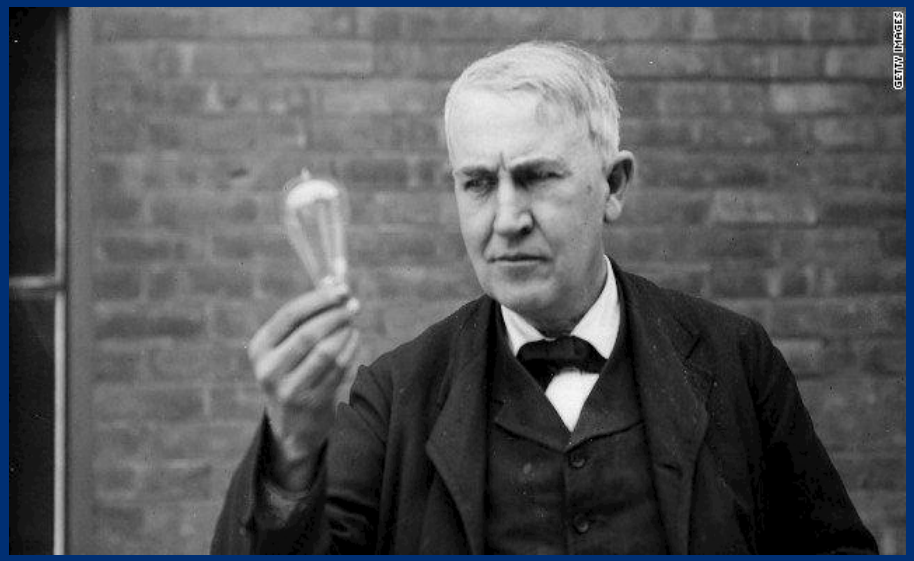


Figure 2 The pooled RR for CV events and death in patients with the metabolic syndrome. There were 11 studies examined for CV events, 18 studies for coronary heart disease (CHD) events, 10 studies for CV death, 7 studies for CHD death, and 12 studies for death. The squares on the graph represent the pooled RRs, and the bars represent the 95% confidence intervals. The data were adapted from Gami *et al.*[13]

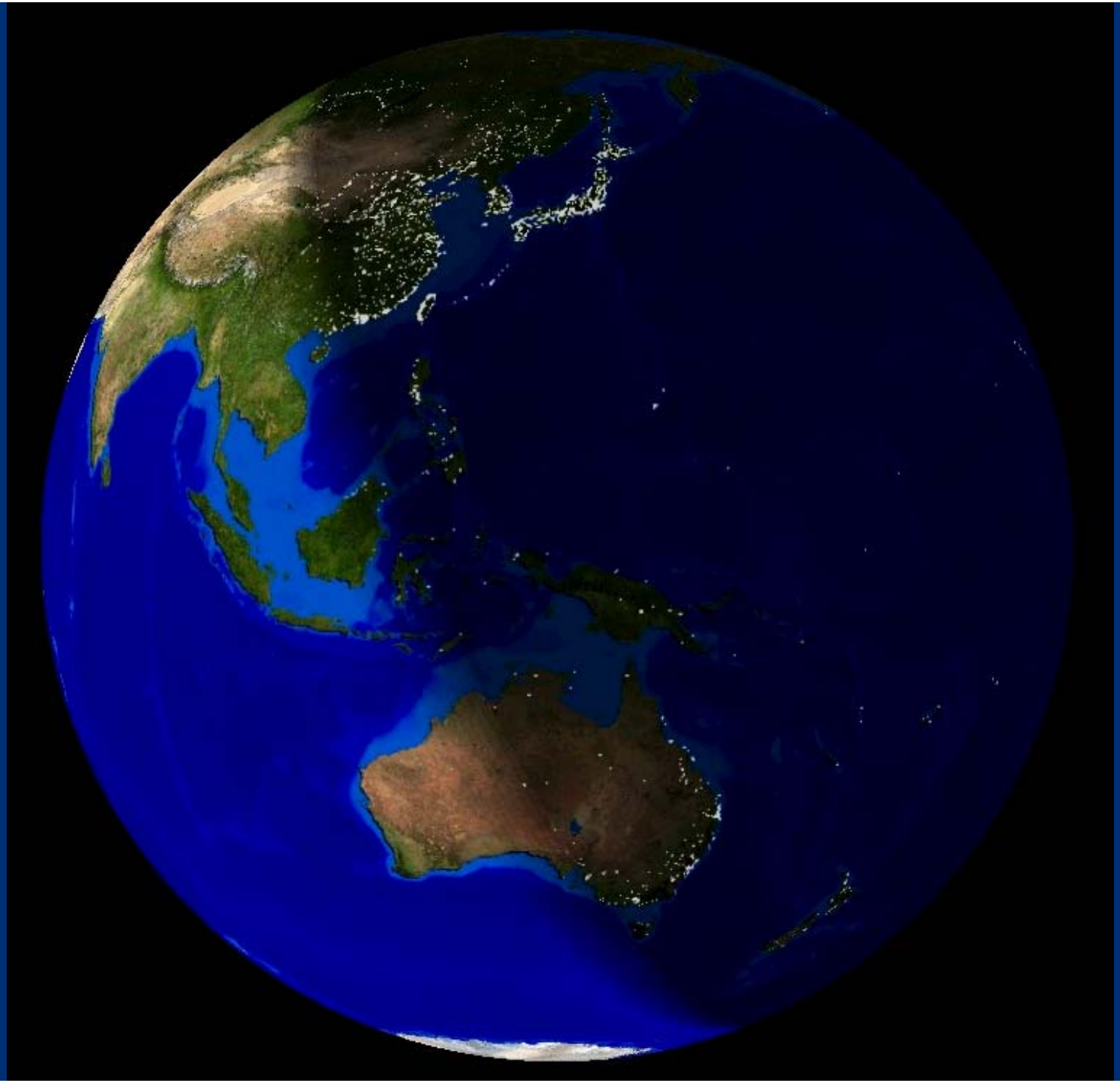
Sleep Apnea and Sleep Duration – Implications for…

- CV risk
- Obesity
- Hypertension
- Insulin resistance
- Metabolic syndrome

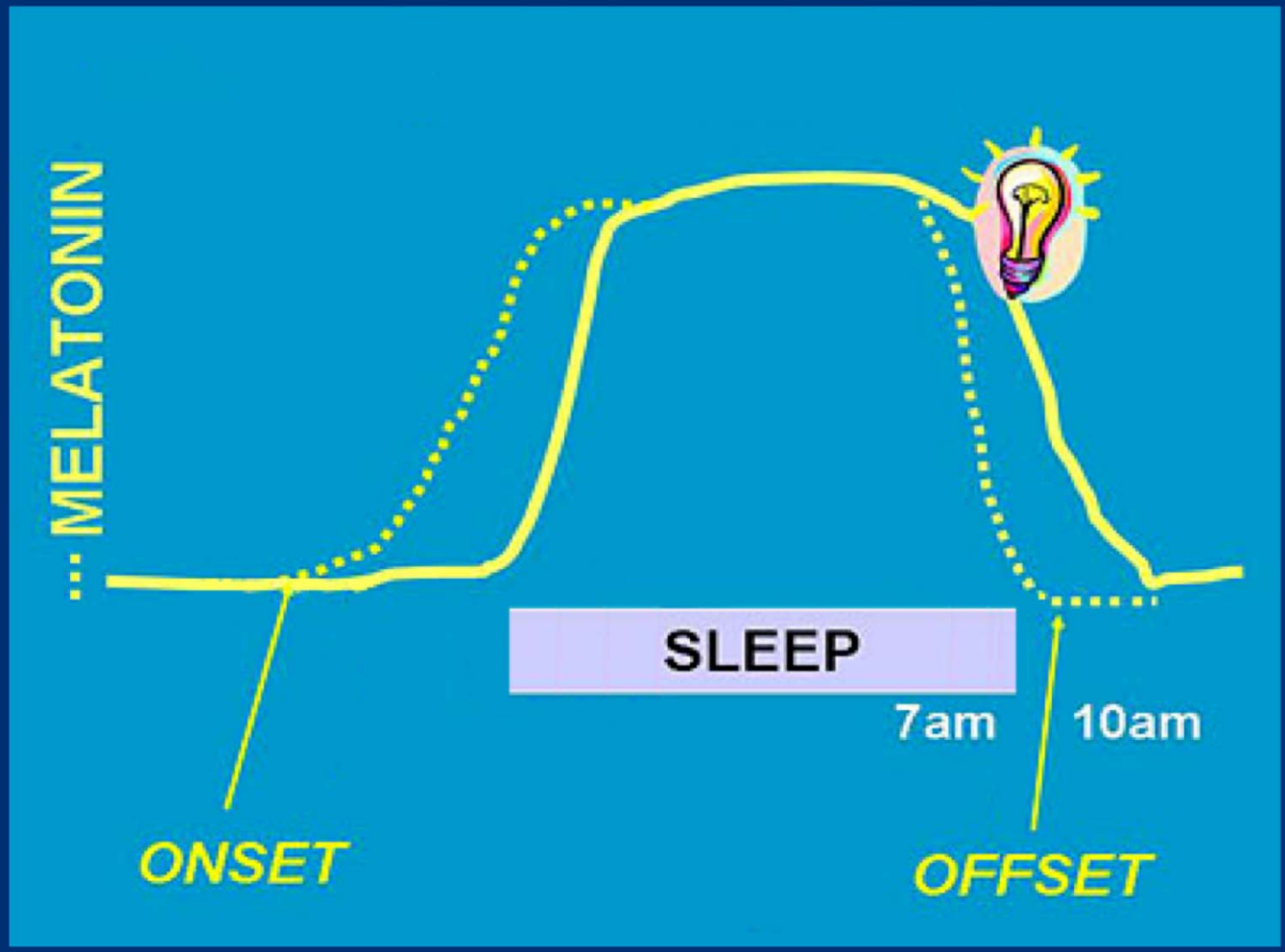


Pretest questions:

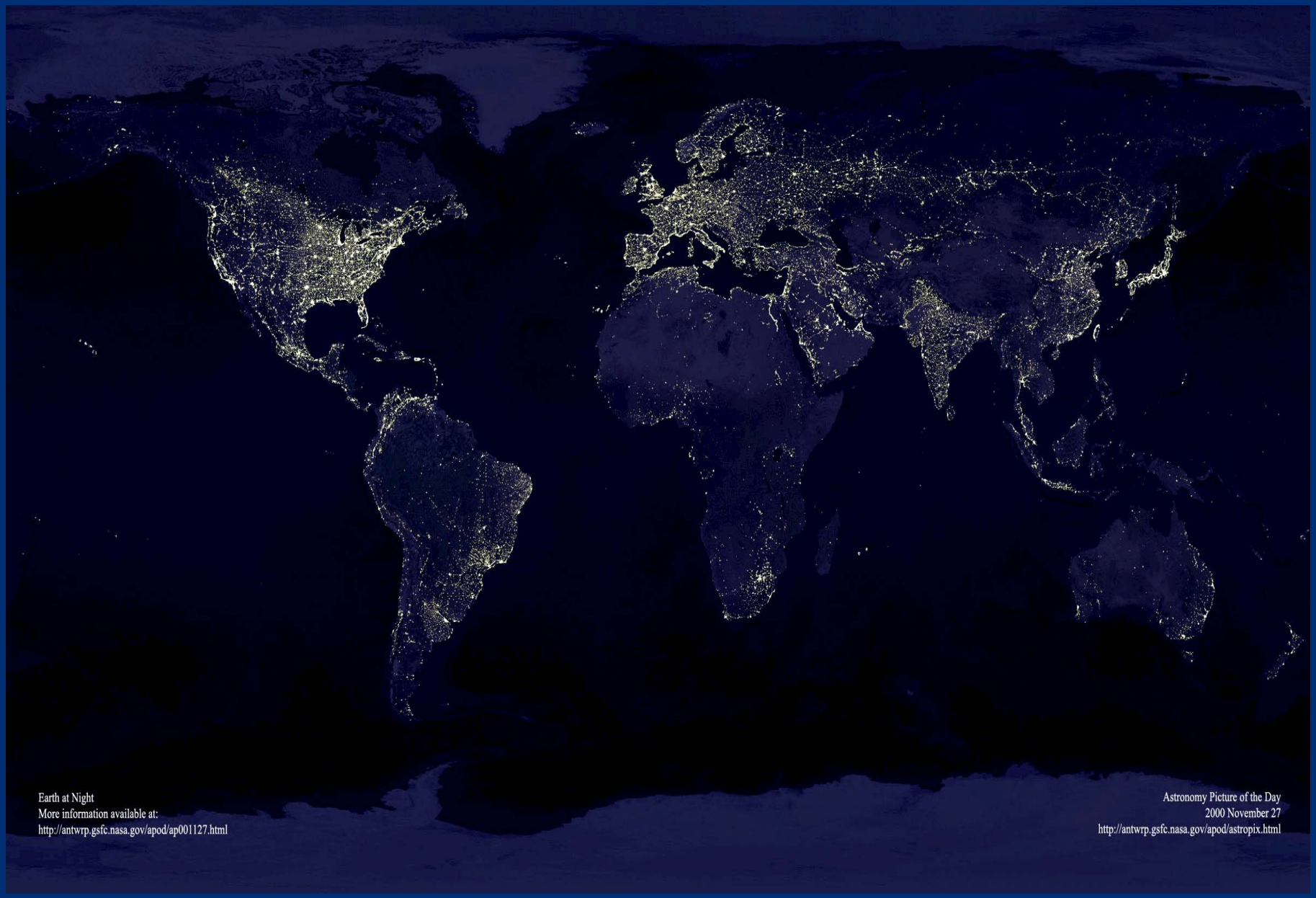
Who are these innovators who have transformed society? What, if anything, do they have to do with the obesity epidemic?



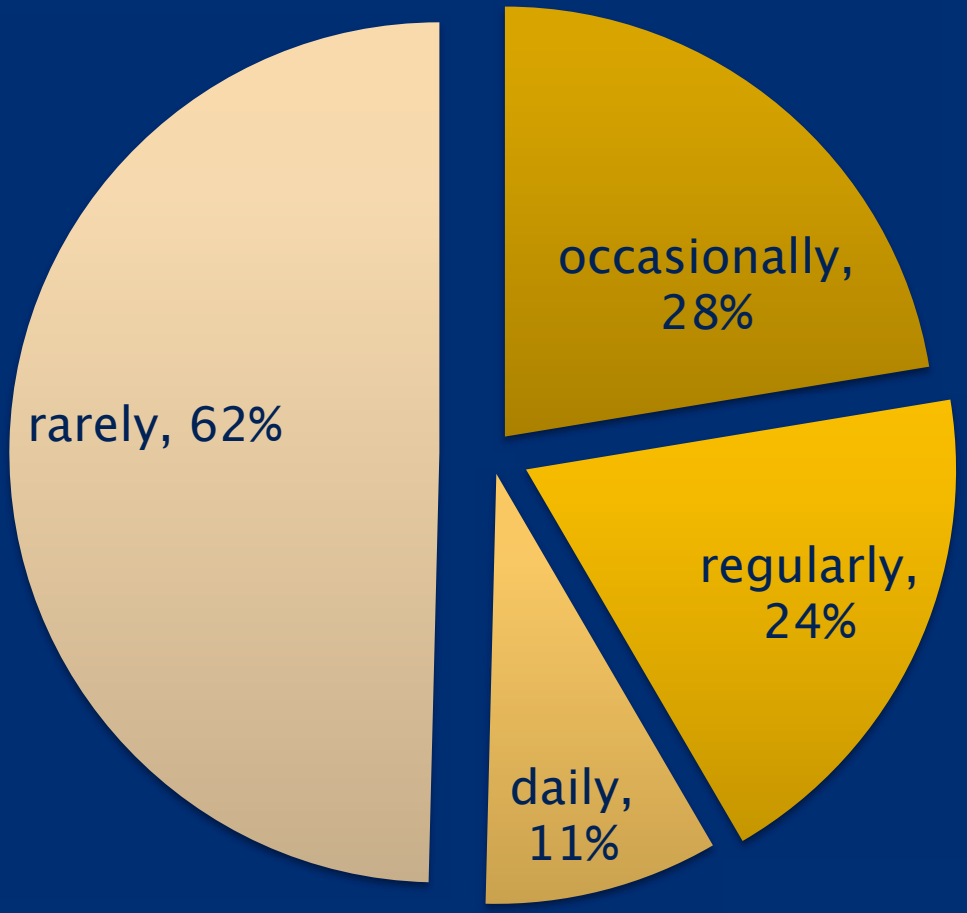
Increase of Melatonin and Induction of Sleep by Darkness



Kripke. 2012


Earth at Night
More information available at:
http://antwrp.gsfc.nasa.gov/apod/ap001127.html
Astronomy Picture of the Day
2000 November 27
http://antwrp.gsfc.nasa.gov/apod/astropix.html

We are chronically sleep deprived - BFB



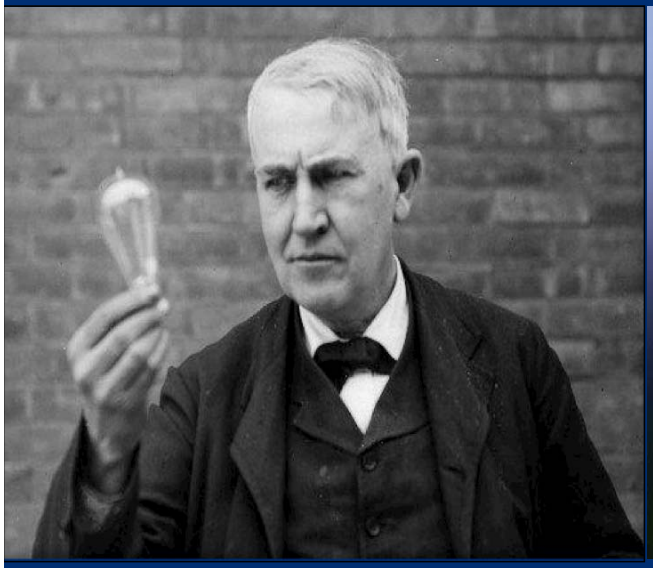
McKnight-Eily. JAMA 2008; Krueger. Am. J. Epidemiol 2009;169:1052-63;
Sleep in America 2002; Aguiar National Bureau of Economic Research 2006

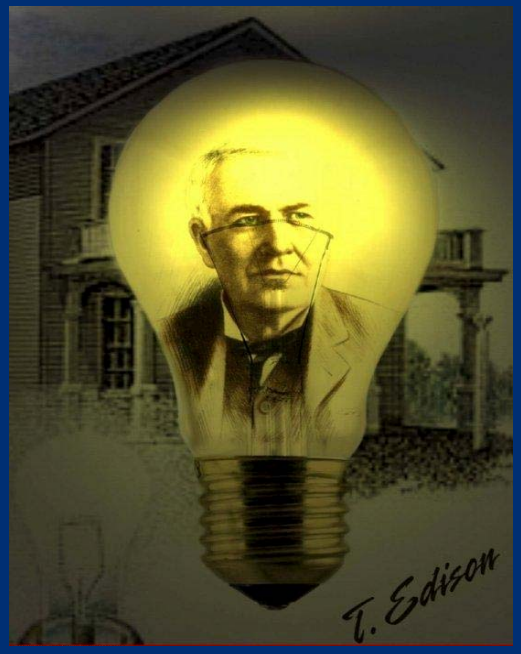

Google

Sleep Deprivation Induced by the Information Highway

(2011 Sleep in America Poll from the NSF)

- Two thirds of Gen Y'ers (19 to 29 yrs) and one third of Gen X'ers use a social networking site before bed
- People who text before bed (half of Gen Y) are more likely to be sleepy and drive while drowsy
- 7 of 10 Brits are tweeting, poking, surfing and writing on walls at night instead of going to sleep (Travelodge Survey/Graham Jones)





Tim Berners-Lee
(html and www)