ΥΠΝΟΣ ΚΑΙ ΠΑΧΥΣΑΡΚΙΑ: ΜΙΑ ΑΜΦΙΔΡΟΜΗ ΣΧΕΣΗ?

ΜΑΡΙΑ ΜΠΑΣΤΑ,
ΕΠΙΚΟΥΡΗ ΚΑΘ. ΨΥΧΙΑΤΡΙΚΗΣ
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Obesity and Sleep

- Obesity and sleep apnea
- Obesity and daytime sleepiness and fatigue
- Sleep loss and Obesity
OBESITY AND SLEEP APNEA, EDS, FATIGUE
Obstructive Sleep Apnea (OSA)

~70% of clinical OSA patients are overweight or obese.
Example of an Obstructive Apnea

...but no airflow from the nose.

“Apnea” = 5 sec breath cessation, out-of-phase strain gauge movement.

“Hypopnea” = 50% ↓ of airflow, 3% ↓ SaO₂ or arousal

AHI (apnea/hypopnea index) = # apneas/hypopneas summed per hour of sleep
Sleep Apnea and Sleep Disruption in Obese Patients

Alexandros N. Vgontzas, MD; Tjiauw L. Tan, MD; Edward O. Bixler, PhD; Louis F. Martin, MD; Duane Shubert, MD; Anthony Kales, MD

Conclusion: Severely or morbidly obese men are at extremely high risk for sleep apnea and should be routinely evaluated in the sleep laboratory for this condition, while for severely or morbidly obese women the physician should include a thorough sleep history in the clinical assessment.
Obesity and Sleep Apnea

- 250 obese patients
- 8-hour polysomnographic study
- 40% of men and 3% of women had apnea warranting treatment
- Obese patients without apnea had disturbed nighttime sleep compared to normal weight controls

Vgontzas et al., 1994
Polycystic Ovary Syndrome

- Most common endocrine disorder of premenopausal women (5-10%)
- Chronic hyperandrogenism, oligoanovulation
- Insulin resistance
PCOS
Healthy Controls

% Sleep Apnea

% EDS

Vgontzas et al. 2001
Sleep apnea in PCOS

- 17%  
  Vgontzas, 2001

- 44%  
  Fogel, 2001

- 21%  
  Gopal, 2002

- 17% (75%)  
  Tasali, 2005

- OSA in PCOS is not explained by the presence of obesity alone
Excessive Daytime Sleepiness

• Is there an “epidemic”?  
• Is obesity a major factor in this “epidemic”?  
Obesity Without Sleep Apnea Is Associated With Daytime Sleepiness

Alexandros N. Vgontzas, MD; Edward O. Bixler, PhD; Tjiauw-Ling Tan, MD; Deborah Kantner, BS; Louis F. Martin, MD; Anthony Kales, MD

Conclusions: Daytime sleepiness is a morbid characteristic of obese patients with a potentially significant impact on their lives and public safety. Daytime sleepiness in individuals with obesity appears to be related to a metabolic and/or circadian abnormality of the disorder.

Arch Intern Med. 1998; 158: 1333-1337
Obesity is Independently Associated with Daytime Sleepiness

- 73 Obese patients & 45 Controls both without SDB
- Obese patients compared to controls:
  - Sleepier during the day
  - Less sleepy during the night

Vgontzas, 1998
Daytime Sleep Latencies in Obese and Healthy Controls
Prevalence of EDS (BMI)

Bixler 2001 JCEM
SLEEP LOSS AND OBESITY
Reduced sleep as a risk factor for obesity

- Sleep restriction is associated with reduced leptin, increased ghrelin and increased appetite
  
  Spiegel 2004

- Obesity is associated with short sleep duration

  Taheri 2004, Vorona 2005
  Gangwish 2005, Hasler 2004
Sleep Restriction and glucose metabolism

Glucose and HOMA responses to identical meals

GLUCOSE (mg/dL)

HOMA (INSULIN (mU/L) * GLUCOSE (mmol/L) / 22.5)

AFTER 6 DAYS OF 4 HOURS IN BED

AFTER 6 DAYS OF 12 HOURS IN BED

AREA UNDER THE CURVE

Glucose (mg/dL) 9772 ± 211 9205 ± 314 0.04
HOMA index 1954 ± 188 1399 ± 152 0.03

Sleep Restriction and glucose metabolism

LEPTIN, GHRELIN, HUNGER AND APPETITE

LEPTIN (ng/ml)
- 18%; p<0.04

GHRELIN (ng/ml)
- 28%; p<0.04

HUNGER (cms)
- 24%; p<0.01

APPETITE (cms)
- 23%; p<0.01

AFTER 2 DAYS OF
10-H BEDTIMES

AFTER 2 DAYS OF
4-H BEDTIMES

Spiegel et al,
Ann Int Med 2004
Leptin and hunger levels in young healthy adults after one night of sleep loss

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¹Sleep Research and Treatment Center, Department of Psychiatry, Penn State College of Medicine, Hershey, PA, USA and ²First Department of Pediatrics and Unit on Endocrinology, Metabolism, and Diabetes, Athens University Medical School, Athens, Greece

Figure 1. Twenty-four-hour leptin values pre (*) and postsleep (C) deprivation. The thick black line in the abscissa indicates the night-time sleep recording period.

<table>
<thead>
<tr>
<th>Time of Meal</th>
<th>Predeprivation</th>
<th>Postdeprivation</th>
<th>Δ (pre – post)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast (07:00)</td>
<td>3.67 ± 0.2</td>
<td>3.33 ± 0.2</td>
<td>0.34 ± 0.3</td>
<td>0.268</td>
</tr>
<tr>
<td>Lunch (12:00)</td>
<td>4.00 ± 0.2</td>
<td>3.95 ± 0.2</td>
<td>0.05 ± 0.2</td>
<td>0.790</td>
</tr>
<tr>
<td>Dinner (18:00)</td>
<td>4.05 ± 0.3</td>
<td>4.33 ± 0.2</td>
<td>-0.30 ± 0.2</td>
<td>0.385</td>
</tr>
</tbody>
</table>
Recurrent sleep restriction & metabolic effects

- Exposure to recurrent sleep restriction in the setting of high caloric intake and physical inactivity results in increased insulin resistance and reduced glucose tolerance (Nedeltcheva JCEM 2009)
- Sleep restriction does not affect glucose control and insulin secretion during diet-induced weight loss (Nedeltcheva Obesity 2012)
- Sleep restriction decreases physical activity in adults at risk for type 2 diabetes (Bromle SLEEP 2012)
Self-reported short sleep duration and obesity: the role of emotional stress and sleep disturbances.

Penn State Cohort

- 1741 men and women studied in the lab
- 1300 completed MMPI
- No difference in terms of age, gender, BMI or sleep complaint
## Obesity and Sleep Complaints Prevalence

<table>
<thead>
<tr>
<th></th>
<th>Lean</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>6.0% (6.1%)</td>
<td>11.1%** (9.2%)</td>
</tr>
<tr>
<td>Sleep Difficulty</td>
<td>17.3% (16.7%)</td>
<td>31.5%* (27.2%)</td>
</tr>
<tr>
<td>EDS</td>
<td>7.5% (7.3%)</td>
<td>15.6%* (13.0%)</td>
</tr>
<tr>
<td>Any Sleep Complaint</td>
<td>25.5% (24.8%)</td>
<td>47.4% * (40.7%)</td>
</tr>
</tbody>
</table>

*p < 0.01     **p < 0.05

In parentheses are the values when obesity is defined as BMI > 27.8kg/m² for men and 27.3kg/m² for women.
Self reported sleep duration and obesity
Obese with sleep complaints report shorter sleep duration.
MMPI profiles in asymptomatic obese vs. obese with sleep difficulty and insomnia

- Insomnia
- Sleep difficulty
- Asymptomatic
MMPI profiles in asymptomatic lean vs. asymptomatic obese

<table>
<thead>
<tr>
<th>Scale</th>
<th>Asymptomatic Lean</th>
<th>Asymptomatic Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>hs</td>
<td>56</td>
<td>54</td>
</tr>
<tr>
<td>d</td>
<td>52</td>
<td>50</td>
</tr>
<tr>
<td>hy</td>
<td>54</td>
<td>52</td>
</tr>
<tr>
<td>pd</td>
<td>50</td>
<td>48</td>
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<td>44</td>
</tr>
<tr>
<td>ma</td>
<td>44</td>
<td>42</td>
</tr>
</tbody>
</table>
CONCLUSION: Self-reported short sleep duration in non-obese individuals at risk of developing obesity is a surrogate marker of emotional stress and subjective sleep disturbances. Objective short sleep duration is not associated with a significant increased risk of incident obesity. The detection and treatment of sleep disturbances and emotional stress should become a target of our preventive strategies against obesity.
Objective sleep duration (%ST)

- BMI, MMPI, Sleep Disturbance
- **Sleep complaint** $\rightarrow \downarrow$ % ST by 15 minutes *
- MMPI (7.7 units) $\rightarrow \downarrow$ % ST by 3 min
- BMI (6.7kg/m²) $\rightarrow \downarrow$ % ST by 3 minutes

* $p < 0.05$
# Sleep and Incident Obesity: The Penn State Cohort

## Table 3. Multivariable adjusted odds ratio (95% CI) of incident obesity and subjective sleep duration, sleep difficulty and emotional stress

<table>
<thead>
<tr>
<th>Subjective sleep duration</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
<th>Model 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥7h</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>6–7h</td>
<td>1.19 (0.62–2.29)</td>
<td>1.26 (0.62–2.57)</td>
<td>1.25 (0.61–2.56)</td>
<td>1.25 (0.60–2.60)</td>
<td>1.02 (0.45–2.29)</td>
<td>1.03 (0.46–2.34)</td>
</tr>
<tr>
<td>5–6h</td>
<td>1.18 (0.76–1.83)</td>
<td>1.15 (0.72–1.85)</td>
<td>1.25 (0.77–2.03)</td>
<td>1.27 (0.83–2.26)</td>
<td>1.25 (0.89–2.73)</td>
<td>1.27 (0.89–2.76)</td>
</tr>
<tr>
<td>≤5h</td>
<td>2.18 (1.25–3.78)**</td>
<td>1.71 (0.87–3.36)</td>
<td>1.69 (0.85–3.37)</td>
<td>1.68 (0.82–3.45)</td>
<td>1.07 (0.48–2.39)</td>
<td>1.08 (0.48–2.41)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sleep difficulty</th>
<th>Normal sleep</th>
<th>1.0</th>
<th>1.0</th>
<th>1.0</th>
<th>1.0</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor sleep</td>
<td>2.48 (1.58–3.91)***</td>
<td>2.19 (1.37–3.48)***</td>
<td>2.07 (1.28–3.35)***</td>
<td>1.80 (1.04–3.12)*</td>
<td>1.78 (1.02–3.13)*</td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>0.81 (0.33–1.99)</td>
<td>0.81 (0.33–2.00)</td>
<td>0.78 (0.30–2.00)</td>
<td>0.49 (0.16–1.45)</td>
<td>0.48 (0.15–1.53)</td>
<td></td>
</tr>
<tr>
<td>Emotional stress</td>
<td>1.25 (1.11–1.42)***</td>
<td>1.24 (1.09–1.41)***</td>
<td>1.39 (1.19–1.62)***</td>
<td>1.38 (1.17–1.63)***</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Obesity and self-reported sleep duration: A marker of sleep complaints and chronic psychosocial stress and unhealthy behaviors

- Short sleep duration is associated with socioeconomic and minority status
  
  *Stamatakis et al 2007, Ann Epidemiol*

- Short sleep is associated with smoking, alcohol use and lack of exercise
  
  *Schoehborn and Adams 2008, DHHS, CDC*

- Short sleep duration is associated with lack of exercise and lower fruit/vegetable consumption
  
  *Stamatakis and Brownson 2008, Prev Med*

- Sleep complaint and emotional stress predictive of short sleep duration in obese
  
  *Vgontzas 2009*
Does lengthening/improving objective sleep reduce weight?
Conclusions: OSA patients using CPAP may gain modest amount of weight with the greatest weight gain found in those most compliant with CPAP.
Conclusions—Results suggest that clinicians and investigators might consider targeting sleep, depression, and stress as part of a behavioral weight loss intervention.
Stress and food intake

• Chronic stress leads to increased consumption of palatable food

  Dallman et al., 2003

• “Comfort food” reduces anxiety and stress system activity

  Pecoraro et al., 2004

• Quality but not quantity of sleep is associated with increased hunger and uncontrolled emotional eating

  Kilkus, et al 2012
Sleep and Obesity
Prospective and Interventional Studies

• No association between baseline objective sleep duration and obesity after 5 years
  Lauderdale, Am J Epid 2009

• CPAP failed to improve weight after 1 year
  Quan, 2006
  Redenius, 2008

• Weight loss improves apnea
  Peppard et al., JAMA 2000
  Johansson et al., BMJ 2009
Sleep and Obesity

Conclusions

• Simplistic Model (Sleep more loose weight)
• Longitudinal interventional studies, measures from multiple domains, sleep (subjective – objective), stress, mental and physical health
• Multidimensional approach – stress management reduction of risky behaviors, healthy lifestyle, better quality and possibly quantity of sleep
The majority of observational cohort and randomized controlled trials (RCTs) show that an increase in the AHI occurs with weight gain and a decrease with weight loss. In fact, relatively small amounts of weight loss may be clinically relevant, as illustrated by a meta-analysis of 9 studies representing 577 OSA patients that demonstrated that a 5 kg weight loss was associated with a 48% reduction in the AHI, improving symptoms related to OSA.

Based on what we know currently, I would encourage Sleep Medicine specialists to incorporate into the practice: (1) Education of their obese OSA patients of the role their obesity likely is playing in their OSA and comorbid diseases; and (2) Strengthen their referral and working relationships with practitioners primarily treating obesity: nutritionists, commercial weight loss program directors and bariatric surgeons so that they can easily and conveniently refer obese OSA patients to these practitioners. It is my hope and anticipation that after a thorough review of the topic, Sleep Medicine professional organizations will join the effort to address the life-threatening challenge the majority of our OSA patients face every day—obesity.
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