Snack ‘n’ Snooze: Sleep and Eating Behavior

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Agenda

- The (Y)HUGE message
- Sleep and eating
- Eating behavior studies
- The problem with BMI
- Biomarkers
- Connections (to our favs)
- Public health implications
Evidence suggests that sleep may modulate eating
- & eating may modulate sleep #bidirectional
There are links between eating disturbances (& metabolism)
& sleeping disturbances
BMI does not (accurately) convey the whole picture
Eating Disorders & Their Relationships

Anorexia Nervosa, Bulimia Nervosa, and Binge Eating Disorder
Anorexia Nervosa

- Severe weight loss due to:
  - reduction of food intake
  - Excessive exercise
  - Purging behaviors
  - Comorbid with depression
  - Low weight maintained (BMI <18.5)
**Anorexia Nervosa**
- Excessive appetite and lack of control
- Maintaining of weight in a normal range or even gain weight

**Bulimia Nervosa**
- Cycles of binging and compensatory behaviors such as self-induced vomiting
- Excessive appetite and lack of control
Similarities (Eating Lens)

- AN → AN-R and AN-BP
- BN → BN-NP and BN-P
- Binge eating symptom of BED, BN, AN-BP and NES
Binge eating disorder (BED)

- Recurrent episodes of consuming unusually large amounts of food in discrete period - binge eating
- Feeling that eating is out of control
- **Absence** of extreme weight control behaviors
- Weight in normal-obese range
  - BMI $\geq 18.5$
Binge Eating Disorder

- Feeling lack of control
- May involve binging; AN and BN have a compensatory weight control behavior, while BED does not
- Pattern of disordered eating

Anorexia Nervosa

Bulimia Nervosa
Sleep

- **Stages**
  - NREM: synchronization
    - Stage 1
    - Stage 2
    - Stage 3 - slow wave sleep
    - Stage 4 - slow wave sleep
  - REM: desynchronization
    - rapid eye movement
    - cortical activation
    - dream state

Figure 3: Wave pattern of different sleep Stages
Sleep

- Dictated by circadian rhythm and lighting conditions (SCN release of sleep-causing melatonin)
- Common problems:
  - Insomnia: difficulty initiating sleep and maintaining sleep
  - Duration: waking early, not enough REM vs NREM
  - Disturbance: waking up several times a night
  - Sleep restriction: too little sleep in experimental settings (sleep deprivation)
  - Sleep latency: sleeping too late
  - Narcolepsy: falling asleep suddenly
Anorexia Nervosa

- Alterations of sleep architecture
  - Decrease SWS
  - Decrease REM
  - Increase Stage 1
  - Increase time period awake
  - Decrease of time asleep
Anorexia Nervosa

- Alterations of Sleep architecture
  - Insomnia
  - Hypersomnia
  - Restless Sleep
  - Excessive daytime somnolence (sleepiness)
  - Night eating

Bulimia Nervosa
Similarities (Sleeping Lens)

- Sleeping difficulties
- EMA
- Mid-sleep awakenings
- Parasomnias
- Hypersomnia
- AN-B/P & BN-P VS. AN-R & BN-NP
Binge eating disorder (BED)

- Lower sleep quality - shorter episodes of continuous sleep, less true sleep time
- Obese patients: snoring, midsleep waking, daytime sleepiness, restless sleep
- Fall asleep and wake 1hr later than controls - sleep latency
  ○ Related to bingeing episodes at evening or night
- In general population, eating before sleep associated with sleep disruption
Binge Eating Disorder

- Difficulties initiating sleep, maintaining sleep
- Binge eating-purging subtypes have more sleep disturbances

Anorexia Nervosa

Bulimia Nervosa
Nocturnal Sleep-related Eating Disorder

- Arousal ~3 hours after sleeping
- Rapid ingestion of food
  - Sloppy eating
  - Weird food combinations
  - Eating inedible substances
- Don’t remember the episode

✩ Found in patients with AN - nocturnal bulimia
✩ Found in patients who binge eat at night
✩ **Daytime eating** proceeds as normal
Night-Eating Syndrome

- Five associated symptoms:
  1. No appetite in the morning
  2. Strong urge to eat after dinner before sleeping
  3. Persistent insomnia
  4. Belief that you need to eat in order to fall asleep
  5. Depressed mood

- **Awareness of eating episodes**
  - Hyperphagia after waking up or after dinner
  - Lower leptin levels at night compared to controls
NSRED: lack of awareness, more similar to sleep-walking or sleep-talking

NES: awareness of the episode, need to eat in order to go back to sleep

Both occur during NREM sleep

Preference for carbohydrate-rich foods
Obesity

- Excess of body fat
- Breathing related sleep disorders
  - Snoring/sleep apnea
  - Late sleep latency
  - Sleep disruption
  - Poor sleep quality
  - Difficulty initiating and maintaining sleep
  - Early morning awakening
  - Sleep restriction
  - Daytime fatigue
  - Low sleep efficiency
Obesity

- poor sleep quality
- multiple types of parasomnias
- poor sleep efficiency
- daytime somnolence
- possibly related to dopaminergic pathway
Obesity

- poor sleep quality
- multiple types of parasomnias
- poor sleep efficiency
- daytime somnolence

The (Y) H U G E Message

- Evidence suggests that sleep may modulate eating & eating may modulate sleep bidirectionally.
- There are links between eating disturbances (metabolism) & sleeping disturbances
- BMI does not (accurately) convey the whole picture
But what’s missing????? BMI
Observational and Experimental Studies

Three groups of studies:

- Sleep difficulties
- Eating disturbances/BMI

- Sleep difficulties
- Eating disturbances/BMI

- Sleep difficulties
- Eating disturbances/BMI
Sleep Difficulties on Eating Disturbances/BMI (1)

- Links between sleep restriction to weight
  - Ecological: Too little (or too much) sleep $\rightarrow$ weight gain
  - Prospective cohort: Too little or too much sleep $\rightarrow$ weight gain
    - Only current sleep is just a correlate, not predictor

- Consequences of sleep deprivation:
  - Experimental: Metabolic disturbances (ghrelin $\uparrow$, leptin $\downarrow$)
  - Increased hunger and appetite for carbohydrates and fats
  - Increased meals during the night
Sleep Difficulties on Eating Disturbances/BMI (2)

- Finer associations from convenience samples
  - Cross-sectional: Sleep difficulties → history of eating disorders
    - College males (SPE ↑) and college females (DC ↑)
    - BMI is not a significant predictor to sleep difficulties
  - Retrospective cohort: Sleep difficulties → partial link to obesity

- Epidemiological associations of NSRED on eating disturbances
  - Sleep disorders → NSRED → AN with nocturnal bulimia and BE
  - Sleep disorders → Some history of an eating disorder?
**Eating Disturbances/BMI on Sleep Difficulties (1)**

<table>
<thead>
<tr>
<th>AN patients</th>
<th>BN patients</th>
<th>BED patients</th>
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<tbody>
<tr>
<td>Decreased SWS</td>
<td>Insomnia</td>
<td>Partial/total amnesia</td>
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<tr>
<td>Decreased REM sleep</td>
<td>Daytime sleepiness</td>
<td>Snoring</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Partial/total amnesia</td>
<td>Mid-sleep awakenings</td>
</tr>
<tr>
<td>Early morning waking</td>
<td>Delayed sleep and wake time</td>
<td>Daytime sleepiness</td>
</tr>
<tr>
<td>Less time slept</td>
<td>Low sleep efficiency</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Low sleep efficiency</td>
<td></td>
<td>Low sleep efficiency</td>
</tr>
</tbody>
</table>
Eating Disturbances/BMI on Sleep Difficulties (2)

**NE§ patients**
- Short sleep duration
- Sleep deficits
- Insomnia
- Daytime sleepiness
- Likely link to other ED

**Obese patients**
- Display of ED behaviors
- Breathing-related sleep disorders
- Poor sleep quality
- Daytime sleepiness
Bidirectional Association Between Sleep and Eating

- Study 1: Eating disturbances/BMI predictive of sleep difficulties?
  - Severe ED behaviors at baseline → DIS, DMS, and sleep difficulties ↑
  - Severe diet concerns at baseline → sleep difficulties ↑
  - BB and SPE are predictors of long-term sleep difficulties
  - BMI not a significant predictor

- Study 2: Sleep difficulties predictive of eating disturbances/BMI?
  - Insomniacs at baseline → consistent and more severe ED ↑, BMI ↓
  - Females with DIS at baseline → BB ↑
  - Males with DIS at baseline → BMI ↓
B MI & its B roblems
Cases Against BMI

- Case 1: Not an accurate predictor for Bulimic Patients
- Case 2: Anorexia Nervosa Binging/Purging Subtype and Bulimia Nervosa Purging subtype
- Case 3: Not consistent across studies
Addressing the Perfect Storm: Biomarkers in Obesity

BMI is not always a measure of fatness

BMI

VS

Other but better things

Visceral adipose tissue
More active than subcutaneous adipose tissue

<table>
<thead>
<tr>
<th>Prevention</th>
<th>Detection</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Disease management</th>
</tr>
</thead>
<tbody>
<tr>
<td>• monitor health • predict disease development</td>
<td>• identify disease • risk stratification</td>
<td>• characterize disease</td>
<td>• monitor compliance • efficacy</td>
<td>• predict response • monitor recurrence</td>
</tr>
</tbody>
</table>

Biomarker requirements:
- specific
- sensitive
- predictive
- robust
- stable
- noninvasive
- high preclinical and clinical value
The Biomarkers

(a) biomarkers of glucose–insulin homeostasis (Hyperinsulinemia, Proinsulin)
(b) adipose-tissue biomarkers (Fat Mass Index)
(c) inflammatory biomarkers
(d) omics-based biomarkers.
Omics-based biomarkers.

METABOLITES (FTO (FTO, α-ketoglutarate dependent dioxygenase) genotype) = obesity and type 2 diabetes have been identified

MICRO RNAs = noncoding RNAs = regulate expression of genes
### Biomarkers: Adipose Tissue Imaging Techniques: Fat Mass Index

<table>
<thead>
<tr>
<th>Measure</th>
<th>Techniques</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat mass</td>
<td>DXA</td>
<td>Low radiation, short imaging time</td>
<td>hard to distinguish between subcutaneous fat and visceral fat</td>
</tr>
<tr>
<td>Fat mass</td>
<td>Ultrasound</td>
<td>Lower cost, easy, and no radiation</td>
<td></td>
</tr>
<tr>
<td>Fat mass</td>
<td>CT</td>
<td>Accurate, measures specific body fat compartments</td>
<td></td>
</tr>
<tr>
<td>Fat mass</td>
<td>PET</td>
<td>Accurate, measures body fat compartments and metabolism including brown fat</td>
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Adipose-tissue biomarkers
“Biomarkers provide an innovative approach to understanding the spectrum of cardiometabolic diseases with potential applications in risk prediction, screening, and diagnosis and prognosis. However, they are prone to several methodological limitations such as high variability, ranging from the individual (biological variability) to the laboratory (methodological variability). It is important to consider reliability, validity, sensitivity, specificity, ascertainment bias, and interpretation of data when using biomarkers.”
Neurobiology

Sleep & metabolism are regulated by the same brain circuits
also part of stress response and reward systems

- Peptides involved: MCH and Hcrt 1 & 2 (a.k.a. Orexin A & B)
- Appetite regulation = metabolic & hormonal interaction
- Sleep disturbances are associated w/ hormonal imbalances
  - E.g., Short sleep duration associated with lower leptin +
    higher glucose & ghrelin
  - ↓ feeding signal → higher BMI and ↑ risk of T2D
Peptides - (a) Melanin concentrating hormone (MCH)

- Activated by binding to 2 GPCRs: MCHR1 & MCHR2
- Postsynaptic inhibitory properties
- Short-term orexigenic features
- Upregulated after fasting
- **promotes ↓ energy expenditure + sleep**
Peptides - (b) Hypocretin/Orexin

- Orexin-A = 33 amino acid peptide
- Orexin-B = 28 amino acid peptide
- Orexin
  - Shares similar amino acid identities as gut hormone secretin
  - Orexin receptor mRNA found in gut
Peptides - (b) Hypocretin/Orexin

- Leptin administration reduces orexin-A in LH
- Fasting/hypoglycemia increases activity of LH orexin neurons
- Increases NPY-expression in ARC neurons
  - Projections to ARC POMC and NPY expressing neurons
    - Inhibited by leptin, stimulated by ghrelin pathway
- Food intake enhancement depends on CRF release
Peptides - (b) Hypocretin/Orexin

- Promotes wakefulness & ↑ energy expenditure
- Excites neuromodulatory systems that desynchronize cortical activity: Ach, histamine, DA, 5-HT, NE
Figure 3: Wave pattern of different sleep stages

- Awake
- Stage 1
- Stage 2
- Stage 3
- REM sleep

Wake
- Monoaminergic Centers: LC, DR, TMN, SN/VTA
  - Orexin ON
  - VLPO OFF

Sleep
- Orexin ON
- VLPO OFF
- Monoaminergic Centers: LC, DR, TMN, SN/VTA
Peptides - (b) Hypocretin/Orexin

- Death of orexin neurons associated with narcolepsy
- Evolutionary response? Starvation → need food, forage and be vigilant!
Peptides - (b) Hypocretin/Orexin

- Stress-related:
  - Needed for maintenance of (behavioral) arousal
  - May be part of response of HPA axis

- Reward-related:
  - Major component of natural reward associated w/ feeding behavior
Other Connections
Metabolic Syndrome
- Putamen and nAcc show enhanced sensitivity to food reward
- Some evidence for elevated ghrelin levels
  - Reduced fat oxidation → loss of lean body mass
- Some evidence for reduced physical activity after sleep loss
- Shift work leads to circadian rhythm desynchrony
Connections

Glucose Metabolism
- Spiegel et al. → after sleep restriction, impaired glucose tolerance & ↓ insulin sensitivity
- β-cell function was NOT sufficient enough to compensate for this reduced insulin sensitivity
Public Health Implications

- Don’t eat immediately before bed
- Don’t exercise before bed
- Maintain a consistent schedule
- Don’t use your phone before bed
- Avoid junk food
- Don’t skip meals
- Maintain an active lifestyle
- Get 8 hours of sleep
- Avoid all-nighters
- Limit caffeine intake
- Stay hydrated
- Don’t eat immediately before bed  Eat better foods before bed
- Don’t exercise before bed  Try relaxing exercise, like stretches/yoga
- Maintain a consistent schedule  lol, can’t do that
- Don’t use your phone before bed  Use a blue-light filter on devices
- Avoid junk food  Balance healthy and unhealthy food
- Don’t skip meals  Vary when and what you eat
- Maintain an active lifestyle  #PetersonStairs
  ○ But actually, take breaks when you work to stretch/walk around
- Get 8 hours of sleep  Try to get at least 6 on most days
- Avoid all-nighters  Try to get at least a few hours, or a nap
- Limit caffeine intake  Limit caffeine intake after ~10 PM
- Stay hydrated  Stay hydrated (there’s no sugarcoating this one)
- Use campus resources
Use campus resources
Walk UCSD: Log, Routes, and Maps

- **Campus Loop (PDF):** 8,000 steps (4 miles), one hill
  Discover the beauty of UCSD's natural environment in this extended walk around the perimeter of the main campus.

- **Chancellor's Challenge 5K (PDF):** 6,200 steps (3.1 miles), one hill
  From the north campus recreation/athletic fields to Library Walk, follow the route of the Chancellor's Challenge 5K Run/Walk for Scholars, held each fall.

- **East-West Connect (PDF):** 3,000 steps (1.5 miles), easy
  This sidewalk route crosses the I-5 to connect the east and west portions of campus. See the Triton Baseball Stadium, UCSD’s Preuss School, and the towering Challenge Course.

- **Eucalyptus Trail (PDF):** 2,000 steps (1 mile), easy to moderate
  A trail on uneven terrain winds through a shady fringe of eucalyptus trees; thousands were planted here for use as railway ties by the Santa Fe Railway.
References
Sleep Disturbances, Body Mass Index, and Eating Behavior

Maria João Soares and António Macedo
Faculty of Medicine, Department of Psychological Medicine, University of Coimbra, Coimbra, Portugal

The metabolic burden of sleep loss

Sebastian M Schmid*, Manfred Hallschmid*, Bernd Schultes*

In parallel with the increasing prevalence of obesity and type 2 diabetes, sleep loss has become common in modern societies. An increasing number of epidemiological studies show an association between short sleep duration, sleep disturbances, and circadian desynchronisation of sleep with adverse metabolic traits, in particular obesity and type 2 diabetes. Furthermore, experimental studies point to distinct mechanisms by which insufficient sleep adversely affects metabolic health. Changes in the activity of neuroendocrine systems seem to be major mediators of the detrimental metabolic effects of insufficient sleep, through favouring neurobehavioural outcomes such as increased appetite, enhanced sensitivity to food stimuli, and, ultimately, a surplus in energy intake. The effect of curtailed sleep on physical activity and energy expenditure is less clear, but changes are unlikely to outweigh increases in food intake. Although long-term interventional studies proving a cause and effect association are still scarce, sleep loss seems to be an appealing target for the prevention, and probably treatment, of metabolic disease.
The physiological role of orexin/hypocretin neurons in the regulation of sleep/wakefulness and neuroendocrine functions

Ayumu Inutsuka and Akihiro Yamanaka

Abstract

Initial research on the functional significance of two novel hypothalamic neuropeptides, orexin-A and orexin-B, suggested an important role in appetite regulation. Since then, however, these peptides have also been shown to influence a wide range of other physiological and behavioural processes. In this paper, we review the now quite extensive literature on orexins and appetite control, and consider their additional effects within this context. Although the evidence for orexin (particularly orexin-A and the orexin-1 receptor) involvement in many aspects of ingestive physiology and behaviour is...
Nocturnal Eating: Sleep-Related Eating Disorder or Night Eating Syndrome? A Videopolysomnographic Study

Roberto Vetrugno, MD, PhD, Mauro Manconi, MD, Luigi Ferini-Strambi, MD, Federica Proveni, MD, PhD, Giuseppe Plazzi, MD, Pasquale Montagna, MD


Behavioral and Neuroendocrine Characteristics of the Night-Eating Syndrome

Grethe Stoa Birketvedt, MD, PhD
Jon Florholmen, MD, PhD
Johan Sundsfjord, MD, PhD
Bjarne Østergard, PhD
David Dinges, PhD
Warren Bilker, PhD
Albert Stunkard, MD

Context Investigators first described the night-eating syndrome (NES), which consists of morning anorexia, evening hyperphagia, and insomnia, in 1955, but, to our knowledge, this syndrome has never been subjected to careful clinical study.

Objective To characterize NES on the basis of behavioral characteristics and neuroendocrine data.

Design and Setting A behavioral observational study was conducted between January 1996 and June 1997 in a weight and eating disorders program at the University of Pennsylvania. A neuroendocrine study was conducted from May through August 1997 at the Clinical Research Center of the University Hospital, Tromsø, Norway.

Sleep-Related Eating Disorders: Polysomnographic Correlates of a Heterogeneous Syndrome Distinct from Daytime Eating Disorders

Carlos H. Schenck, MD, Thomas D. Hurwitz, Scott R. Bundlie, Mark W. Mahowald


Published: 01 September 1991  Article history v
Review of nocturnal sleep-related eating disorders
Dr. Carlos H. Schenck M.D., Mark W. Mahowald M.D.

Computerized Method for Automatic Evaluation of Lean Body Mass from PET/CT: Comparison with Predictive Equations
Tao Chan

ATVB in Focus
Ectopic and Perivascular Fat: Basic Mechanisms and Clinical Consequences
H. Wang, Y.E. Chen, Daniel T. Eitzman

Abstract—Obesity is a worldwide epidemic and is associated with multiple comorbidities. The mechanisms underlying the relationship between obesity and adverse health outcomes remain poorly understood. This may be because of several factors including the crude measures used to estimate adiposity, the striking heterogeneity between adipose tissue depots, and the influence of fat accumulation in multiple organs. To advance our understanding of fat stores and associated comorbidities in humans, it will be necessary to image adiposity throughout the body and ultimately also assess its functionally. Large clinical studies are demonstrating the prognostic importance of adipose tissue imaging. Newer techniques capable of imaging fat metabolism and other functions of adipose tissue may provide additional prognostic use and may be useful in guiding therapeutic interventions. (Arterioscler Thromb Vasc Biol. 2014;34:2217-2223.)

Key Words: abdominal fat ■ adipose tissue ■ brown fat ■ inflammation ■ obesity ■ white fat