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REVIEW ARTICLE

Sleep Disturbance as a Contributor to Pediatric Obesity: Implications and Screening

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Abstract

Obesity causes more than 200 medical disorders including cardiovascular disease, diabetes, hypertension, sleep apnea. In particular, the prevalence and rate of obesity in children and adolescents have increased with over 1/3 of the US pediatric population afflicted with overweight and obesity. Though there is a multifactorial etiology including complex biological and physiological mechanisms involved in energy regulation that may predispose toward an obesity phenotype, we highlight an often missed and overlooked etiology of obesity in clinical assessment in children- sleep disturbance and its causation to weight gain. We also highlight pertinent findings on clinical history and examination, with particular attention to the pediatric population, along with routinely used screening tools for sleep disturbances in the clinical assessment of the patient with obesity.

Keywords

Sleep disturbance, Childhood obesity, Adolescent obesity, Sleep apnea, Sleep disorders on children, Metabolic syndrome

Introduction

Obesity is one of the leading causes of morbidity and mortality in the United States and globally. The prevalence of overweight and obesity in children in the US currently approaches 33% with increasing severity with age: 41.5% of US 16-19 year-old adolescents are classified with obesity and 4.5% meet the criteria for Class III obesity (BMI > 140th of the 95th percentile) [1]. The prevalence of chronic sleep restriction in children and adolescents is approximately 27% of school-aged children and 45% of adolescents; lower levels of parental education, increased caffeine consumption, and presence of electronics in the child's bedroom overnight may be predictive of insufficient sleep duration [2].

Studies as early as 2002 illustrate a link between obesity in children and sleep duration. Limitations from these studies include data collected from parental report and study design [3-5]; however, later studies address these concerns resulting in further associations between sleep disturbances, pediatric obesity, and poor metabolic health, including a meta-analyses suggesting that insufficient sleep is associated with increased risk of obesity in children (range 58-89%) [6,7]. Further, sleep disturbance is linked to insulin resistance, cardiovascular disease and type 2 diabetes [8-12], which are increasingly common in children with obesity [13].

Sleep disturbance is identified as a novel risk factor for increased vulnerability to obesity and cardiometabolic disease as a result of dysregulation of appetite, increased glucose intolerance, and elevation of blood pressure [12-18]. Our understanding of sleep as a key modulator of metabolic syndrome and obesity phenotype provides additional opportunity to intervene early and provide mitigating strategies to either slow progression of weight gain or lose weight. Prompt recognition of the association between sleep pathology and obesity, especially in children, paves a potential path-

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Table 1: Sleep Disturbances - Classifications, Sub-Types, Characteristics.

Classification	Sub-Types	Characteristics
Insomnias	-Acute -Chronic -Comorbid	-Difficulty initiating & maintaining sleep -Chronic: exists > 3 months & > 3 times/week -Comorbid: associated with affective disorders, stimulants, alcohol use
Sleep Related Breathing Disorders (SRBD)	-OSA (chronic vs. short term) -Central sleep apnea syndromes -Sleep-related hypoventilation -Sleep related hypoxemia	-Snoring, labored/breathing -Daytime consequences: Sleep deprivation, -Hypercapnia
Central Disorders of Hypersomnolence	-Narcolepsy -Kleine-Levin syndrome -Hypersomnia due to medical or psychiatric disorder -Idiopathic	-Excessive daytime sleepiness disorders which are not included in other categories
Circadian Rhythm Sleep-wake Disorders	-Delayed Sleep Phase Disorder (DSPD) -Night Eating Syndrome (NES)	-Internal (endogenous) abnormalities of the body's circadian rhythm (sleep/wake cycle) -Entrained to 24 hours by external factors, specifically light -Short-term circadian rhythm disturbance includes jet lag -Chronic circadian rhythm disturbance exhibited in night-shift workers
Parasomnias: Non-Rapid Eye Movement Types (NREM) Rapid Eye Movement Types (REM)	**NREM:** -Confusional arousals, sleepwalking, sleep terrors, and sleep-related eating disorder (SRED) **REM:** REM sleep behavior disorder and nightmare disorder **Other parasomnias include:** sleep enuresis, exploding head syndrome, sleep-related hallucinations	-Disorders associate with sleep stages and partial arousal
Sleep Related Movement Disorders	-Restless leg syndrome, -Periodic movement disorder -Myoclonus, bruxism, and sleep-related movements due to medical condition or medicine	-Simple, repetitive movements during sleep -Associated with dysesthesias or cramps

way for more effective treatment of a chronic, debilitating disease [19].

In this review, we highlight a frequently overlooked etiology of pediatric obesity in clinical assessment-sleep disturbance and its causation to weight gain. We emphasize pertinent findings on clinical history or examination along with routinely used screening tools for sleep disturbances in children. Common sleep disturbances are summarized in Table 1 and Classification section; a more in-depth discussion (including screening, evaluation, and treatment) of obstructive sleep apnea (OSA), restless leg syndrome (RLS), delayed sleep phase disorder (DSPD), sleep related eating disorder (SRED), and night eating syndrome (NES) follows. A brief discussion of the associations between pediatric obesity and pediatric sleep disorders concludes the paper.

Children and Sleep

The activity of sleep is life sustaining; it is estimated that older children and adolescents spend up to 40% of their day in sleep; younger children significantly more. This complex activity is highly regulated to allow for restorative functions of the body which include neurocognitive functioning, memory, mood stabilization, and any number of neurobiologic and neuroendocrine functions. Sufficient, effective sleep is basic to the optimal functioning for humans [20].

Conversely, chronic, insufficient sleep is related to the consequences of the body not meeting this basic need. These consequences range from mild (drowsiness, sluggishness) to more chronic debility (difficulty maintaining wakefulness, lapses in attention, poor cognitive performance, and emotional instability); there are a host of behavioral and cognitive conditions that may result from chronic, insufficient sleep [21].

Sleep patterns and behaviors evolve in infancy, childhood, and adolescence just as many other physiological and behavioral processes develop; intrinsic (physiological) and extrinsic (environment including parenting) processes affect each child and their smooth progress through optimal sleep development. It is through this lens that "normal struggles" in managing sleep transitions from infancy to toddlerhood and progressing through normal developmental stages is to be expected and part of normal development; these struggles tend to be transient. These normal struggles are in contrast

to sleep disorders which tend to be chronic in nature; children with chronic diseases are a higher risk for these sleep disturbances [22].

Sleep/Obesity Association in Youth

Youth with the chronic disease of obesity are at particular risk for associated sleep disorders. The processes that contribute to the association of obesity and sleep disorders continue to be studied; a current theory is this relationship involves metabolic and neuroendocrine/hormonal physiology and is multifactorial. The association seems to be bidirectional [13,15,17]. The excess accumulation of adiposity resulting in obesity is now known to involve complex pathways with afferent and efferent feedback and neurohormonal signaling to the cognitive or emotional brain, affecting energy regulation [23]. The perturbance in this intricate energy regulation system driven by macro-environment, micro-environment, biological, behavioral, developmental, and/or psychosocial factors may impact food intake and satiety leading to weight gain [23]. The neuron cluster centers controlling hunger (neuropeptide Y (NPY) and agouti-related peptide (AgRP)) and satiety (proopiomelanocortin (POMC) and cocaine- and amphetamine-related transcript (CART)) lie in the arcuate nucleus of the hypothalamus and play a 'ying-yang' relationship where overall energy homeostasis is determined by multiple variables affecting either stimulation and/or inhibition of the two. NPY/AgRP and POMC/CART are sensitive to the effects of insulin and leptin. Neurons of the arcuate nucleus project intrahypothalamically affecting neuroendocrine circuitry whereas other types of neurons project to various regions of the hypothalamus. Gut hormones (i.e. insulin, ghrelin, glucagon-like-peptide 1, PYY) cross the median eminence to influence energy regulation [23]. In particular, the suprachiasmatic nucleus regulates sleep-wake cycles and disturbance in these 24-hour oscillation patterns will influence appetite-regulating hormones.

Sleep curtailment has been intricately associated with hormones controlling appetite and feeding behavior. Sleep loss has been linked to increase in appetite in relation to the heightened wakefulness. Leptin, secreted predominantly by adipose tissue in response to satiety with a peak between 22:00 and 03:00 hours during sleep in healthy adults, is markedly decreased after sleep deprivation in human studies where subjects have been well-fed, thus implicating a state of famine despite satiety. Ghrelin, the hunger hormone secreted by the fundus of the stomach, typically is lowest during sleep, peaks pre-prandially, and decreases after energy intake, has also been noted to be elevated during episodes of sleep deprivation, leading to increase in feeding behavior [15,19,24]. Sleep deprivation has also been linked to glucose intolerance and insulin resistance. Imbalance in sleep patterns influence the autonomic nervous system, resulting in over-activation of the sympathetic system that promotes insulin resistance and metabolic syndrome [25].

A few studies in youth link sleep deprivation and the development of metabolic syndrome components. Weiss, et al. demonstrated a reduction of leptin levels along with increased caloric consumption and slight increase in weight in a group of thirty-six 8-11 year-old with sleep restriction [26]. Other studies found associations between sleep deprivation and higher glycemic load diet, desire for sweets, and higher fasting and post-prandial insulin levels [27-29].

Sleep Disturbance-Definition and Classification

The American Academy of Sleep Medicine's International Classification of Sleep Disorders (ICSD) 3rd Edition organizes sleep disorders into 7 categories: insomnia, sleep-related breathing disorders (SLBD); central disorders of hypersomnolence; circadian rhythm sleep-wake disorders; parasomnias, sleep-related movement disorders; and other sleep disorders [30]. A functional way to classify these groups is (1) Insufficient sleep quantity, (2) Poor sleep quality, (3) Inappropriate timing of the sleep period, and (4) Primary disorders of excessive daytime sleepiness [31,32]. Classification sub-types and characteristics of these sleep disorders are summarized in (Table 1) [33-35].

General Screening and Assessment for Sleep Disturbances in Children

The diagnostic process for sleep disturbances is similar to other medical problems: general assessment to define most likely differential diagnoses followed by focused history, evaluation, and physical examination to identify specific diagnoses. Sleep disturbances frequently co-exist and often exacerbate each other. Different developmental stages may elicit different presenting scenarios within the same diagnostic category.

Assessment begins with a complete sleep history via discussion with family (and patient as developmentally appropriate) to determine areas of concern. Highlighting variability in sleep patterns will help guide screening, evaluation and ultimately the treatment plan. Variability in tolerance of sleep disturbances may elicit parental concerns that are very different to the clinician's concerns. All will need to be addressed for the parent-child-clinician triad to function optimally.

Several screening tools exist for pediatric sleep disorders; some tools are age-specific based on developmental age [31,36,37]. The BEARS screening tool organizes questions around the categories of Bedtime problems, Excessive daytime sleepiness, Awakenings during the night, Regularity and duration of sleep, and Sleep-disordered breathing [31] Questions are available for preschool, school-age, and adolescent groups; questions pertain to both child and parent. Other screening tools used in adults (Epworth Sleepiness Scale; STOP-Bang Sleep Apnea questionnaire) have been modified for older adolescents. The Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD) is validated to assess

daytime sleepiness in adolescents 12-18 years [38]. The STOP-Bang tool which stratifies risk of OSA in adults has been modified for use in adolescents 9-17 years with ongoing validation in process [39].

Sleep history includes information about sleep patterns, schedules, habits, and routines. Assessment of the sleep environment provides insight into aspects of family dynamics and stressors which may need support to ultimately achieve the primary goal of improved sleep. A thorough family, medical, developmental, school (age appropriate), cultural, and psychosocial history along with behavioral assessment and physical examination (with emphasis on neurologic and head/neck) yields valuable information for discussion with the family; and an excellent opportunity for education [31,40].

After a synthesis of information from the sleep history, the clinician and family decide on additional testing as indicated to further define specific sleep disturbances. These may include sleep diaries, actigraphy, and overnight polysomnography.

Sleep Disturbances and Relationship to Pediatric Obesity

OSA (sleep related breathing disorder classification) is defined as repeated episodes of prolonged upper airway obstruction during sleep with continued or increased respiratory effort; often results in hypoxia, hypercapnia and fragmented sleep [15,41]. OSA is classified as a decrease in patency of the upper airway, increased collapsibility of upper airways, or decrease in central ventilatory drive [14]. OSA etiologies include medical conditions categorized as craniofacial syndromes, neurological disorders, and several miscellaneous syndromes (Choanal stenosis, Down syndrome, subglottic stenosis, Prader-Willi syndrome, and obesity for examples) that can lead to partial upper airway obstructions. The resultant hypercapnia, intermittent hypoxia, and fragmented sleep contribute to cardiovascular, metabolic, neurocognitive, and behavioral co-morbidities [13].

Evaluation of OSA includes a full sleep assessment with particular emphasis on sleep habits, presence of snoring or disrupted sleep, daytime sleepiness, hyperactivity, and audible pauses in breathing while sleeping. Clinical guidelines for evaluation of OSA in children include those by the American Academy of Pediatrics, American Academy of Sleep Medicine, and American Academy of Otolaryngology-Head and Neck Surgery [42]. All 3 recommendations guide the clinician through the pediatric algorithm of diagnostic criteria. OSA is graded in adults > 18 years of age as normal (Apnea/Hypopnea Index (AHI) < 5.0), mild (AHI 5-15); moderate (AHI 15-30) and severe (AHI > 30) [15]. In children and adolescents less than 18 years of age, OSA grading is more stringent: mild (AHI 0-1.5); moderate (AHI 1.5-5.0); and severe (AHI > 5.0); treatment is recommended when AHI is greater than 5 [15]. Treatment options are case specific but generally include tonsillectomy/adenoidectomy (T&A), positive airway pressure support, oral appliances, pharmacologic therapy, positional therapy, and supplemental oxygen [43]. Weight loss may be beneficial to children with elevated BMI percentiles; 33-76% of children with OSA and obesity will continue to have a positive sleep study after T&A; a repeat sleep study is encouraged postoperatively [36,44].

Delayed Sleep-Wake Phase Disorder

Delayed Sleep-Wake Phase Disorder (DSWPD) is a circadian rhythm disorder characterized by a significant and ongoing shift of an entire sleep/wake cycle; a shift that interferes in daily routine, commitments (school), daytime sleepiness, and frequently behavior problems [45,46]. Often, sleep is normal if the segment of sleep is not constricted by societal or environmental responsibilities or expectations. Often the patient reports an inability to sleep prior to 2-3 am with a preference to wake late morning. DSWPD may have a genetic predisposition. Onset of the disorder is typically in adolescents, affecting males more than females. After a thorough history and physical examination, evaluation consists of sleep logs, actigraphy, and secondary effects of poor sleep. The goal of therapy is to shift and maintain the sleep-wake cycle to earlier in evening and earlier in morning. Possible therapies include optimizing sleep hygiene which includes elimination of stimulants in evening; bright light therapy immediately after awakening, a very gradual shift nightly to an earlier bedtime, and possible medication therapy (melatonin) [46].

Night Eating Syndrome (NES)

Night Eating Syndrome is a delay in the circadian intake of food with at least 25% of daily food intake ingested during evening and/or night. Characteristics of NES include 1) Morning anorexia; 2) Strong urge to eat between dinner and bed and/or nighttime; 3) Insomnia or delayed sleep onset > 4 times a week; 4) Belief one must eat to be able to sleep; 5) Mood frequently depressed; may be worse in evening; 6) Awareness and recall of late night eating; and 7) Pattern has been present for at least 3 months [47,48].

Prevalence of NES is 1.5% of general population; in patients with obesity, the prevalence is 10-20%. There is an increased risk of NES in adults with obesity, other eating disorders, depression, anxiety, and emotional or substance abuse [49]. Evaluation is performed using the Night Eating Diagnostic Questionnaire (clinically useful diagnostic categories) [50] and Night Eating Questionnaire provides severity scale [47]. Other etiologies for presenting symptoms may include substance abuse, medication, or undiagnosed medical or psychiatric disorder. Treatments may include anti-depressants, cognitive behavioral therapy, relaxation techniques, and trial of melatonin [51-53].

NES may be confused or concurrent with other eating disorders, particularly binge eating disorder (BED) and sleep related eating disorder (SRED). Key areas of difference include: patients with BED eat large amounts of food in one sitting while patients with NES eat smaller amounts throughout the night. NES is also associated with nocturnal anxiety while BED is not. Distinctions between NES and SRED are related to timing and state of consciousness during nocturnal eating.

There is scant research related to NES and obesity in youth. Cleater, et al. reviewed the relationship of severe obesity and NES in adults; they found a heterogeneity of the development of NES in their subjects ranging through childhood, adolescence, and adulthood [54]. Other researchers whose general study populations ages ranged from 13-26 years found weak or no relationship between NES and obesity [55,56]. However, Utzinger, et al. using data from the Teen Longitudinal Assessment of Bariatric Surgery Consortium (242 youth, ages 13-19 years), reported on eating disorders discovered in the study participants at preoperative baseline [57]. 5% of the cohort tested positive for NES. Although there are several limitations to the study, it suggests that a subset of youth with the onset of severe obesity at a young age also exhibit NES. More research is needed to examine this association and guide clinicians.

Sleep Related Eating Disorder (SRED)

Sleep Related Eating Disorder is classified as a parasomnia. Episodes of SRED typically occur in the first half of the night and include: 1) Out of control eating; 2) Impaired consciousness while preparing/eating food with little memory of these episodes the next morning; 3) Eating high carbohydrate, high-fat, or odd combinations of food; and 4) Not easily awakened or redirected during the episode [48]. Prevalence is 5% in general population and 9-17% in patients with other eating disorders. Age of onset typically late teens; 65% are female and > 40% have diagnosis of overweight or obesity. While the cause is unknown, SRED often occurs in adolescents with history of sleepwalking or stress.

Diagnosis requires history and physical examination to rule out any underlying causes, a review of sleep habits, sleep-wake pattern, and level of daytime sleepiness. A sleep diary can be helpful; input from the patient and other household members is important. A complete review of medications is done; primarily assess for zolpidem, triazolam, amitriptyline, olanzapine, and risperidone which have been associated with SRED. Patients with SRED are at increased risk of developing other sleep disorders including OSA, sleepwalking, narcolepsy, and RLS. SRED is associated with a daytime eating disorder (bulimia, anorexia), mental health disorders (anxiety or depression), and sleep deprivation. Treatment of SRED consists of optimizing sleep hygiene, eliminating medications that may be triggers, treating other sleep disorders, increased safety in the home environment to manage nocturnal episodes and pharmacotherapy [48,58,59].

Restless Leg Syndrome (Willis-Ekbom disease)

Restless leg syndrome (RLS), a sleep related movement disorder, is a neurological, sensory condition characterized by overwhelming desire to move the legs; it is often accompanied by unpleasant sensations (dysesthesias). These episodes usually occur during periods of rest or inactivity; resuming activity appears to relieve the symptoms to some degree. Symptoms tend to increase if the period of inactivity is prolonged. Children with RLS often have difficulty falling asleep and delay in bedtime activities [32].

RLS is a diagnosis of exclusion. In some patients, iron levels are low and can be confirmed by obtaining serum ferritin level. Often, EMG or muscle biopsies are performed to rule out other neuromuscular disease. Treatment consists of maximizing sleep hygiene, treating any iron anemia, avoiding stimulants (liquid or medications), biofeedback, and other stress reduction techniques. Medical therapy may include dopaminergic agents, clonidine, neurontin and klonopin if symptom relief is not achieved by non-medication techniques [60,61].

Pediatric Obesity and Sleep Disturbances

The relationship between sleep disturbances and pediatric obesity seems to be bidirectional [13,15,16]. Several studies [6,12,13,15-18,24,62] and two meta-analyses [63,64] report an association between inadequate sleep duration and elevated BMI percentiles (both obese and severely obese ranges). Both sleep disturbances and obesity are associated with increased risk of metabolic syndrome, Type 2 diabetes, dyslipidemia, and insulin resistance [12,15,17,18,62,65-67]. Obesity seems to increase the risk of sleep related breathing disturbances in children and adolescents [13].

The presence of OSA and obesity may potentiate each condition; also, the severity of each condition often is in parallel [15]. Other associated co-morbidities of OSA and obesity in children include excessive daytime sleepiness, poor quality of life, neurocognitive, behavioral and functional deficits [21], and cardiovascular burden. OSA is often accompanied by inadequate, poor quality sleep which is associated with increased risk of obesity; poor sleep quality is consequently associated with worsening obesity [6].

Beyond metabolic consequences resulting from pediatric obesity and sleep disorders in children, there are associations between these conditions and cognition and behavior. Spruyt & Gozel (2012) report multidirectional relationships studying weight, sleep-disordered breathing (SDB) and cognitive processing in 351 children in a community cohort; cognitive functioning was negatively affected by the presence of obesity and SDB

[68]. While limitations of this and other studies [69-71] suggest the need for further research, the interrelationships of these and related disorders should be addressed during the care of children with these chronic conditions.

Yet to be established is whether improvement in sleep quality and duration have a positive impact on weight reduction, quality of life, and obesity related cardiometabolic health in children and adolescents [13,16]. Future studies are needed to determine if particular groups are more vulnerable to sleep disturbances thus enabling the development of targeted treatment strategies [15].

Conclusion

Given the rise in obesity and severe obesity in children and adolescents, it becomes increasingly prudent for primary care providers to screen for potential etiologies of weight gain. Though the causation of obesity is multifactorial, important elements of the history and physical should encompass adequate assessment of sleep disturbances, including sleep deprivation and circadian rhythm perturbation which are common in adolescents. As children and adolescents continue in the developmental cycle towards adulthood, impaired memory, cognition, and school performance may be reversible sequelae of chronic sleep disturbance. Disruptions in normal sleep patterns may result in weight gain, metabolic syndrome, insulin resistance, and deteriorating cardiometabolic health, all ultimately contributing to worsening obesity phenotype [15,16].

The evidence continues to grow regarding the negative impact of sleep disturbances upon weight and cardiometabolic health in youth. Thus, a clear need emerges to investigate if improvement in sleep quality and duration have a positive impact on weight reduction, quality of life, and obesity related cardiometabolic health in children and adolescents.

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