The Underlying Interactome of Childhood Obesity: The Potential Role of Sleep

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Abstract

Fine-tuning and integration between social rhythms and biological rhythms should be a priority for all, especially for children. As such, the opportunity to sleep should fit the evolving needs for sleep in a child. Unfortunately, children today are highly unlikely to obtain sufficient sleep or live under stable and regular schedules. Poor or dysregulated sleep affects the regulation of homeostatic and hormonal systems underlying somatic and intellectual growth, maturation, and bioenergetics. Therefore, in the prevention and management of childhood obesity, assessments of the “obesogenic” lifestyle, such as dietary and physical activity patterns, need to be coupled with accurate evaluation of the quality and quantity of sleep and with the potential co-existence of sleep-disordered breathing or other sleep disorders. Incorporation of sleep as an integral component of many childhood research studies on obesity should be done *a priori* rather than as an afterthought. Although parents and health professionals have meticulously delineated, observed, and quantified normal patterns of activities such as eating or playing, the absence of reliable sleep health data in children is all the more puzzling considering that young children engage in sleeping activities more than in any other activity during the 24-hour cycle. Therefore, the most forgotten, overlooked, or even actively ignored behavior of this century is undoubtedly childhood sleep. Trends aiming to reduce sleep in children have emerged, and regrettably continue to gain momentum. In parallel with such undesirable consequences, leading to the blatant disregard of sleep as a vital function rather than a commodity, a reciprocal increase in obesity rates has emerged. The mechanistic links between sleep and metabolism are now emerging, and should prompt incorporation of measures aiming to align sleep with any other antiobesity campaign. To paraphrase a well-known dictum “*Somni sano in corpore sano*” (healthy sleep in healthy bodies).

Introduction

A review of literature with respect to pediatric sleep and overweight or obesity reveals a substantial conglomerate of multifactorial components potentially contributing to the current childhood obesity epidemic. Many of those factors will be discussed in other articles in this issue of the journal. However, we should point out that there is a substantial overlap between the multifactorial components of obesity in children, and that the nature of the interactions among such factors is worthy of intense scientific discussion and investigation. Similar to physical activity and diet, sleep plays an uniquely important role in growth, maturation, and health, especially during childhood in which sleep needs are much greater than later in life. Adequate sleep plays fundamental roles in the regulation of homeostatic and hormonal systems underlying somatic and intellectual growth, maturation, and bioenergetics.

Here, we will highlight associations between sleep and obesity in children, and provide an evidence-based guide that can serve as a benchmark for future research.

The Conglomerate of Multifactorial Components Potentially Contributing to the Accrual of Obesity in Children

Studies have clearly shown¹⁻⁷ that children are highly unlikely to obtain sufficient sleep on a stable and regular schedule. Two polls by the National Sleep Foundation^{1,2} indicated that parents routinely overestimate their children’s sleep duration, and that, in fact, children sleep much less than what was deemed appropriate for their stage of development. Furthermore, it is estimated that as a society and across all age groups, people sleep ≈ 1 hour less than what they used to sleep one century ago. It is clearly apparent that both parents and professionals pay particular attention and derive more satisfaction from their children’s accomplishments (e.g., first steps, first words, school grades, extracurricular activity performances), such that it can be readily inferred that our society places the most emphasis on daytime functioning, and, in doing so, all too often forgets or omits to consider the critically important role of sleep.

There is conclusive evidence that healthy sleep plays a vital role in brain maturation, somatic growth, informa-

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tion processing, memory consolidation, learning, and other important neurobehavioral functions. Because sleep subserves so many aspects of overall well-being, maladaptive or disturbed sleep can exert multidimensional adverse effects. Considering the multitude of environmental factors and daytime activities that tend to intrude into daily life and potentially rob children of their sleep needs, it is not surprising that preservation of healthy sleep will suffer from such intrusions. For example, 43% of school-aged children and 57% of adolescents have a television in their bedroom.^{1,2,8} As many as 42% have a mobile phone in their bedroom, and many other electronic devices, such as computers, video games, and others, are preeminently and frequently present in children's bedrooms.^{8,9} Perceptual denigration of the night and the dark as a "negatively loaded" period has also been pervasively communicated to children, such that 60%–72% of children routinely have a nightlight in their bedroom.¹ Moreover, a continued urge for sustained uninterrupted social e-contact is increasingly observed in youngsters, and at lower and lower ages. In summary, historical trends point to decreased opportunities for sleep in children and also to the increased "pollution" of that sleep opportunity by a variety of intrusions that may further lead to reduced sleep duration or sleep disruption.

Lately, increasingly more studies have been published on sleep duration in children, with most of these studies aiming to evaluate the potentially adverse impact of poor sleep on health outcomes. To provide a representative picture regarding the complexity of documenting sleep duration in children, a synopsis of several scientific papers on the sleep–weight debate from 1990 onward was tabulated (Table 1^{10–21}). Even to the naked eye, it becomes readily apparent that although these studies are methodologically heterogeneous, the reported associations require further investigation. As such, factors such as the age of the child, the body weight normative criteria, the normal sleep criteria, the implementation of either objective or subjective assessment of sleep, and the myriad of other covariates and/or confounders reflective of the sociocultural niche in which one develops need to be incorporated into the sleep–weight interaction to enable a reliable estimate of the magnitude of such interactions. These considerations should lead to a call for large-scale representative and longitudinal studies on objective sleep–wake patterns in children, particularly if we want to address the impact of sleep on health in general and on body weight in particular from a valid ecological standpoint.

The covariates and confounders shown in Table 1 further emphasize that in addition to its composition, the family caters to many health-related components, *e.g.*, exposure and accessibility, modeling, provision, and sociocultural niche. In fact, the family domain is important with respect to sleep–wake patterns^{22,23} as well as markedly influencing food and health provisions of the developing child. Therefore, the presence of parental

overweight has been found to be of substantial importance to childhood overweight.²⁴ Parental beliefs and perceptions likely shape parental feeding behaviors as well, such that if mothers believe that a heavy infant is a healthy infant and the latter is reflective of good parenting, then early introduction of solid foods, insistent administration of food to infants, and use of food as an aid to shape behavior are likely to promote obesity.²⁵ As such, parenting style²⁶ and likely family composition potentially shape the household habits, and the latter may then interact with sleep. For instance, when US preschoolers were exposed to three household routines, namely evening meal as a family for more than 5 nights per week, sleeping ≥ 10.5 hours/night on weekdays, and ≤ 2 hours/day television, video, or other screen-viewing behavior, the obesity prevalence decreased by 40% than when no such simple routines were present.²⁷

In general, the consensus emanating from the available studies on sleep–weight associations suggest that less sleep is more likely to be associated with being overweight or obese (see Table 1). Although a dose–response relationship has been proposed,²⁸ it should be emphasized that pooled odds ratios range from 1.15 to 11.0!²⁹ In a recent study in which sleep and weight were carefully monitored using objective measures, we found that regular sleep is a significant risk factor for the occurrence of weight problems in children, and that a nonlinear trend between sleep and weight is present.³⁰ We further found that obese children are less likely to "catch-up" sleep during weekends, and the combination of shorter sleep duration and more variable sleep patterns was associated not only with increased weight risk but also with adverse metabolic outcomes (*i.e.*, insulin resistance, elevated serum lipids, increase high-sensitivity C-reactive protein levels). Therefore, we would advocate that educational campaigns aimed at families and promoting longer and more regular sleep may yield favorable changes in obesity rates and improve metabolic dysfunction in school-aged children.

The biological plausibility of the link between sleep, appetite regulation, and adiposity is quite compelling. Due to space restrictions, we will not be able to review this important topic in depth. However, mechanistic evidence linking circadian clocks to cellular metabolism and regulation of appetite and food intake has clearly emerged (for review see ref. 31). Similarly, since the initial demonstration of the effects of sleep restriction on insulin bioavailability, a flurry of studies in both animals and humans has conclusively demonstrated the marked impact of sleep patterns on all aspects of organismal bioenergetic balance, including food preference, appetite, and energy disposition (for reviews, see refs. 32 and 33). Thus, any perturbations of the endogenous circadian cycle or in the integrity of sleep homeostatic mechanisms is likely to be fraught with adverse consequences whose confluence would translate to increased probability of obesity and metabolic disturbances.

Table 1. Synopsis of Sleep–Weight Debate in Scientific Literature

Year/author	Country	Demographics	Weight criteria	Sleep criteria	Associative conclusion	Confounders/covariates
2004/Agras ¹⁰	US	n = 150 0 yr	>85 th percentile	Duration ^Q	Negative linear relation (β -0.21) ~30 min shorter sleep	Parent overweight, child temperament, low parental concern about weight, food tantrums daily sleep at ages 3–5 yr
2005/Reilly ¹¹	UK	n = 7758 3 yr	≥95 th percentile	>12 hr ^Q	Watching TV ≥8 hr/wk at age 3 yr Short sleep (≤10.5 hr) at age 3 yr (OR 1.45)	Gender, maternal education, energy intake at 3 yr
2007/Snell ¹²	US	n = 2281 3–12 yr	Overweight and obesity (WHO 1997)	9–10 hr ^D	<8 hr (OR -0.009) 8–9 hr (OR -0.014) 10–11 hr (OR -0.070) ≥11 hr (OR -0.171)	Gender, race, family income, parental education, age at time 1 and 2
2002/ Von Kries ¹³	Germany	n = 6862 5–6 yr	≥90 th percentile ≥97 th percentile	≤10 hr ^Q	≤10 hr (prevalence 14.5%) 10.5–11.5 hr (prevalence 10%) >11.5 hr (prevalence 7.4%) negative linear relation for both BMI and fat measured by impedance	Parental education, parental BMI birthweight, weight gain, screen time, snack taking
2002/Sekine ¹⁴	Japan	n = 8941 3–5 yr	Overweight and obesity (WHO 1997)	≥11 hr ^Q	<9 hr (OR 1.57) 9–10 hr (OR 1.34) 10–11 hr (OR 1.20)	Gender, age, parental obesity, outdoor playing time
2002/Sekine ¹⁵	Japan	n = 8274 6–7 yr	Overweight and obesity (WHO 1997)	≥10 hr ^Q	<8 hr (OR 2.87) 8–9 hr (OR 1.89) 9–10 hr (OR 1.49)	Gender, age, parental obesity, physical activity, screen time, frequency of taking breakfast, frequency of taking snack; risks were higher for boys than girls
2005/Padez ¹⁶	Portugal	n = 4511 7–9 yr	Overweight and obesity (WHO 1997)	<9 hr ^Q	Overweight 9–10 hr (OR 0.46), ≥11 hr (OR 0.44) Obese 9–10 hr (OR 0.44), ≥11 hr (OR 0.39)	Gender, age
2006/ Chaput ¹⁷	Canada	n = 422 5–10 yr	Overweight and obesity (WHO 1997)	≥12 hr ^Q	8–10 hr (OR 3.45) 10.5–11.5 hr (OR 1.42)	Gender, age, parental obesity, parental education, family income, single parenthood, screen time, exercise, breast-feeding time
1992/ Locard ¹⁸	France	n = 1031 5–10 yr	French obesity reference z-score	≥12 hr ^I	<10 hr (OR 4.9) 10–11 hr (OR 2.8) 11–12 hr (OR 2.0)	Parental overweight for the <11 vs. ≥11 hr OR; ≥11 hr (OR 1.4)
2003/Hui ¹⁹	China	n = 1031 5–10 yr	Overweight ≥ 92 nd percentile	<9 hr ^Q	9–11 hr (OR 0.54) ≥11 hr (OR 0.31)	Paternal and maternal obesity
2011/Sung ²⁰	US	n = 133 10–16.9 yr	Continuous BMI z-score (CDC)	Duration ^{Q,A}	No association between parent report, self-report, actigraphy and BMI (β -0.03 to -0.01)	Age, gender, race, socioeconomic status, Log-transformed Apnea Hypopnea Index
2011/Hense ²¹	Europe North: Sweden, Belgium, Estonia, Germany South: Italy, Spain, Hungary, Cyprus	n = 7867 2–9 yr	Overweight and obesity (International Obesity Taskforce criteria)	>11 hr ^Q (computer- based)	Dose-dependent inverse association <9 hr (OR 3.81) 10–11 hr (OR 1.73) stratified for region only <9 hr remained significant North (OR = 1.70) vs. South (OR = 2.84)	Personal, social, environmental, and behavioral factors of each child; screen time and parental education level, dietary habits, physical activity, daylight duration, temperature

Q, questionnaire data or survey; D, diary; I, interview; A, actigraphy (motion-logger); β , beta from regression analyses; OR, odds ratio; WHO, World Health Organization.

As further evidence of the importance and operationality of such mechanisms, albeit viewed from another angle, we will mention the Pickwickian syndrome. This condition, initially immortalized by Dickens in his description of the fat boy Joe in his novel *The Pickwick Papers*, epitomizes an extreme phenotype of obstructive sleep apnea (OSA), hypoventilation, and obesity, and is probably the best caricatural example that exemplifies the concurrence between obesity and (disturbed) sleep.³⁴ Obese children are at increased risk for developing sleep-disordered breathing, and the risk and severity of respiratory disturbance during sleep appears to be proportional to the degree of obesity.³⁴ Even though the pathogenic pathways of OSA and adiposity are not identical,^{35,36} OSA (*i.e.*, the occurrence of repeated events of partial or complete upper airway obstruction during sleep) results in disruption of normal ventilation, hypoxemia, and sleep fragmentation. Evidence has now emerged that OSA and obesity in children may adversely impact dietary preferences and may be particularly detrimental to daily physical activity patterns. Furthermore, increased levels of the hormone ghrelin support the presence of increased appetite and caloric intake in obese patients with OSA, which in turn may further promote the severity of the two concurrent conditions.³⁷ Consequently, OSA has now been shown to induce marked changes in lipid profiles and insulin sensitivity and to promote a low-grade systemic inflammatory state that appears to be additive when obesity is present concurrently.^{35,38–42}

Conclusion

In summary, sleep and weight share a conglomerate of multifactorial components that are embedded in the child, the family, and even the society, all of which can potentially contribute to the excessive accrual of weight problems in children. Future studies should focus on the nature and characteristics of such interactions while integrating a longitudinal perspective. Clearly, food, exercise, and sleep habits emerge as integral components of the developing “(un)healthy” lifestyle. In this context, the impact of poor sleep in the developing child is tremendously underrated and virtually unexplored. The most consistent consequence from insufficient or disrupted sleep is increased daytime somnolence, which can become manifest in multiple and diverse ways in the developing child, including obesogenic behaviors. Our studies suggest that poor sleep adversely impacts learning, weight, diet, quality of life, and physical activity, and their interactions.^{30,43,44} On the basis of these considerations, we will provocatively ask: Is the obese, sleepy child the reflection of our 21st century society?

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