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# Sleep disorders and the development of insulin resistance and obesity

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## Synopsis

Sleep, which comprises a third of the human lifespan, consists of two major states, non-rapid eye movement (NREM, stages N1–3) and rapid eye movement (REM). Sleep is a physiologic state of decreased metabolism and likely serves a reparative role, marked by increased glycogen stores and peptide synthesis. Normal sleep is characterized by reduced glucose turnover by the brain and other metabolically active tissues, particularly during NREM sleep. Circadian and sleep-related changes in glucose tolerance occur in normal subjects, but there are conflicting data regarding lipid metabolism during sleep. Sleep duration has decreased over the last several decades, and with this have come cross-sectional and longitudinal data suggesting a link between short sleep duration and the prevalence of type 2 diabetes. Forced decreased sleep duration in healthy individuals has also been linked to impaired glucose homeostasis. Moreover, short sleep duration has been suggested to lead to obesity, although this is less conclusive since psychological and social factors also considerably impact food intake. Obstructive sleep apnea (OSA) is a disorder of sleep characterized by diminished or abrogated airflow, which results in intermittent hypoxia and sleep fragmentation. Based on a large body of evidence, this disorder seems to be associated with impaired glucose tolerance. Obesity is a major risk factor for the development of OSA, but whether OSA leads to obesity is unclear. Thus, the quality and quantity of sleep may have a profound effect on obesity and type 2 diabetes, and therefore should be routinely assessed in endocrine clinic.

### Keywords

Obstructive sleep apnea; Metabolism; Diabetes; Sleep duration; Glucose homeostasis

## I. Metabolic Changes in Sleep

Sleep is a physiologic recurring state of reduced consciousness, absence of voluntary activity, and suspension of sensory activity. Approximately one-third of the human lifespan



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is spent asleep, yet its fundamental purpose remains a mystery (1). However, it has been recognized for decades that sleep is necessary for optimal cognitive, motor, and metabolic function (2;3). The drive to sleep is controlled by homeostatic regulation, whereby sleep propensity increases with time awake; and circadian regulation, where sleep propensity waxes and wanes according to the time of day (4).

According to a standardized scoring system by the American Academy of Sleep Medicine (5), adult sleep is divided into two electroencephalographic stages: non-rapid eye movement (NREM) and rapid-eye movement (REM) sleep. NREM sleep is further subdivided into progressively deeper sleep stages referred to as N1, N2, and N3 (or slow-wave) sleep. During sleep, sympathetic tone, blood pressure, heart rate, and metabolic rate decrease, with a more marked suppression of these parameters in NREM compared to REM stages (6). In fact, REM is often described as “active” sleep since neural activity during REM bears a resemblance to wakefulness. Respiratory, hemodynamic, and metabolic changes are also more erratic during REM sleep. A typical sleep period in adults consists mostly of NREM sleep with REM periods occurring at 60 to 90 minute intervals. Slow-wave sleep usually occurs in the first few hours of sleep, while periods of REM lengthen towards the latter hours of sleep.

One of the functions ascribed to sleep is that of energy conservation and cellular repair. Sleep induces a fall in core body temperature, and oxygen consumption decreases by approximately 10%. These changes were first described in the mid-20$^{th}$ century (7) and were reaffirmed by subsequent studies (8), some of which showed trends of progressively lower metabolic rate from REM to N3 sleep (9;10). Glycogen stores (11), ATP levels (12) and peptide synthesis (13) increase in the brain during mammalian sleep. Several hormonal changes that foster growth and repair also occur during NREM sleep. For example, growth hormone (GH) is secreted in the first few hours of a usual sleep period, coinciding with slow wave sleep (14–16). This surge in GH induces peripheral lipolysis and insulin resistance, which may serve to spare the catabolism of protein and glucose stores (17). Conversely, most hypothalamic-pituitary-adrenocortical hormones are suppressed during NREM sleep (18).

In parallel with decreased metabolic demand, glucose turnover decreases during sleep. The changes in energy requirements during sleep are driven by a decrease in the high glucose demands of the brain (19–21). During NREM sleep, the uptake of glucose in the brain falls progressively, while hepatic glucose output decreases, commensurate with reductions in cerebral blood flow (22;23). Other metabolically active tissues such as skeletal muscle exhibit reduced blood flow and glucose uptake (24;25). The underlying mechanisms involved in lowered glucose turnover during sleep are not known. Patterns of insulin, cortisol, and glucagon secretion make these hormones unlikely mediators (26). Substrate availability does not limit brain metabolism, since glucose levels are usually unchanged during sleep (22;26).

Increases in glucose during sleep have been reported, but in the setting of specialized research or clinical conditions. Frank et al. infused glucose continuously in volunteers as they slept, either at night or during the day. This protocol revealed a rise in evening glucose and a superimposed glucose elevation during sleep, regardless of the time of day that sleep occurred (27). Thus, circadian and sleep-related changes in glucose tolerance occur in normal subjects. This physiologic glucose intolerance may play a role in the “dawn phenomenon” which describes hyperglycemia in the early morning in diabetic subjects (28). This phenomenon was also later reported to a lesser degree in non-diabetics (29). The pathogenesis of the dawn phenomenon is not known, but it is associated with increased catecholamines (29;30) and GH (31–33), both of which induce insulin resistance.

Lipid metabolism during sleep has received comparatively less scrutiny. Glycerol and free fatty acids (FFA) decreased progressively during sleep in one study (26), and authors speculated that reduced adipose tissue lipolysis may signal a reduction in hepatic gluconeogenesis. However, another study showed that lipid turnover decreases during early sleep, then subsequently rises in a GH-dependent manner (34). Discrepancies between these studies may relate to the extent and distribution of slow wave sleep, when GH is primarily secreted. In fact, a "rebound" in slow wave sleep that occurs after sleep deprivation is accompanied by significant elevations of GH, plasma glycerol and FFA (35).

Circadian rhythms, independent of sleep, also affect hormone profiles and metabolism. For example, cortisol levels peak early in the morning, regardless of sleep-wake state (36;37). Ghrelin, a peptide synthesized in multiple tissues that stimulates appetite, is secreted in a pulsatile fashion in anticipation of daily meals (25). However, ghrelin is also secreted in early sleep, suggesting a correlation with GH (38). Closer analysis of the interacting influences of sleep and circadian rhythm require protocols that disrupt the timing of cues that ordinarily serve to delineate a 24-hour day. Scheer et al. subjected volunteers to a week of 28-hour "days" to parse the effects of sleep and circadian rhythm on glucose metabolism. This study showed that, independent of the time of day, glucose and insulin increased following meals, and both decreased during sleep. Mild diurnal fluctuations in glucose also occurred, without changes in insulin (39). More striking, they found that circadian misalignment caused significant insulin resistance and elevations of blood pressure (40). In the sections that follow, we will examine how altered quantity, timing, or quality of sleep can affect glucose metabolism and obesity.

### Key points

- Sleep, particularly NREM sleep, is a physiologic state of decreased global metabolism which likely serves a reparative role.
- Normal NREM sleep is characterized by decreased glucose turnover, but there are conflicting data regarding lipid metabolism during sleep.
- Brain metabolism in REM sleep is similar to wakefulness.

## II. The Metabolic Effects of Sleep Duration

Today's "around the clock" society, characterized by demands for high work performance, prolonged daily commutes, and leisure activity, has significantly compromised sleep duration. Self-reported sleep times have decreased from over 8 hours in the 1960s to approximately 6.5 hours in 2012. Up to 30% of middle-aged Americans sleep less than six hours a night (41–46). Similar results were reported in other countries (47;48) and were confirmed in population-based cohorts where sleep duration was objectively measured (49;50). Sleep duration is also compromised by sleep disorders such as insomnia and obstructive sleep apnea. Whether it is voluntarily or involuntarily compromised, sleep loss has significant health consequences. These consequences range from impaired cognitive function (51;52) to increased all-cause morbidity and mortality (53–56). Derangements in sleep also affect glucose homeostasis and appetite control. Impaired sleep thus might contribute to the rising prevalence of type 2 diabetes (T2DM) and obesity in modern society. In the following section we will examine evidence linking short sleep duration to decreased glucose tolerance, insulin sensitivity, and insulin secretion. Of note, excessive sleep has also been associated with metabolic dysfunction (57;58); however, this association has not been adequately explored, and may be confounded by medical comorbidities (e.g. sleep apnea, depression) that can lengthen sleep time.

Cross-sectional studies suggest that short sleep duration is associated with an increased prevalence of T2DM or impaired glucose homeostasis. Data from large cohorts (Sleep Heart Health Study, Finnish Type 2 Diabetes Study, Quebec Family study, Behavioral Risk Factor Surveillance System, National Health Interview Study, and Isfahan Healthy Heart Program) have demonstrated that middle-aged to elderly subjects with self-reported short sleep duration are approximately twice as likely to be diagnosed with T2DM, and are at higher risk for impaired glucose tolerance. These results were independent of common T2DM risk factors in all studies (58–62) but one (63). Similar associations between short sleep and T2DM have been observed in hypertension clinic patients (64), young subjects with a family history of T2DM (65), obese adolescents (66) and pregnant women (67;68). Interestingly, the association may be statistically stronger in women than men (59;60). However, a smaller study conducted in middle-aged adults observed no association between sleep duration and diabetes (69). Self-perceived insufficient, poor or short sleep is also associated with pre-diabetic metabolic impairments such as elevated glucose and insulin levels, HBA1c or whole-body insulin resistance (61;67;69–77). Moreover, inadequate sleep has been shown to worsen glucose control in patients with preexisting T2DM (78;79). Despite various definitions of short sleep time among cross-sectional studies, outcomes of these studies are rather uniform, suggesting a significant association between short sleep duration and worsened glucose homeostasis. However, cross-sectional studies cannot establish causality. In fact, it has been reported that T2DM negatively impacts sleep architecture, making an inverse or bi-directional relationship between sleep and glucose regulation plausible (80–82).

Stronger evidence for a causal link between short sleep duration and diabetes is provided by prospective studies following diabetes-free individuals with various sleep durations over time. Twelve published studies have been conducted in the USA, Japan, Germany, Sweden, and South Korea, investigating 661 to 70,026 adult subjects for incident diabetes, over a 4–32 year follow-up period (83–94). All of these studies except the two most recent (93;94) were included in a meta-analysis of 90,623 subjects (57), which showed an increased relative risk of developing diabetes in subjects with short (RR = 1.28) as well as long sleep duration (RR = 1.48), compared to subjects with normal sleep duration (typically 7–8 hours), after adjusting for known confounding variables. Similarly, more recent studies confirmed short sleep as a risk factor for newly developed diabetes (79;93); however, this association became insignificant in one study after adjusting for multiple confounding variables (93). Limitations of these prospective studies include differing definitions of short sleep duration, reliance upon self-reported data, and the potential for residual confounding bias. Nonetheless, prospective and cross-sectional studies provide strong circumstantial evidence for the independent role of short sleep in the development of T2DM.

Experiments in human volunteers demonstrate how short-term changes in sleep duration can directly impact glucose homeostasis. After total sleep deprivation lasting from 24 hours to five days, studies report decreased insulin sensitivity (95–97) and impaired fasting or postprandial glucose levels (98–102). Additionally, sleep deprivation reduced postprandial insulin secretion (98), suggesting impaired pancreatic β-cell function. However, not all parameters of glucose metabolism were affected equally across studies and some authors did not find impairments in glucose homeostasis after total sleep deprivation (103), probably due to methodological differences and inter-individual variability. Still, no study to date has reported *improved* glucose metabolism after sleep loss. Some studies have restricted sleep to 4–5 hours/night, more closely modeling the sleep habits of today's society. Although a few studies have not observed impairments in glucose metabolism (104;105), the majority of studies show that glucose tolerance and/or insulin sensitivity are substantially impaired when sleep is restricted for a few days to several weeks in a laboratory or in the home environment (106–113). The metabolic phenotype induced by partial sleep deprivation is

characterized by features typically observed in T2DM, such as diminished muscle glucose uptake, enhanced hepatic glucose output and inadequate glucose-induced insulin secretion (106;108;109;114).

Mechanisms inducing impairments in insulin sensitivity and glucose metabolism during acute sleep deprivation are complex and poorly understood. The suggested endocrine and molecular mediators are typically supported by limited and often indirect evidence. For example, sleep deprivation increases circulating levels of cortisol (elevated evening cortisol and 24h profile) (102;106–108;115–117) and induces sympathetic activation (107) accompanied by elevated catecholamine levels (111). However, metabolic impairments were also reported in studies where cortisol or catecholamine levels remained unchanged (108–110;114). Moreover, sleep restriction was reported to reduce TSH and testosterone levels (107;118), disrupt the pattern of GH secretion (119), and elevate levels of pro-inflammatory cytokines (120). These complex endocrine changes might contribute to impaired insulin signaling in peripheral tissues. In adipocytes, changes in production of circulating adipokines occurred after short sleep duration (97;121;122). Though mechanisms are not fully understood, metabolic impairments induced by experimental sleep deprivation are reversible after sleep recovery in young and older individuals (109).

Sleep loss also affects appetite and food intake, thereby promoting obesity. Following partial sleep deprivation, subjects increase caloric intake by approximately 20%, (104;123–126) with a preference for foods rich in carbohydrates and fat (124;126–130). Additionally, a meta-analysis of several studies confirmed that short sleep increases appetite (131). Among many factors that regulate food intake (132), leptin (which suppresses appetite) and ghrelin (which stimulates appetite) have been investigated extensively under conditions of sleep restriction. Considering the numerous interacting factors that affect food intake, it is not surprising that results are mixed. Decreased leptin and increased ghrelin levels were observed in some studies following sleep deprivation (107;127;133–136) and in some cross-sectional studies (137;138), but opposite results or no changes have also been reported elsewhere (102;104;112;117;125;135;139;140). Although methodological differences might be responsible for inconsistent results, it is also possible that other mechanisms, such as decreased levels of satiety promoting peptide YY (141), might contribute to increased food intake. If these appetite-stimulating effects of acute sleep loss are extrapolated to chronic sleep loss, one might expect obesity to develop in those with reduced sleep time. Indeed, cross-sectional and prospective studies have linked short sleep with weight gain and abdominal fat accumulation (142;143). Interestingly, short sleep was associated with lower fat loss during caloric restriction in overweight subjects (135). Some mechanistic studies of sleep loss and energy regulation have been attempted in animals. In rodents, sleep deprivation appears to lead to weight loss and energy catabolism, culminating in death. However, dramatic metabolic differences between species and stressful sleep deprivation protocols have limited the clinical applicability of these findings (144).

There is evidence that the timing of sleep, in addition to the duration, may be a critical factor for metabolic health. Approximately 20% of workers in the U.S. perform their jobs under flexible or shift schedules (145;146) which misaligns sleep timing with circadian rhythms. Shift work induces profound and sustained misalignment between circadian and homeostatic or behavioral rhythms (39;147;148). As previously noted, an acute circadian misalignment is associated with impaired glucose tolerance and pancreatic β-cell dysfunction, leading to elevated postprandial glucose excursions (39), independent of sleep duration. Furthermore, decreased leptin levels and an inverted cortisol profile across sleep and wake might further deteriorate glucose regulation and food intake. Thus, adequate and properly timed sleep may be important for normal glucose and weight regulation.

### Key points

- Pressures of modern society have resulted in decreased sleep duration over the past several decades.
- Cross-sectional studies suggest a link between short sleep duration and the prevalence of T2DM. These results are echoed by longitudinal studies which have even described a worsening of preexisting glucose intolerance.
- Short-term studies in healthy volunteers also demonstrate a variety of measures of impaired glucose homeostasis with short sleep time.
- Decreased sleep duration is associated with the development of obesity, though the mechanisms which underlie this are not clear.

## III. Effects of Obstructive Sleep Apnea on Insulin Resistance and Obesity

One sleep disorder with a potential impact on metabolic health is obstructive sleep apnea (OSA). OSA is a common sleep disorder with an estimated prevalence of 4–5% in the general population. It is about twice as common in men as women (149). OSA is characterized by repeated collapse of the upper airway during sleep, causing intermittent oxygen desaturations and arousals from sleep. During sleep, a patient or bed partner may recall snoring, gasping, or witnessed pauses in breathing. While awake, the patient may complain of excessive daytime sleepiness, fatigue, or morning headaches. A patient may also describe poor workplace performance or impaired vigilance during driving or other monotonous activity. When OSA is suspected, a polysomnogram (PSG) should be performed, a test which monitors a patient's sleep architecture, breathing patterns, and gas exchange during sleep. A diagnosis of OSA is made by an examination of airflow and breathing effort during sleep. Obstructive *apneas* are noted when oro-nasal airflow ceases for over 10 seconds despite continued breathing effort. Obstructive *hypopneas* are noted when airflow decreases significantly (but does not completely cease), leading to a fall in oxygen level or an arousal from sleep. The combined rate of apneas and hypopneas per hour, or the apnea-hypopnea index (AHI), is used to classify OSA severity. An AHI of 5–15, 15–30, or >30 events/hr describes mild, moderate, or severe OSA, respectively. The first-line treatment for OSA is a nasal mask which delivers continuous positive airway pressure (CPAP), thereby splinting the airway open. This often results in much more restful sleep, markedly reduced daytime symptoms, and improved gas exchange. Besides its more obvious impact on quality of life (150;151), OSA is associated with significant long-term health consequences. Sleep apnea is a risk factor for cardiovascular disease (152;153), and more recently an association has also been shown between OSA and a variety of metabolic disorders including hypertension, dyslipidemia, non-alcoholic fatty liver disease, glucose intolerance, and T2DM. In this section, we will briefly examine the evidence supporting links between OSA and insulin resistance and obesity.

Theoretically, OSA is a plausible cause of insulin resistance and T2DM, since it can induce sleep loss and hypoxia, each of which can impact glucose metabolism. The nature of sleep loss in OSA is best described as "sleep fragmentation," whereby deeper stages of sleep are replaced by less restful, lighter stages of sleep. When healthy volunteers are frequently awakened from sleep with acoustic and mechanical stimulation, they exhibit decreased morning insulin sensitivity, and increased morning cortisol levels and sympathetic activity (154). Tasali and colleagues showed qualitatively similar results when slow-wave sleep was specifically interrupted, and that the effect was "dose dependent,"—that is, the magnitude of the disruption correlated with the magnitude of the blunting of insulin sensitivity (155). Acute hypoxia also causes glucose intolerance (156–159), and one study showed that intermittent hypoxia in healthy volunteers decreased insulin sensitivity and increased sympathetic tone (160). Mouse models of OSA which involve exposures to intermittent

hypoxia have further implicated reactive oxygen species (161), increased sympathetic tone (161;162), inflammation (163), and pancreatic beta cell apoptosis (164;165) as possible causes of glucose intolerance and impaired insulin secretion. Additionally, intermittent hypoxia induced arousals in mice (166), which demonstrates the interconnectedness between the two defining characteristics of OSA.

Biological plausibility itself is insufficient proof that sleep apnea *causes* worsened insulin resistance, however, so we must examine the clinical evidence as well. Cross-sectional studies have provided some of the support for an association between the two. In diabetics, the average prevalence of OSA has been reported at 71% (167) and as high as 86% among obese diabetics in one recent study, with most having moderate to severe OSA (168). This suggests that considerably more diabetic patients have OSA than are diagnosed. Twenty years ago, Levinson et al. showed that men with OSA had twofold the expected prevalence of impaired glucose tolerance compared with published data from a control population (169). Subsequent studies attempted to account for the confounding influence of obesity, which is an obvious shared risk factor for OSA and T2DM. Ip and colleagues showed that OSA was associated with a higher degree of insulin resistance as measured by HOMA-IR, even after correction for body mass index (BMI) (170). Similar results were shown in another study that examined oral glucose tolerance among apneics after adjusting for BMI and body fat, and hypoxia appeared to drive the association between OSA and impaired glucose tolerance (171). McArdle showed that men with OSA had a significantly higher HOMA-IR when compared with controls matched for age, BMI, and smoking status (172). Numerous other cross-sectional studies support a robust association between OSA and insulin resistance (167;173).

Longitudinal studies have the potential to provide stronger evidence for a causal association between OSA and T2DM. Reichmuth et al. examined the baseline prevalence and incidence of T2DM in a cohort of 1387 patients from Wisconsin, some with OSA. OSA was associated with a higher prevalence of T2DM, but the incidence of T2DM over four years was not increased by OSA when adjusted for waist girth (174). A Swedish study found that OSA (defined only by nocturnal intermittent hypoxia) was associated with increased incidence of T2DM over 16 years in women, but not men, although this increase was not statistically significant (175). However, the Busselton Health Study found that subjects with moderate to severe OSA were more likely to develop T2DM over 4 years after adjusting for age, gender, waist circumference, and BMI, but only 9 of the subjects developed T2DM during the study, resulting in wide confidence intervals (176). A larger study of Veterans Affairs patients identified OSA as an independent risk factor for incident diabetes over 2.7 years, and CPAP appeared to attenuate this risk in those with more severe OSA (177). A recent longitudinal study of 141 men over 11 years showed a four-fold increased risk of T2DM in those with nocturnal hypoxia (178). Collectively, these studies point to an impact of OSA on glucose metabolism but they are limited by sample size, and difficulties in accounting for effects of CPAP treatment during the trail periods.

Does CPAP treatment improve glucose metabolism in OSA? This finding would provide the strongest degree of evidence for a causal link between OSA and T2DM. To date, nine randomized, controlled trials have examined the effect of CPAP (compared with sham CPAP) on glucose metabolism (167). The studies ranged in duration from one week to three months and examined various markers of insulin sensitivity including fasting glucose, HOMA, HbA1c, and hyperinsulinemic euglycemic clamp testing. Four studies showed a beneficial effect of therapeutic CPAP, while the other five did not. The largest study randomized 86 patients with OSA to three months of CPAP or sham, and then crossed patients over to the other treatment group after a 1-month washout period. Several components of the metabolic syndrome were improved after CPAP, including a significant

but modest absolute reduction in HbA1c (0.2%). However, CPAP did not alter fasting glucose, insulin or HOMA (179). It appears that most studies showing a benefit of CPAP were characterized by subjects with more severe OSA (180), or who were more adherent to CPAP (181). Hence, although some studies show improvements in markers of insulin sensitivity with CPAP use, no firm conclusions can be drawn from the available evidence. Moreover, even if CPAP attenuates diabetes risks, poor adherence to this therapy remains a significant clinical problem.

Much clearer is the relationship between obesity and the development of OSA. Approximately 70% of patients with OSA are obese (182), while 60% of obese patients have OSA; this figure is nearly 100% of the morbidly obese (BMI ≥40) (183). Young et al. examined a cohort of 600 patients who underwent PSG and determined that a single standard deviation higher of any measure of body habitus was associated with a threefold increased risk of having an AHI ≥5 (184). Moreover, weight loss has been shown both to decrease the AHI in patients with OSA (185), and to decrease the collapsibility of the upper airway (186). However, one study found that some patients who lose weight and subsequently achieve a cure of their sleep apnea may later develop an increased AHI on repeat PSG after long-term follow-up, despite maintaining their weight loss (187). This suggests that while obesity clearly contributes to the development of OSA, it is indeed a complex, multifactorial illness.

Because of mounting evidence linking OSA to the development of other facets of the metabolic syndrome, there has also been speculation that OSA itself can cause obesity. However, the data supporting this reciprocal relationship are scant. A small study by Loube et al. showed that patients who were compliant with CPAP use (>4 hours per night) were more likely than noncompliant patients to have significant weight loss (10 pounds or greater) on follow-up after six months; in fact, none of the 11 patients who were nonadherent to CPAP achieved this degree of weight loss (188). However, other studies have not replicated this finding, and at least one study has demonstrated no weight loss, and some weight gain in a subset of patients compliant with CPAP (189). Intriguingly, there is evidence that CPAP may reduce visceral body fat even if overall weight is not significantly altered (190). Therefore, no clear conclusion can be drawn about the possibility of OSA causing obesity based on the currently available evidence.

## Key points

- A growing body of evidence, including data from cross-sectional and longitudinal studies, links OSA with the development of insulin resistance.
- The effect of CPAP on insulin resistance and type 2 diabetes has not been consistent in several randomized clinical trials; large randomized clinical trials should be conducted to better assess this effect.
- Though a multifactorial illness, obesity clearly is a major risk factor for the development of OSA. The effect of OSA on obesity is not well-defined.

In conclusion, sleep is a necessary human activity, and although the exact functions are unclear, it is associated with a state of decreased metabolism and energy conservation. Impairments in the timing and particularly the duration of sleep seem to be associated with worsened glucose tolerance and perhaps the development of T2DM. Sleep disorders such as OSA may predispose to the development and the progression of T2DM. Because of disturbing worldwide trends in sleep habits, obesity, and T2DM, it will be critical for clinicians and researchers to recognize and address the potential impact of sleep disorders on metabolic health.

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**KEY POINTS**

- Sleep is a physiologic state of decreased metabolism and likely serves a reparative role, marked by increased glycogen stores and peptide synthesis.
- Sleep duration has decreased over the last several decades, and with this have come cross-sectional and longitudinal data suggesting a link between short sleep duration and the prevalence of type 2 diabetes.
- Forced decreased sleep duration in healthy individuals has also been linked to impaired glucose homeostasis.
- Obstructive sleep apnea (OSA) is a disorder of sleep characterized by diminished or abrogated airflow, which results in intermittent hypoxia and sleep fragmentation. Based on a large body of evidence, this disorder seems to be associated with impaired glucose tolerance.