

Sleep and Obesity in Children and Adolescents

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Obesity and Sleep Loss: Epidemiologic Evidence

- The increasing prevalence of obesity in both children and adults is affecting all industrialized countries.
 - The average weight of a child in the U.S. has increased by over 5 kg in the last 30 years.
 - Over a third of our country's children are overweight or obese.
- Nightly sleep duration has decreased with the increase in the prevalence of obesity.
 - Well-documented laboratory studies have shown that, when given a 10-hour opportunity to sleep for several days, children between 10 and 17 years of age sleep for about 9 h, indicating that sleep need is not less than 9 h.
 - Self-reported sleep durations by American children in this age range is often less than 9 hours and drops to 7 h or less in 16- to 18-year-olds.

Leproult, R., Van Cauter, E., Role of Sleep And Sleep
Loss in Hormonal Release and Metabolism,
Endocrine Development 2010;17:11-21

Recommended sleep requirements for children and adolescents

- Infants (4-11 months): 12-15 hours
- Toddlers (1-2 years): 11-14 hours
- Preschoolers (3-5): 10-13 hours
- School age children (6-13): 9-11 hours
- Teenagers (14-17): 8-10 hours
- Younger adults (18-25): Sleep range is 7-9 hours

Hormones, Metabolism, and Sleep

- Leptin
- Ghrelin
- Cortisol
- Glucose
- Melatonin
- Growth Hormone

Leptin

- Hormone produced mainly by adipose tissue.
- Released into the circulatory system by the adipose tissue as a function of the energy stores.
- After release by the adipose tissue, leptin signals to the brain, giving information about the status of the body energy stores.
- This results in a decrease in food intake and an increase in energy expenditure to maintain the size of the body fat stores.
- Leptin induces weight loss by suppression of food intake and by stimulation of metabolic rate.

Klok, M. et al. Leptin and ghrelin, and their role in energy balance in humans. *Obesity Reviews* 8, 21-

Leptin

- Signals satiety to the brain and thus suppresses appetite.
- Regulation of leptin is markedly dependent on sleep duration.
 - After 6 days of bedtime restriction to 4 hours per night, the plasma concentration of leptin was markedly decreased, particularly during the nighttime.
 - The magnitude of this decrease was comparable to that occurring after 3 days of restricting caloric intake by approximately 900 kcal/day.
 - The subjects in the sleep-restriction condition received identical amounts of caloric intake and had similar levels of physical activity as when they were fully rested.
 - Leptin levels were signaling a state of famine in the midst of plenty.

Klok, M. et al. Leptin and ghrelin, and their role in energy balance in humans. *Obesity Reviews* 8, 21-

Leptin and OSA

- Patients with OSA may have elevated plasma leptin levels, even when adiposity has been taken into account.
- Because leptin functions to reduce serum insulin concentrations, hyperleptinemia may be a compensatory response to normalize insulin resistance and other metabolic abnormalities.
- Hyperleptinemia in the presence of obesity and OSA may be indicative of “leptin resistance,” the appetite-regulating signals of leptin are not appropriately detected in the hypothalamus, resulting in persistent obesity and/or weight gain.

Klok, M. et al. Leptin and ghrelin, and their role in energy balance in humans. *Obesity Reviews* 8, 21-

Ghrelin

- Ghrelin is a hormone secreted by the stomach.
- Ghrelin functions as an appetite-stimulatory signal.
- Functions as a meal-initiation signal for short-term regulation of energy balance.
- Secretion is inhibited by the parasympathetic system
 - During normal sleep parasympathetic activity increases, with sleep restriction there is less P.S. activity and more ghrelin
 - More ghrelin, more hunger upon rising

Klok, M. et al. Leptin and ghrelin, and their role in energy balance in humans. *Obesity Reviews* 8, 21-

Leptin and ghrelin in obese people

- Although it would be expected that in obese humans leptin levels are decreased and ghrelin levels are increased, circulating leptin levels turned out to be increased and circulating ghrelin levels were decreased.
- Development of leptin resistance most likely involves a period of over-eating, resulting in the leptin system getting so disturbed that it leads to sustained defects.
- It is possible that decreased plasma ghrelin concentrations represent a physiological adaptation to the positive energy balance associated with obesity.

Klok, M. et al. Leptin and ghrelin, and their role in energy balance in humans. *Obesity Reviews* 8, 21-

Cortisol

- The first effect of partial sleep loss on circulating levels of pituitary-dependent hormones is an increase in the early evening levels of the stress hormone cortisol
- Normally at that time of day, cortisol concentrations are rapidly decreasing to attain minimal levels shortly before habitual bedtime.
- The rate of decrease of cortisol concentrations in the early evening was significantly slower in subjects who had undergone 6 days of sleep restriction than in subjects who were fully rested.
- Elevations of evening cortisol levels in chronic sleep loss are likely to promote the development of insulin resistance, a risk factor for obesity and diabetes.

Glucose

- The brain is almost entirely dependent on glucose for energy and is the major site of glucose disposal.
- Major changes in brain activity, such as those associated with sleep-wake and wake-sleep transitions, impact glucose tolerance.
- During sleep (when we go long stretches without eating) glucose levels remain stable or fall only minimally, but decrease during fasting in the waking state.
- These important modulatory effects of sleep on glucose regulation suggest that sleep loss may have adverse effects on endocrine function and metabolism.

L.Morselli et al./Best Practice & Research Clinical
Endocrinology & Metabolism 24(2010) 687-702

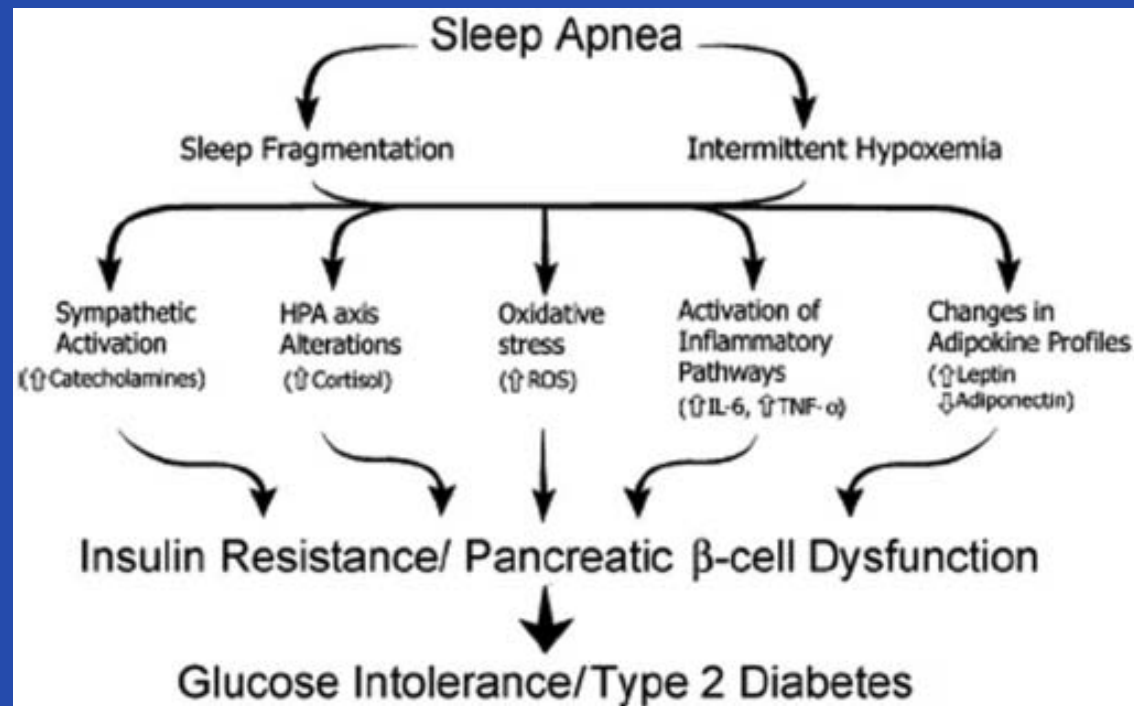
Glucose

- During the deeper stage of non-REM sleep, slow wave sleep (SWS), brain glucose utilization and sympathetic nervous activity are decreased and parasympathetic nervous activity is increased, relative to both wake and REM sleep.
- A review of 10 studies investigating the impact of partial sleep deprivation on healthy, non-obese young adults shows decreased insulin sensitivity, increased glucose, decreased glucose tolerance.
- Authors conclude that recurrent sleep restriction is associated with impaired glucose metabolism.

Potential Mechanisms of Glucose and Insulin Disturbances in Sleep Disordered Breathing (SDB)

- Intermittent hypoxia and sleep fragmentation from OSA may elicit changes in glucose and insulin homeostasis through a number of mechanisms;
 - increased sympathetic nervous system activity,
 - abnormalities in adipokines (cell signaling proteins) secreted by adipose tissue and inflammatory cytokines,
 - alterations in the hypothalamic-pituitary-adrenal (HPA) axis, and oxidative stress .
 - animal and physiologic human studies have shown that sympathetic nerve activity, inflammatory cytokines, and HPA axis dysfunction contribute to insulin resistance and/or impaired glucose tolerance.

Potential mechanisms of glucose intolerance and insulin resistance in OSA



Melatonin and Obesity

- The melatonin cycle has a number of essential physiological actions.
- Inform cells in the organism as to whether it is day or night, the cells then using this information to adjust their metabolic activity accordingly
- Assists animals, including humans, to adapt to and remain in synchrony with their external environment.
- Wide-spread use of artificial light, which distorts circadian rhythms results in suppression of elevated night-time melatonin levels
- Decreased melatonin levels may contribute to sleep fragmentation.

Reiter, R et al (2012) Obesity
and metabolic syndrome: Association with
chronodisruption, sleep deprivation, and
melatonin
suppression, *Annals of Medicine*, 44:6, 564-577

Melatonin and Obesity

- Necessary for a healthy metabolism and for the optimization of energy balance and body weight regulation
- Acts by potentiating central and peripheral insulin action
- Powerful chronobiotic influencing the circadian distribution of other metabolic processes synchronizing them to the activity-feeding/rest-fasting cycle.
- Responsible for the establishment of adequate energy balance mainly by regulating energy flow to and from the stores and directly regulating the energy expenditure through the activation of brown adipose tissue.
- Decreased melatonin production, as in shiftwork and illuminated environments during the night, induces insulin resistance, glucose intolerance, sleep disturbance, and metabolic circadian disorganization.
 - Creates a vicious cycle, ultimately leading to obesity.

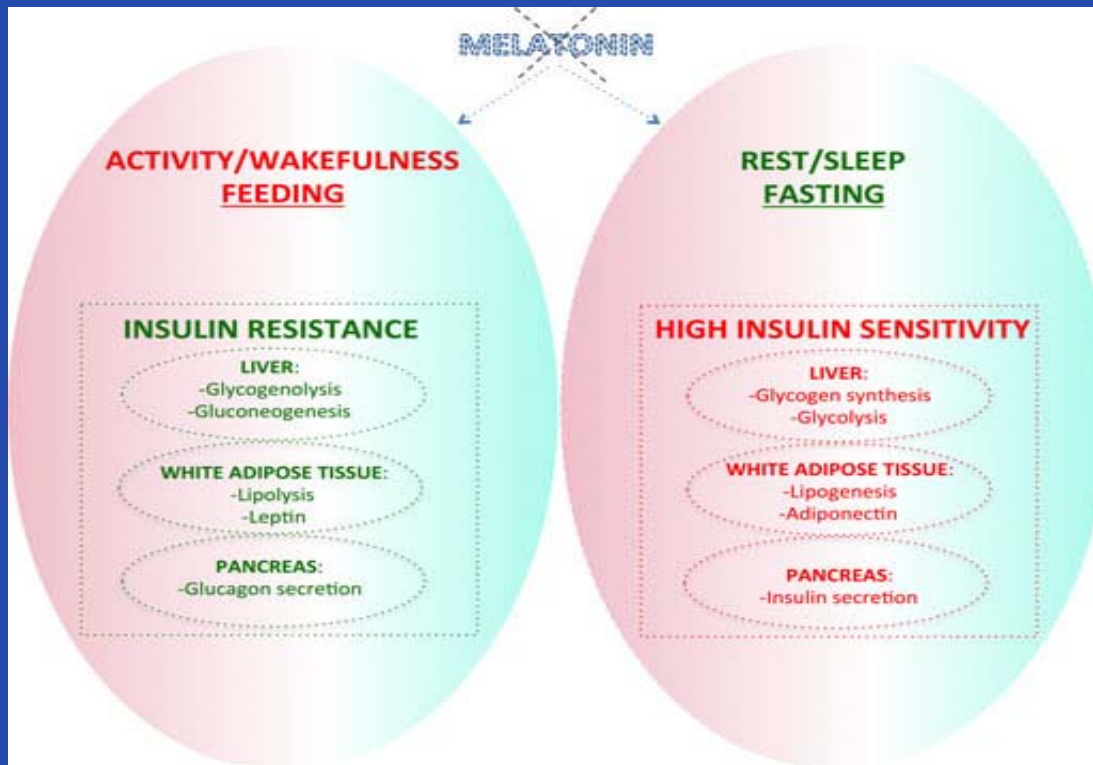
Journal of Pineal Research

[Volume 56, Issue 4, pages 371-381, 5 APR 2014 DOI:](#)

[10.1111/jpi.12137](#)

<http://onlinelibrary.wiley.com/doi/10.1111/jpi.12137/full#jpi12137-fig-0001>

Deficiency in melatonin production leads to a state of internal circadian desynchronization between the circadian activity-feeding/rest-fasting rhythm and the metabolic periods of high insulin sensitivity and insulin resistance



Journal of Pineal Research

Volume 56, Issue 4, pages 371-381, 5 APR 2014 DOI: 10.1111/jpi.12137

<http://onlinelibrary.wiley.com/doi/10.1111/jpi.12137/full#jpi12137-fig-0001>

Growth Hormone (GH)

- It has been well-documented that GH is a hormone essentially controlled by sleep-wake homeostasis
- SWS is associated with marked elevations of growth hormone (GH) levels
- Decreased amounts of slow wave sleep may result in decreased release of growth hormone
- GH deficiency results in altered lipid metabolism, increased subcutaneous visceral fat, decreased muscle mass, decreased bone density, low exercise performance
- Obesity disrupts the physiological and pathological factors that regulate, suppress or stimulate GH release
- High circulating insulin levels may be a major determinant in the suppression of GH output in the obese

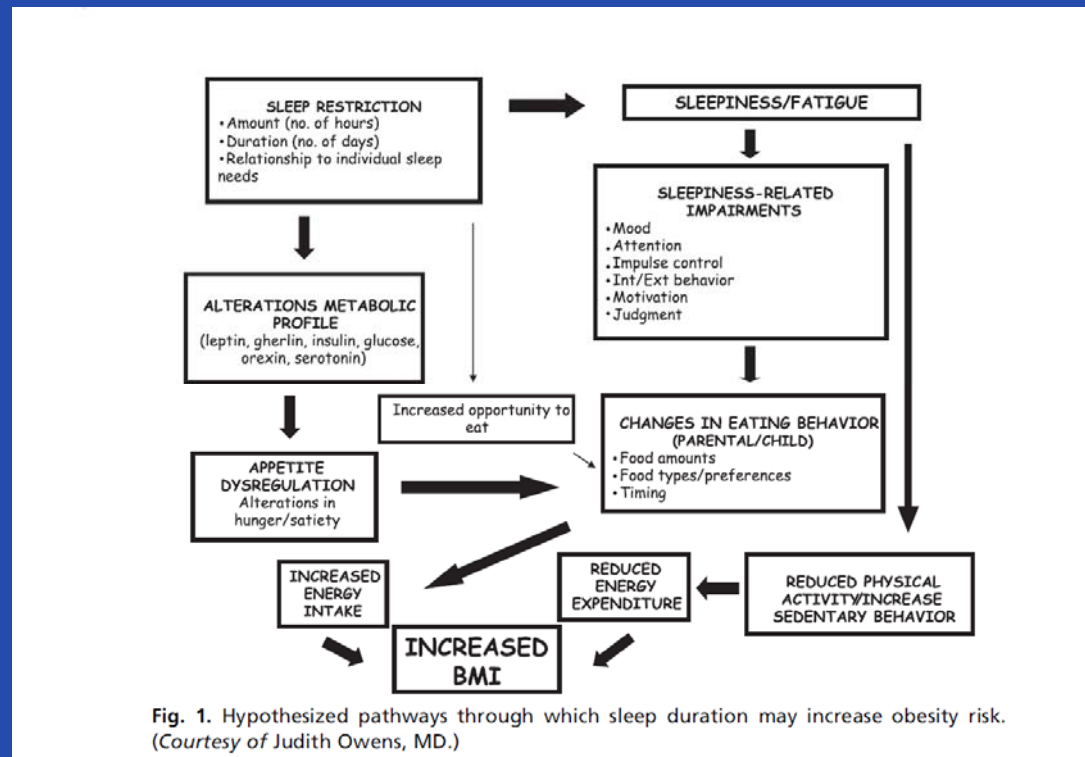
Sleep and Obesity in Children and Adolescents

Hart, C., et al *Pediatric Clinics of North America* 58 (2011) 715–733

- Only studies that focused on children and adolescents (birth to 18 years of age) and represented original empirical work were included
- Included 30 studies from 16 countries
- The reference values for sleep length used to determine obesity risk varied from less than 7 hours of sleep per night to more than or equal to 12 hours per night. Despite these differences all studies demonstrated negative associations between sleep duration and obesity risk.
- Even after controlling for potential confounding variables like parental BMI, television viewing, birth weight.

Sleep and Obesity in Children and Adolescents

Hart, C., et al *Pediatric Clinics of North America* 58 (2011) 715–733



Sleep duration and obesity

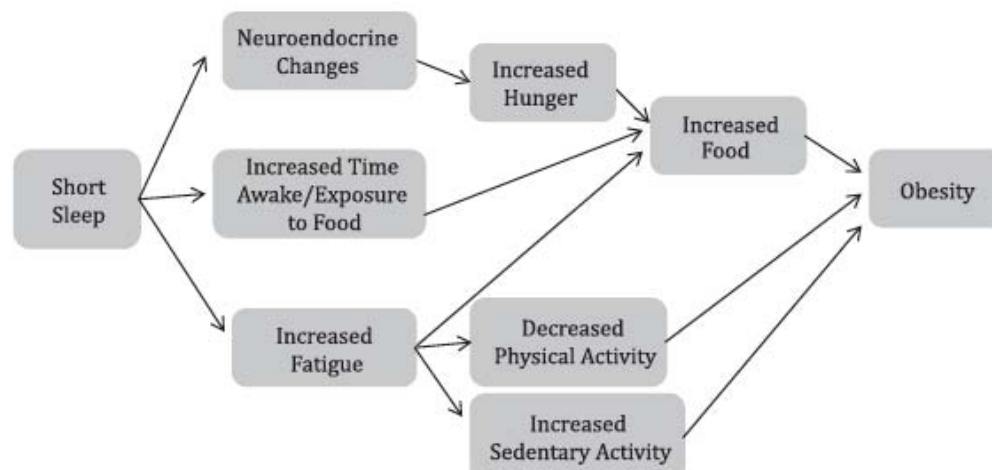


Fig. 1. Pathways through which sleep duration could affect obesity risk.

The Role of Sleep and Sleep Loss in Metabolism

- Epidemiologic studies have documented that children's sleep duration is associated with obesity risk
- This association is more consistent in children than it is in adults
- Across 22 prospective observational studies of children aged 6 months to 18 years at baseline, from diverse backgrounds, children with a shorter sleep duration had twice the risk of overweight/obesity compared with their longer-sleeping peers. The association was stronger among younger compared with older children.

Fatima Y, et al. Longitudinal impact of sleep on overweight and obesity in children and adolescents: a systematic review and bias-adjusted meta-analysis. *Obes Rev* 2015;16(2):137-49

“Changes in Children’s Sleep Duration on Food Intake, Weight, and Leptin”

Hart, C., et al. *Pediatrics*. 132(6) 1473-80

- This controlled experimental study demonstrates that compared to sleeping less, when children increase sleep, they report decreased caloric intake, have lower fasting leptin levels, and weigh less.
- The authors suggest that such changes, if maintained, could help prevent excess weight gain over time.
 - Children reported consuming 134 kcal/day less during the increase than the decrease condition.
 - Fasting morning leptin was significantly lower during the increase than the decrease condition, there was no difference for fasting morning ghrelin,
 - Children weighed less at the end of the increase than the decrease condition with a mean difference in weight of 0.22 kg,
 - Increase in children’s average nightly sleep of 2 hours, 21 minutes.

“Sleep debt and obesity”

Bayon, V., et al, *Annals of Medicine*, 2014;46:264-272

- Epidemiological data have identified an association between short sleep duration and overweight and/or obesity. This association is more consistent in children than in adults.
- Sleep restriction results in metabolic and endocrine alterations (increased levels of ghrelin, decreased levels of leptin, increased hunger and appetite, decreased glucose tolerance, decreased insulin sensitivity, increased evening concentrations of cortisol).
- Insufficient sleep is associated with increased food intake, snacking, and poor diet quality.

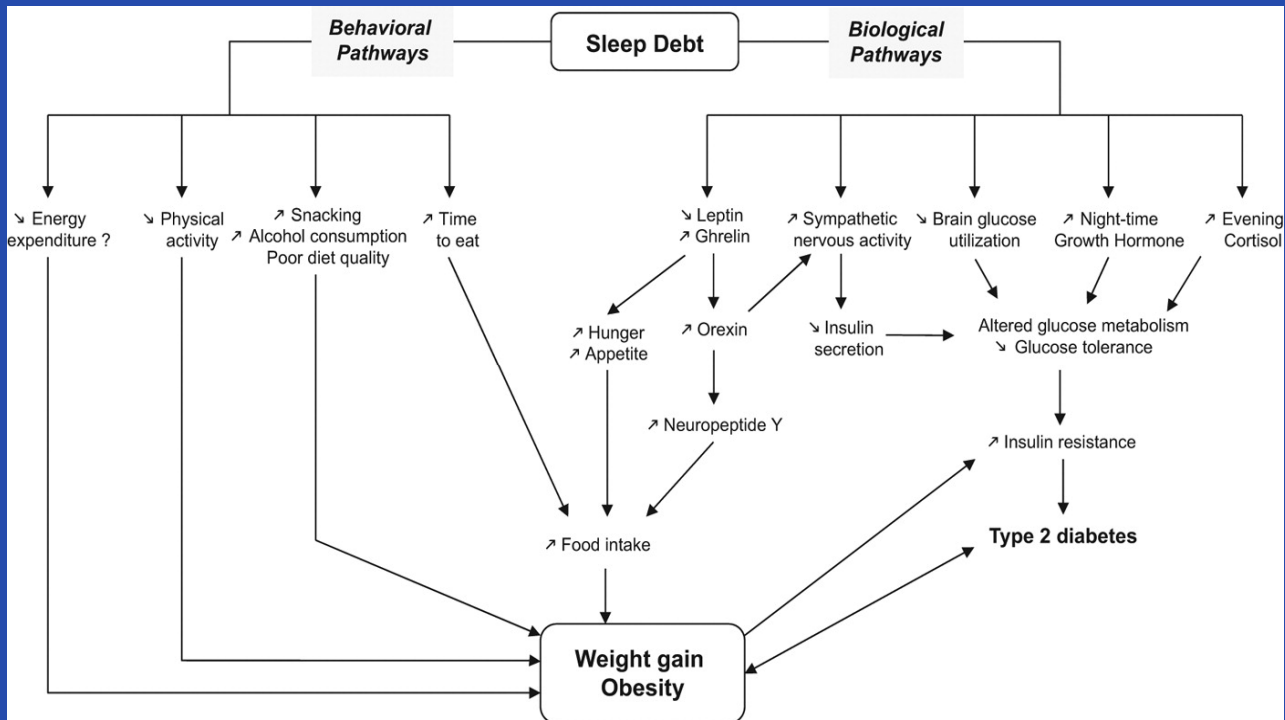


Figure 1. Schematic representation of the possible biological and behavioral pathways linking sleep debt and obesity.

Published in: Virginie Bayon; Damien Leger; Danielle Gomez-Merino; Marie-Françoise Vecchierini; Mounir Chennaoui; *Annals of Medicine* 2014, 46, 264-272.

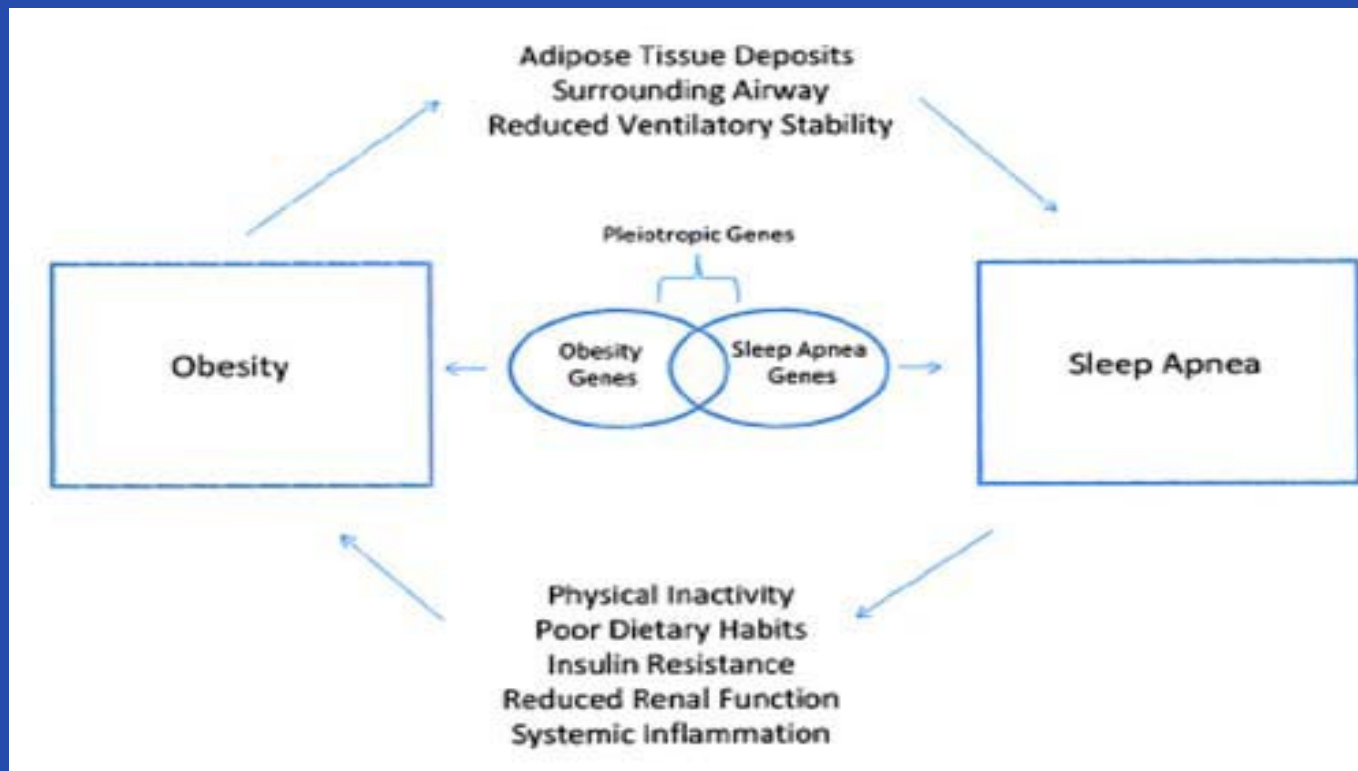
DOI: 10.3109/07853890.2014.931103

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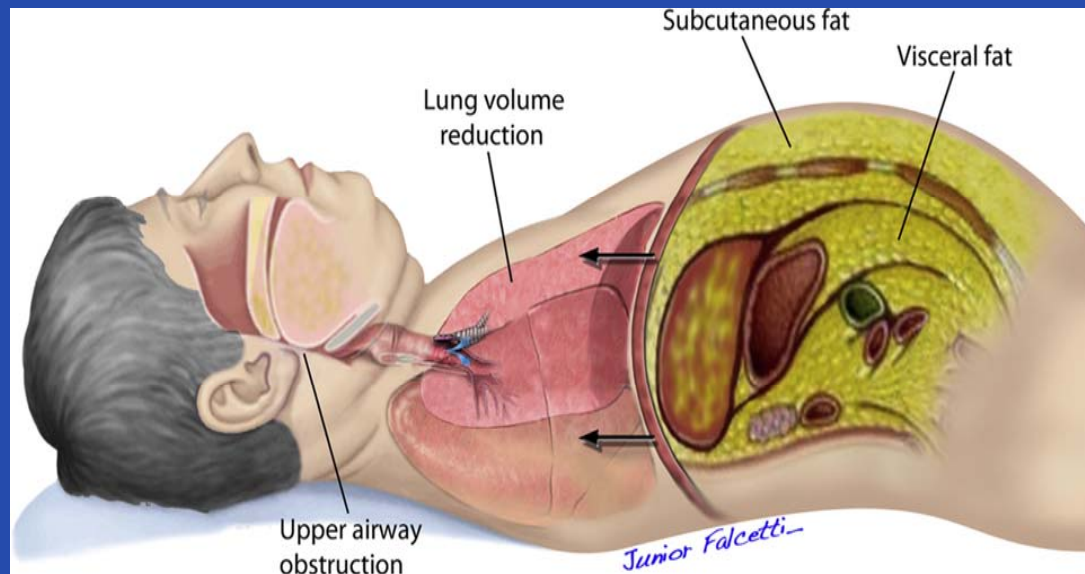
Obstructive Sleep Apnea and Obesity

- Obesity is one of the most significant risk factors for the development of OSA.
- Increased fat and muscle tissue in the neck may narrow airway size and increase upper airway resistance.
- Deposition of fat in tissues surrounding the upper airway produces a greater mechanical load on the upper airway that increases the likelihood of obstruction during sleep.
- Deposition of fat over the chest wall and abdomen reduces chest wall compliance and lowers lung volumes.

Potential mechanism involved between obesity and Obstructive Sleep Apnea(OSA)



Carter, RC, Watenpaugh, DE. Obesity and obstructive sleep apnea: or is it OSA and obesity? Pathophysiology, 2008;15:71-77.



Obesity Predisposes to Obstructive Sleep Apnea
Anatomic factors that predispose obese patients to obstructive sleep apnea.

Obstructive Sleep Apnea and Obesity in children and adolescents

- Obstructive sleep apnea in children is characterized by recurrent events of partial or complete upper airway obstruction during sleep, resulting in disruption of normal gas exchange (intermittent hypoxia and hypercapnia) and sleep fragmentation
- The usual nighttime symptoms and signs of OSA in children include snoring, noisy breathing, snorting episodes, paradoxical chest and abdominal motion, retractions, witnessed apnea, labored breathing, cyanosis, sweating, recurring nightmares, and restless sleep

Pathophysiology of OSA in Children

- Obstructive sleep apnea occurs when the upper airway patency is restricted or collapses during inspiration. Such collapse is a dynamic process that involves interactions between sleep state, upper airway mechanics, and respiratory drive
- The most significant anatomic risk factor for OSA in non-obese healthy children is adenotonsillar hypertrophy. The adenoids and tonsils grow progressively during childhood and reach their peak in the prepubertal years, coinciding with the peak incidence of childhood OSA
- Volumetric measurements of the upper airway using MRI have shown that the volume of the upper airway was smaller in children with OSA compared with controls, and that the combined size of the adenoids and tonsils correlates with the severity of OSA

Obstructive sleep apnea syndrome in children
[Riva Tauman](#) and [David Gozal](#)
Expert Review of Respiratory Medicine. 5:3 (June
2011): p425.

Pathophysiology of OSA in Children

- Disproportionate proliferation of the adenoids and tonsils occurs in children with allergic rhinitis, asthma, and children exposed to cigarette smoking or upper airway respiratory infections, particularly viruses
- Although childhood OSA is associated with adenotonsillar hypertrophy, it is not exclusively due to large tonsils and adenoids alone
- Increased risk for pediatric OSA occur in children with allergy, a family history of OSA, children born prematurely, in African-American children and in children with chronic upper and lower respiratory tract diseases

Obstructive sleep apnea syndrome in children
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2011): p425.

Obesity as a risk factor for pediatric OSA

- Obese children are at increased risk for developing OSA and the degree of OSA is proportional to the degree of obesity
- Adenotonsillar hyperplasia/hypertrophy is not always as prominent in the development of OSA in obese children
- The interaction(s) between obesity and OSA involves upper airway narrowing resulting from fatty infiltration of upper airway structures promoting pharyngeal collapsibility

Obstructive sleep apnea syndrome in
children

[Riva Tauman](#) and [David Gozal](#)

[Expert Review of Respiratory Medicine](#). 5.3

(June 2011): p425.

Obesity as a risk factor for pediatric OSA

- Adiposity and central obesity reduce the intrathoracic volume and diaphragmatic descent during inspiration, particularly in the supine position, resulting in lower oxygen reserves and increased work of breathing during sleep
- Reduced lung volumes decrease airway stiffness by reducing the tracheal tethering effect and may further increase the risk of airway collapse and OSA.
- Obesity could also result in blunted ventilatory responses to hypoxia and hypercapnia.

Obstructive sleep apnea syndrome in children
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Expert Review of Respiratory Medicine. 5.3 (June
2011): p425.

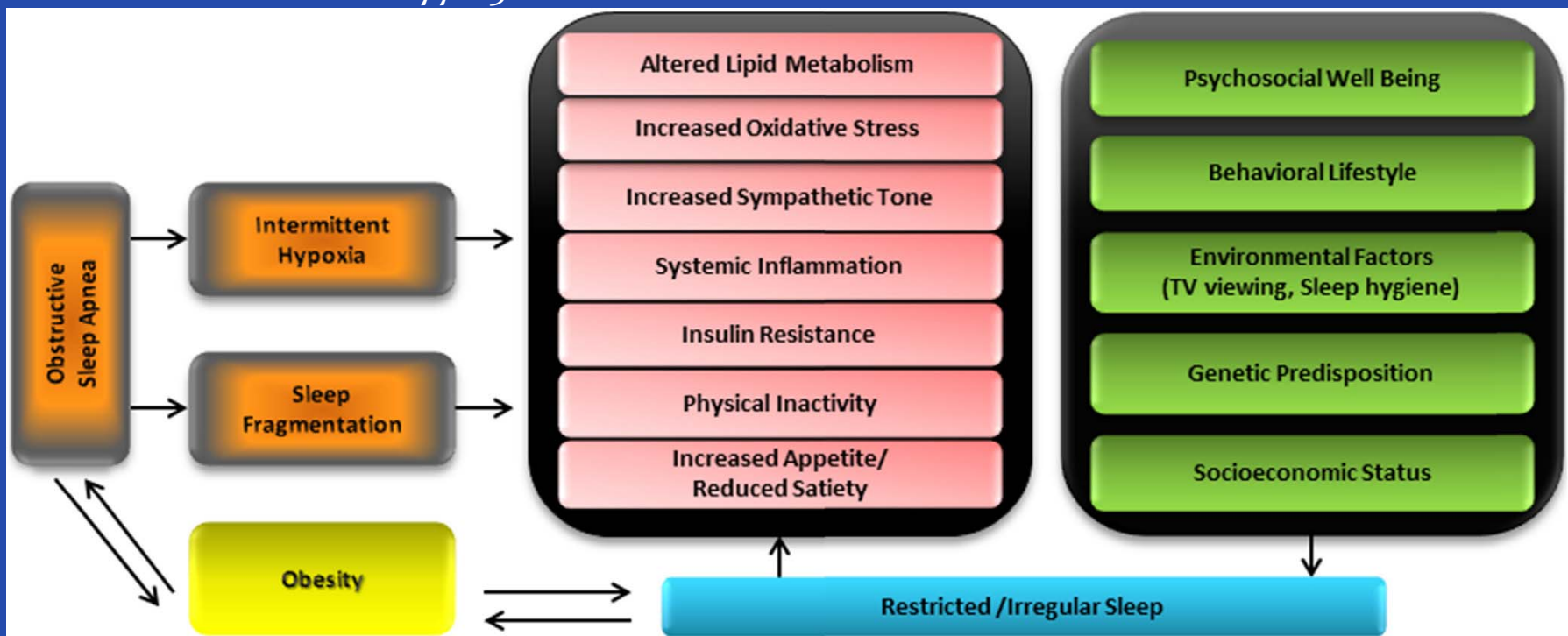
OSA contributing to development of obesity

- The presence of OSA could promote or aggravate obesity and associated morbidities.
- OSA is associated with daytime sleepiness and sleepiness promotes physical inactivity particularly in those children who are at risk for obesity
- There is also compelling evidence that OSA promotes the initiation and propagation of both localized and systemic inflammatory processes.
- OSA is currently viewed as a chronic low-grade inflammatory disease

Fahed Hakim, MD,* Leila Kheirandish-Gozal, MD,
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Semin Pediatr Neurol 22:77-85 C 2015 E

“Obesity and Altered Sleep: A Pathway to Metabolic Derangements in Children?”

Fahed Hakim, MD,* Leila Kheirandish-Gozal, MD, MSc,† and David Gozal, MD†
Semin Pediatr Neurol 22:77-85



Metabolic syndrome in children/adolescents

- Metabolic syndrome consists of hyperinsulinemia, dyslipidemia, and abdominal obesity.
- Patients with metabolic syndrome exhibit three of five of the following abnormalities: 1) waist circumference $>75\%$ of normal for age and gender, 2) mean BP or diastolic BP $>90\%$ of normal or current treatment with anti-hypertensive medication, 3) elevation of triglycerides, 4) low levels of high-density lipoprotein (HDL), or 5) abnormal oral glucose tolerance or elevated fasting glucose.
- Adolescents with OSA are seven times more likely to suffer from metabolic syndrome. The prevalence of metabolic syndrome in the general adolescent population has been reported to be 4%. In overweight children, the prevalence is markedly increased and approximated at 30% to 50%.

Pediatric Obesity, Metabolic Syndrome, and
Obstructive Sleep Apnea Syndrome
[Nevin, Mary, *Pediatric Annals* 42.10](#) (Oct
2013): 205-10

Metabolic syndrome in children/adolescents

- Gas exchange abnormalities and sleep arousals in OSA have a proatherogenic effect on serum lipid concentrations; low-density lipoprotein (LDL) is increased, whereas cardioprotective HDL is decreased.
- The severity of OSA has been found to independently correlate with impairments in glucose homeostasis and the severity of dyslipidemia
- An apnea hypopnea index (AHI) of greater than or equal to 5 was associated with a 6.5-fold increase in the odds of developing metabolic syndrome

Pediatric Obesity, Metabolic Syndrome, and
Obstructive Sleep Apnea Syndrome
[Nevin, Mary. *Pediatric Annals* 42,10 \(Oct
2013\): 205-10](#)

Concluding thoughts

- Nurse practitioners working in a multitude of practice settings can educate their patients about the relationships that exist between sleep and metabolic health
- Sleep duration should routinely be assessed in clinical practice, taking on increased importance in the context of obesity and/or metabolic concerns
- Consider routine monitoring of sleep duration in weight management programs
- Clear links exist between chronic insufficient sleep and obesity
- Clear links exist between obesity and OSA
- Future studies looking at interventions involving lengthening children's sleep as a treatment for obesity are promising.