Metabolic effects of sleep disturbance

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Agenda

• Diabetes and sleep
• Circadian metabolic networks and their adaptation to sleep
• Obesity and obstructive sleep apnoea
The metabolic syndrome

- Hyperinsulinaemia/Insulin resistance
- Hyperlipidaemia
- Hypertension
- Abdominal Obesity
The metabolic syndrome

- Hyperinsulinaemia
- Insulin resistance
- Hyperlipidaemia
- Hypertension
- Abdominal Obesity
- Inflammation
The Metabolic Syndrome

Diagnosis is established when ≥3 risk factors are present:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference*</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&gt;102 cm (&gt;40 in)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;88 cm (&gt;35 in)</td>
</tr>
<tr>
<td>TG†</td>
<td>≥1.7mmol/l</td>
</tr>
<tr>
<td>HDL-C†</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&lt;1mmol/l</td>
</tr>
<tr>
<td>Women</td>
<td>&lt;1.3 mmol/l</td>
</tr>
<tr>
<td>Blood pressure†</td>
<td>≥130/≥85 mm Hg</td>
</tr>
<tr>
<td>Fasting glucose†</td>
<td>≥5.6 mmol/mol</td>
</tr>
</tbody>
</table>

*Lower cutpoints (≥90 cm in men and ≥80 cm in women) for Asian Populations. Or BMI >30 kg/m² (IDF)
†Or on drug treatment for the risk factor

Diabetes and Sleep

<table>
<thead>
<tr>
<th>Sleep duration</th>
<th>&lt;or=5h</th>
<th>7 h</th>
<th>8h or</th>
<th>ODDS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.95</td>
<td>1</td>
<td>3.12</td>
<td></td>
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</tbody>
</table>

(Yaggi et al, Diabetes Care 2006)

- Short and long sleep durations increase the risk of developing diabetes, independent of confounding factors
- Sleep fragmentation and deprivation linked to obesity and diabetes e.g. in shift workers
Circadian rhythm and metabolism

Normal Hypothalamo-Pituitary-Adrenal Axis Activity
Balbo M et al. 2010
Circadian rhythm and metabolism

Impact of Sleep and Its Disturbances on Hypothalamo-Pituitary-Adrenal Axis Activity
Buxton et al. Sleep 2000
Insomnia and cortisol profile
Too much and too little

- Elevation of cortisol levels
Sleep deprivation and inflammation

- TNF-α and MCP-1 in the late evening and early night hours increased after 5 days of sleep restriction

Sleep deprivation II

[Graphs showing time of day and concentration levels for MCP-1 and Monocytes]
Disturbance of hypothalamic HPA axis

• In subjects with insomnia and stress
• Elevated cortisol levels found in subjects with obesity
• Subjects with depression
• In subjects with disordered breathing such as OSA
• No rocket science!
Spaceflights "environment" negatively affects sleep and its functions

How stressful are 105 days of isolation? Sleep EEG patterns and tonic cortisol in healthy volunteers simulating manned flight to Mars

Stressful conditions, even with cortisol fluctuations in the normal range, alter sleep structure and sleep EEG spectral content, mirroring pathological conditions such as primary insomnia or insomnia associated to depression.
Obesity and OSA

• 40-90% of OSA in men with severe obesity (BMI > 40 kg/m²) and greater OSA severity
• Associated with increased abdominal fat distribution (Vgontzas, NEJM 2000)
• More common in men and bariatric patients
• 10% increase in weight 30% increases in AHI (Peppard et al, JAMA 2000)
Body weight and OSA severity

Peppard et al, JAMA 2000

Longitudinal Study of Moderate Weight Change and Sleep-Disordered Breathing with follow up of 4 years n=690
Obesity and upper airway mechanics

• Higher neck circumference
• reductions in lung volume
• Increased pharyngeal collapsibility
• blunting of upper airway neuromuscular responses
• Increasing hypoventilation
The metabolic syndrome

- Hyperinsulinaemia/Insulin resistance
- Hypertension
- Hyperlipidaemia
- Abdominal Obesity
- OSA
Diabetes and OSA:

- OSA is associated with insulin resistance and β-cell dysfunction independent of obesity.

- OSA is associated with an increased prevalence of the metabolic syndrome (Drager, PlosOne, 2010) (but probably not contributing as much as obesity).

- OSA is related with poor glucose control in diabetic men independent of body weight (West, 2006).
Studies Examining The Effect Of CPAP Treatment on Glucose Metabolism

• 17 studies show a significant improvement in HbA1C or markers of glucose metabolism especially with longer term use of CPAP in diabetic or non-diabetic men e.g. studying HOMA-IR, HbA1C or hyperinsulinemiac euclygemic clamps

• not reproduced by all e.g. West et al when using Sham CPAP devices

• Review: Guest et al, Diabetes Care, 2014
Alternative treatments

• 10 to 15% reduction in body weight leads to an approximately 50% reduction in sleep apnoea severity (AHI) in moderately obese male patients

• Bariatric surgery for treatment of OSA
Our study

Hypothesis:
• OSA aggravates subclinical inflammation and hypoxia in adipose tissue

Poster of Clare Thorn
Inflammatory cytokines in OSA

BMI 24.6 ± 0.7  40.5 ± 3.21  32.0 ± 3.7  28.5 ± 2.7

Vgontzas A. J Clin Endocrinol Metab 1997, 82, 1313-6
Summary

- OSA independently affects adipose tissue biology and aggravates inflammation
Take home messages

• Patients with OSA may have diabetes, screen with HbA1C

• Treatment of sleep disorder will improve metabolic health

• Weight management helps with OSA
• Many thanks for your attention