Sleep and Healthy Aging Symposium

Atul Malhotra, MD

Research Chief of Pulmonary, Critical Care
Sleep Medicine and Physiology
UC San Diego
Disclosures

Officer of the ATS (2012-2017)

ResMed gave philanthropic donation to UCSD

MedXCloud no personal income

Equillium, Livanova, Corvus

NIH funds my lab
Outline

• 1. Sleep Deprivation
• 2. Obstructive Sleep Apnea
• Dinges et al.
• Almost all require 7-9 hrs sleep/nt
• Measurable decline in cognitive performance after 18hrs: 1 drink
• At 24hrs: legally drunk
• Optimal neurocognitive function may require 9 hours per 24hr period

AJRCCM 2015; Dawson Nature 1997
Age-adjusted Relative Risks of Incident Coronary Heart Disease (n=71,617)

*Archives Int. Med. 2003*

Relative Risk

Reported Sleep Duration

- 5 hrs
- 6 hrs
- 7 hrs
- 8 hrs
Sleep Issues in COVID

• 1. Sleep Duration improved ~1hr

Is Increased Sleep Responsible for Reductions in Myocardial Infarction During the COVID-19 Pandemic?

The COVID-19 pandemic caused by the highly contagious SARS-CoV-2 virus has had dev-

Am. J. Cardiol. 2020

• 2. OSA as a possible risk factor

OSA as a probable risk factor for severe COVID-19


David McSharry, MD1; Michael T. Lam, MD2; Atul Malhotra, MD2

1Acute Medicine, Transplant and Pulmonary Departments, Mater Misericordiae University Hospital and University College Dublin, Ireland
2UC San Diego School of Medicine, San Diego, California

Potential influences of obstructive sleep apnea and obesity on COVID-19 severity

David McSharry, MD1; Atul Malhotra, MD2

1Acute Medicine and Pulmonary Department, Mater Misericordiae University Hospital and University College Dublin, Ireland
2Professor of Medicine, UC San Diego School of Medicine, California
Spiegel et al. Lancet 1999
Tasali et al. PNAS 2008

• Induced sleep deprivation in normals
• Measured impaired glucose tolerance
• Elevated sympathetic activity
• Increased cortisol levels
• Slow wave sleep seems critical
Effect of sleep restriction on leptin and ghrelin

Spiegel et al.; Annals Intern Med 2004
Age Adjusted Weight Trends

- Red diamonds: 5 Hours
- Green squares: 6 Hours
- Orange triangles: 7 Hours
- Blue circles: 8 Hours
- Purple triangles: 9 Hours

Year:
- 1986
- 1988
- 1990
- 1992
- 1994
- 1996
- 1998
- 2000
- 2002

Weight (kg):
- 65
- 70
- 75
- 80
Results: Sleep curtailment decreased the proportion of weight lost as fat by 55% (1.4 vs. 0.6 kg with 8.5 vs. 5.5 hours of sleep opportunity, respectively; $P = 0.043$) and increased the loss of fat-free body mass by 60% (1.5 vs. 2.4 kg; $P = 0.002$). This was accompanied by markers of enhanced neuroendocrine adaptation to caloric restriction, increased hunger, and a shift in relative substrate utilization toward oxidation of less fat.

Conclusion: The amount of human sleep contributes to the maintenance of fat-free body mass at times of decreased energy intake. Lack of sufficient sleep may compromise the efficacy of typical dietary interventions for weight loss and related metabolic risk reduction.
Short sleep duration and incident coronary artery calcification

Christopher Ryan King, BS¹, Kristen L Knutson, PhD¹, Paul J Rathouz, PhD¹, Steve Sidney, MD, MPH², Kiang Liu, PhD³, and Diane S Lauderdale, PhD¹

1 Department of Health Studies, University of Chicago, Chicago, Illinois
2 Division of Research, Kaiser Permanente, Oakland, California
3 Department of Preventive Medicine, Northwestern University, Chicago
Summary Sleep Deprivation

- Inadequate sleep has health consequences
- Impaired brain function not surprising
- Increased metabolic and cardiovascular complications also present
- Data are rapidly evolving
Outline

• 1. Sleep Deprivation
• 2. Obstructive Sleep Apnea
Sleep Apnea Background

- Stoppages in breathing during sleep
- Associated with neurocognitive and cardiovascular sequelae
- Risk factors including aging, obesity, male gender
Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis


Lancet Respiratory Medicine 2019
Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study


A Sleep-disordered breathing

- Men
  - Mild: >60 years old (40%), <60 years old (30%)
  - Moderate: >60 years old (30%), <60 years old (20%)
  - Severe: >60 years old (20%), <60 years old (10%)

- Women
  - Mild: >60 years old (10%), <60 years old (5%)
  - Moderate: >60 years old (5%), <60 years old (10%)
  - Severe: >60 years old (10%), <60 years old (5%)

Multivariate: AHI predicts HTN, DM, depression

Concept: OSA is highly prevalent, but not all are likely to get cardiovascular benefit from CPAP
Take Home:
OSA affects up to 1 billion people. Numbers vary with scoring criteria and equipment but we need to think how to address this global burden.
CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

R. Doug McEvoy, M.D., Nick A. Antic, M.D., Ph.D., Emma Heeley, Ph.D., Yuanming Luo, M.D., Qiong Ou, M.D., Xilong Zhang, M.D., Olga Mediano, M.D., Rui Chen, M.D., Luciano F. Drager, M.D., Ph.D., Zhihong Liu, M.D., Ph.D., Guofang Chen, M.D., Baoliang Du, M.D., Nigel McArdle, M.D., Sutapa Mukherjee, M.D., Ph.D., Manjari Tripathi, M.D., Laurent Billot, M.Sc., Qiang Li, M.Biostat., Geraldo Lorenzi-Filho, M.D., Ferran Barbe, M.D., Susan Redline, M.D., M.P.H., Jiguang Wang, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Bruce Neal, M.D., Ph.D., David P. White, M.D., Ron R. Grunstein, M.D., Ph.D., Nanshan Zhong, M.D., and Craig S. Anderson, M.D., Ph.D., for the SAVE Investigators and Coordinators*

Therapy with CPAP plus usual care, as compared with usual care alone, did not prevent cardiovascular events in patients with moderate-to-severe obstructive sleep apnea and established cardiovascular disease. (Funded by the National Health and Medical Re
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Patient Engagement Using New Technology to Improve Adherence to Positive Airway Pressure Therapy
A Retrospective Analysis

Atul Malhotra, MD; Maureen E. Crocker, BS; Leslee Willes, MS; Colleen Kelly, PhD; Sue Lynch, RN; and Adam V. Benjafeld, PhD

N=952,819 patients with 137,089,667 nights of recording.
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Figure 2 – Distribution of mean nightly positive airway pressure usage. See Figure 1 legend for expansion of abbreviations.
Brief Communication

Short-term CPAP adherence in obstructive sleep apnea: a big data analysis using real world data

Peter A. Cistulli a,g, *, Jeff Armitstead b,g, Jean-Louis Pepin c,g, Holger Woehrle d,g, Carlos M. Nunez e,g, Adam Benjafied e,g, Atul Malhotra f,g

Table 1
Adherence data from the first 90 days of therapy.

<table>
<thead>
<tr>
<th>Adherence measures</th>
<th>Values (n = 2,621,182) Median (IQR)</th>
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<tbody>
<tr>
<td>CMS compliance in first 90 days, n (%)</td>
<td>1,955,961 (74.6)</td>
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<tr>
<td>Time to achieve CMS compliance, days</td>
<td>23.00 (21.00, 27.00)</td>
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<tr>
<td>Device usage, h/session</td>
<td>6.18 (4.79, 7.35)</td>
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<tr>
<td>Daily usage (all days), h/night</td>
<td>5.54 (3.42, 7.64)</td>
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<tr>
<td>Proportion of days with non-zero usage, %</td>
<td>93.3 (72.2, 98.9)</td>
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<tr>
<td>Proportion of days compliant (usage ≥ 4 h/night), %</td>
<td>80.0 (46.7, 95.6)</td>
</tr>
</tbody>
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CMS, Center for Medicare and Medicaid Services; IQR, interquartile range; SD, standard deviation. CMS Compliance definition: ≥4 hours' PAP use on 70% of nights in a consecutive 30-day period in the first 90 days of therapy.
Nasal CPAP is the Treatment of Choice

- Improves symptoms
- Improves blood pressure
- Transformative for some patients
- A defeatist attitude towards CPAP is not justified
- Need new therapies based on ongoing research