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Association of sleep disturbances with obesity, insulin resistance and the metabolic syndrome

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ABSTRACT

Insufficient sleep, which has become endemic in recent years, has been variably associated with increased risk of obesity, disorders of glucose and insulin homeostasis, and the metabolic syndrome; to a lesser degree, so has excessive sleep. This review summarizes recent epidemiological and pathophysiological evidence linking sleep disturbances (primarily abnormalities of sleep duration) with obesity, insulin resistance, type 2 diabetes and the metabolic syndrome in children and adults.

1. Introduction

The prevalence of obesity has increased dramatically in the adult and pediatric populations world-wide [1]. In the U.S., over 35% of adult men, 40% of adult women, and 17% of children and adolescents are now obese [2,3]. Along with the increase in obesity rates has come an increase in the incidence and prevalence of insulin resistance and the metabolic syndrome, a collection of related cardiovascular risk factors. In order to meet criteria for the metabolic syndrome, three or more of the following criteria must be met: hypertension, elevated triglycerides, low HDL, central obesity, and/or elevated fasting glucose. The metabolic syndrome, along with insulin resistance, predisposes to type 2 diabetes mellitus (T2DM) and cardiovascular disease [4–6]. The metabolic syndrome is found in over 1/3 of U.S. adults [7] and 8.6% of U.S. children [8,9]; prevalence of the metabolic syndrome increases in parallel to increasing obesity [6,10–15]. Numerous reasons are postulated to account for this increase in the prevalence of obesity and the metabolic syndrome, including dietary changes [16], a decline in physical activity [17], increase in sedentary activity [18] and others, but these factors are not sufficient to explain the rise in rates of obesity and the metabolic syndrome; other factors must be sought out to explain this increase. One potential additional contributor may be sleep.

Evidence has emerged in recent years that sleep plays an important role in modulating weight gain, neuroendocrine signaling, and consequently insulin and glucose homeostasis. Alterations in sleep duration (both short and excessively long sleep) have been associated with metabolic and neuroendocrine changes predisposing to excess weight gain and increased risk of the metabolic syndrome and related components. In this review, we will examine the evidence linking disordered sleep (primarily insufficient and excessive duration) with risk of obesity and its cardiometabolic sequelae in adults and children.

2. Sleep Restriction Epidemiology

Chronically insufficient sleep (also known as sleep deprivation) has grown increasingly common in recent decades [19]. In the 2014 Behavioral Risk Factor Surveillance System (BRFSS) survey, over 33% of participating adults reported sleeping <7 h on a typical night, with higher age-adjusted prevalence of sleep deprivation among non-Hispanic Blacks, American Indians/Alaskan Natives and Pacific Islanders/Native Hawaiians vs. non-Hispanic Whites [20], falling shy of the recommended 7–9 h sleep for adults ages 25–60 [21]. Chronic sleep deprivation is also common in children – national polls have found that 27% of school-age children and 45% of adolescents report sleeping less than the recommended durations for their ages [22,23], which is 9–12 h each night for children ages 6–12 years and 8–10 h each night for adolescents ages 13–18 years [24]. The prevalence of sleep deprivation in children increases with age: self-reported sleep duration on school nights declines from an average of 8.4 h/night in the sixth grade to an average 6.9 h/night by twelfth grade [25]. Risk factors for short self-reported sleep duration in adults include race/ethnicity (African American background in multiple studies, Mexican American or other Hispanic/Latino and Asian/other in some studies and Caucasian background in other studies), lower socioeconomic status, food

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insecurity, lower education levels, female sex, being unmarried, and being uninsured or having public vs. private health insurance [26,27]. For children, a non-white ethnic background, a lower parental level of education, and the presence of electronic devices in the bedroom all associate with increased odds of sleeping an insufficient amount [28].

The high prevalence of sleep deprivation is concerning. It has long been recognized that insufficient sleep impairs cognitive and motor function. In adults, the impairment in cognitive function is equivalent to legal alcohol intoxication [29]. In children, insufficient sleep is associated with a wide array of unfavorable cognitive outcomes: poorer working memory [30], higher odds of having poorer neurobehavioral processes in mid-childhood [31], poorer grades in adolescents [23], and lower myelin content in the optic radiation in one study of school-age children [32]. In recent years, data has been accumulating to suggest that insufficient sleep may increase risk of the metabolic syndrome. This data is reviewed below.

3. Sleep Duration and Obesity Risk

3.1. Insufficient Sleep and Obesity

The rate of obesity in the population has risen in parallel with the rate of sleep deprivation. Numerous epidemiological cross-sectional and longitudinal studies in both adults and children have examined the question of whether sleep duration and obesity risk are associated. Many though not all studies have found that short sleep duration associates with increased risk of generalized or central obesity [33–36]. Several meta-analyses of adult and pediatric studies examining the epidemiology of sleep duration as associated with adiposity risk have found that short sleep duration (generally defined as less than 10 hours in children and less than 5 h in adults) increases odds of obesity [37,38]. Analysis of 13,742 adults participating in the 2005–2010 National Health and Nutrition Examination Survey (NHANES) study, in which those sleeping ≤6 h, ≥10 h and between 7–9 h each night were categorized as having short, long and average sleep duration respectively, similarly found that sleep duration was inversely linearly associated with BMI and with waist circumference; of note, these associations were strongest in young and early middle age adults ages 20–39 years [39]. Another study of over 16,000 adults participating in the NHANES 2007–2012 found an inverse linear association between sleep duration and obesity, controlling for number of prescription medications participants were taking. Logistic regression analyses found that each hour of additional sleep restriction (i.e. each hour by which participants reported sleeping less) was associated with a 10% increased odds of obesity [40]. A recent meta-analysis by Miller and colleagues examined the relationship between sleep duration and longitudinal obesity risk in studies in which participants were followed for at least one year [41]. In this comprehensive review, the authors found that short sleep duration was associated with increased risk of developing overweight or obesity over time in infancy (relative risk [RR] 1.40, 95% confidence interval [CI] 1.19–1.65), early childhood (RR 1.57, 95% CI 1.40–1.76), middle childhood (RR 2.23, 95% CI 2.18–2.27) and adolescence (RR 1.30, 95% CI 1.11–1.53). Thus, insufficient sleep predisposed to excess weight gain in every age group studied, although the degree of the association differed, peaking in mid-childhood and declining somewhat thereafter.

Of note, although the majority of studies have found an association between sleep duration and obesity risk, this is not universally the case in the literature – at least one study found no association or a very weak association between insufficient sleep and obesity [42]. One possible explanation for this discrepancy is that many studies utilize self-reported sleep duration data, which is often inaccurate, frequently leading to a significant over-estimation of sleep duration. Nonetheless, the preponderance of data suggests that insufficient sleep is a risk factor for obesity in both children and adults.

3.2. The Relationship Between Sleep Duration and Obesity in Adults may not be Linear

In the above section, we highlighted data suggesting the existence of an independent negative association between sleep duration and risk of obesity, suggesting that the relationship may be of an inverse linear nature (i.e. that lower sleep duration associates with greater obesity risk). However, several adult studies have found that the association between sleep duration and adiposity in a is U-shaped rather than linear – i.e. that there is also an increased risk of obesity in those whose sleep duration is excessively long. A subset of the Wisconsin Sleep cohort study, which examined 1024 adults, found that those sleeping an average of 7.7 h/night had the lowest BMI [43]. Similarly, a longitudinal cohort study found that over a 6-year follow-up period, short and long sleepers (≤6 and ≥9 h respectively) accumulated more visceral adipose tissue (VAT, as assessed by computerized tomography, or CT scan) than those sleeping between 7–8 h. Interestingly, those whose sleep duration increased from baseline to follow in this study, going from sleeping ≤6 h to sleeping 7–8 h, accumulated less VAT over the follow-up period than did the short sleepers who did not change their sleep duration. This data suggests that in adults, the association between insufficient sleep and visceral adiposity may be causal; no such conclusion may be drawn about the association between excessive sleep duration and visceral adiposity risk in this study [35].

3.3. Sleep and Obesity Risk Across the Lifespan

In children, by contrast to adults, the majority of studies examining the relationship between sleep duration and obesity risk is linear as discussed above, although one study of Chinese children also found a U-shaped association between sleep and obesity risk [44]. The difference between the data in adults and children is likely one facet of a broader picture, which is that the association between sleep duration and adiposity in adults varies by age. A study of 332 African American and 775 Hispanic adults (ages 18–81) participating in the IRAS Family Study found that participants ages 18–40 years who slept ≤5 h and ≥8 h accumulated more VAT and sustained a greater increase in BMI compared with study participants sleeping 6–7.9 h (the reference population of "optimal sleepers"), However, no significant association was seen between sleep duration and risk of developing general or visceral adiposity over the study follow-up in adults older than 40 years [45]. Interestingly, a recent analysis of NHANES data of a large population ranging from children to adults also found that the association between sleep duration and obesity varies across the lifespan. The NHANES data found a generally linear relationship in childhood, where a greater degree of insufficient sleep conferred a greater risk of obesity (different from the study of Chinese children discussed above), while a more U-shaped relationship between sleep duration and obesity risk was seen in middle adulthood (with both extremes conferring increased obesity risk). Finally, in older adults, the relationship between sleep duration and obesity was rather inconsistent [46]. One possible explanation for the disparity in findings may relate to the differential sleep need between children and adults – children have greater sleep requirements than adults, and it may prove difficult to find a sufficient number of "long sleepers" in younger children (logistically, sleeping >13–14 h per day may be difficult to sustain on a long-term basis) to be able to examine a U-shaped relationship. At the other end of the age spectrum, in older adults, other risk factors for obesity may become more prominent, and the contribution of sleep duration may be diluted. Thus, the association between sleep and obesity risk appears to vary across the lifespan.

3.4. Other Factors Modulating the Associations Between Sleep Duration and Obesity Risk

Racial and ethnic background may modulate the relationship between sleep duration and adiposity risk. Several studies have found