THEORETICAL REVIEW

Association between long sleep duration and increased risk of obesity and type 2 diabetes: A review of possible mechanisms

Xiao Tan*, Colin D. Chapman, Jonathan Cedernaes, Christian Benedict**

Department of Neuroscience, Uppsala University, SE-751 24 Uppsala, Sweden

ARTICLE INFO

Article history:
Received 26 April 2017
Received in revised form 7 November 2017
Accepted 13 November 2017
Available online 20 November 2017

SUMMARY

For the last two decades research has revealed an alarming association between short sleep duration and metabolic disorders. In tandem, the hormonal, behavioral, and genetic mechanisms underlying this relationship have been extensively investigated and reviewed. However, emerging evidence is revealing that excessive sleep duration has remarkably similar deleterious effects. Unfortunately, to date there has been little attention to what drives this connection. This narrative review therefore aims to summarize existing epidemiological findings, experimental work, and most importantly putative molecular and behavioral mechanisms connecting excessive sleep duration with both obesity and type 2 diabetes mellitus. It will also address recent findings suggesting a worrisome bidirectional effect such that metabolic disorders create a positive feedback loop which further perpetuates excessive sleep.

© 2017 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Nearly half of all adults sleep either too little (commonly defined as ≤6 h sleep per day; up to 33% in the general population) or too much (commonly defined as ≥9 h sleep per day; up to 18% in the general population) [1–5]. This is alarming, as both too little and too long sleep have been associated with an increased risk of obesity and type 2 diabetes mellitus (T2DM) [6,7]. For example, in a Swedish cohort study involving ~5000 women (aged 38.1%, respectively), as compared with reports of habitual normal sleep duration (defined as 6–9 h) and habitual long sleep (defined as ≥9 h), sleep duration (defined as ≥9 h) correlated with a higher prevalence of obesity (31.3% and 38.1%, respectively), as compared with reports of habitual normal sleep duration (defined as 6–9 h, 8.9%) [6]. Moreover, by utilizing self-reported sleep duration data from nearly half a million adult participants (of ages covering the entire adult lifespan) with follow-up periods ranging from 2.5 to 16 y, a recent meta-analysis of prospective studies found the relative risk for T2DM to be increased by about 9% for each 1-h decrement of average sleep duration among individuals who slept less than 7 h per day, and 14% for each 1-h increment of sleep duration among individuals with long sleep duration (defined as >8 h) [7]. Collectively, these studies appear to indicate a U-shaped association between sleep duration and weight gain and T2DM.

Mounting experimental evidence points to a causative role of short sleep duration in obesity and T2DM. A recent study collecting fat tissue biopsies from seven healthy young adults following 4 d of sleep restriction (i.e., 4.5 h in bed) has for instance found an insulin-resistant state in human adipocytes [8]. Moreover, it has been demonstrated that both acute total sleep loss and short-term sleep restriction (i.e., 4 vs. 9 h in bed for six nights) increase brain activation to food stimuli in young adults, including brain areas involved in the regulation of the drive to eat (e.g., prefrontal cortex and anterior cingulate cortex) [9–11]. While behavioral, hormonal and molecular mechanisms underlying the association between short sleep and the risk of obesity and T2DM have been extensively reviewed elsewhere [12–17], there is no comprehensive review of what is driving the association between long sleep duration and the risk of obesity and T2DM in humans. With this in mind, the objective of the present review is to frame recent epidemiological and experimental findings into a comprehensive overview of candidate mechanisms through which long sleep duration drives obesity and T2DM development, and vice versa.

Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide 1; IL-6, interleukin-6; NHANES, US National health and nutrition examination survey; OSA, obstructive sleep apnea; PSQI, Pittsburgh sleep quality index; REM, rapid-eye movement; SWS, slow-wave sleep; T2DM, type 2 diabetes mellitus; TNFα, tumor necrosis factor alpha.

* Corresponding author. Department of Neuroscience, Uppsala University, Husargatan 3, Box 593, 751 24 Uppsala, Sweden.
** Corresponding author. Department of Neuroscience, Uppsala University, Husargatan 3, Box 593, 751 24 Uppsala, Sweden.
E-mail addresses: xiao.tan@neuro.uu.se (X. Tan), christian.benedict@neuro.uu.se (C. Benedict).

https://doi.org/10.1016/j.smrv.2017.11.001
1087-0782/© 2017 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
State of the epidemiological evidence

Long sleep duration and risk of obesity

Cross-sectional studies have reported a higher body mass index (BMI) and prevalence of obesity (BMI ≥30 kg/m²) among adults reporting habitually excessive sleep duration (typically defined as ≥9 h) [14,18,19]. These observations based on self-reported sleep duration have been confirmed by further studies that objectively measured sleep duration and body weight. For instance, in a Dutch study involving about 1000 community-dwelling elderly people (age range: 57–97 y), long sleep duration (defined as ≥8 h) measured by actigraphy over multiple consecutive nights increased the relative risk of obesity by about 193%, compared with participants who slept 7–8 h [20]. These cross-sectional data comport with results from longitudinal studies. For example, in a sample of 226 adults aged 21–64 y from the Canadian Quebec Family Study in which sleep duration was estimated by a questionnaire, long-duration sleepers (defined as 9–10 h per day) gained 1.58 kg body fat more than did average-duration sleepers (defined as 7–8 h per day) over a 6 y stretch [21]. While this may not seem extraordinarily much, reports of long sleep duration in this study were linked with a 21% increased risk of developing obesity (compared to the risk of normal-duration sleepers). Similar findings in which sleep duration derived from questionnaires have been reported for Swedish women who were followed over 10 y [6].

Interestingly, there are also population-based cross-sectional and longitudinal studies in which no association was found between long sleep duration and the risk of weight gain or obesity [22–25]. For instance, in a cohort of 83,377 US men and women aged 51–72 y at baseline, followed up with an average of 7.5 y, no association was observed between reporting ≥9 h sleep/night and obesity [25]. However, there are essential methodological differences between these studies that may contribute to some of the controversial findings in the field. One explanation could relate to whether sleep duration was estimated based on a retrospective recall method (e.g., by questionnaires) [18,19,21,23–25] or multiple-night recordings (e.g., by sleep diary) [14]. Inclusion of subjective and objective measures of sleep duration may also explain why some researchers consider current evidence base to be not strong enough to conclude that sleep duration is a risk factor for obesity [26]. Some of the inconsistency of results in the literature could also be explained by the fact that in some studies, sleep duration was related to all days, i.e., sleep on weekend and workdays was not discriminated [19,21,23–25], whereas in other studies duration was only based on workdays [18,22]. This is consequential as sleep behavior tends to show dramatic differences between workdays and weekends [27]. It must also be noted that in many studies nocturnal sleep duration was considered a primary variable of interest [14,18,23,24], whereas other studies also included daytime naps in the estimation of 24-h sleep duration [19,21,25]. Another source of inconsistency between studies emerges from which cut-offs were used to define long sleep duration (e.g., ≥8 h sleep in e.g., [20] vs. ≥9 h sleep in e.g., [25]). Finally, variation in confounding factors considered for the analyses, such as age, education level, physical activity, and smoking may limit the generalizability of results from epidemiological studies investigating the association between sleep duration and metabolic traits.

Long sleep duration and risk of T2DM

Strong evidence points to an association between excessive sleep and the risk of developing T2DM. A cross-sectional study involving 740 adults aged 21–64 y showed that in comparison with adults who reportedly slept 7–8 h of sleep, those who reported sleeping 9–10 h had an odds ratio of 1.58 for having impaired glucose tolerance or T2DM, after adjusting for various confounders such as age, physical activity level, and waist circumference [28]. Through longitudinal studies, the association between reports of habitual long sleep duration and future incidence of T2DM was first reported among women and men in 2003 and 2006, respectively [29,30]. Since then, increasing prospective studies have found consistent results across a variety of populations. Two meta-analyses (including 482,502 and 107,756 adults, respectively) covering the entire adult lifespan demonstrated a clear longitudinal relationship between reports of long sleep duration at baseline (defined as ≥8 h) and future incidence of T2DM [7,31]. Extending these findings, in an observational study involving 59,031 women aged 55–83 y at baseline, a habitual increase of average daily self-reported sleep duration by ≥2 h has been shown to increase incidence of T2DM by about 15% over a period of ~14 y [32].

Possible mechanisms linking long sleep duration with obesity and T2DM

As described in the subsequent sections, multiple pathways could mediate the association between long sleep duration and the risk of obesity and T2DM, and vice versa. A schematic representation of some of these candidate mechanisms is provided in Fig. 1.

Prolonged sleep duration due to impaired nocturnal sleep quality

Epidemiological data show that poor quality sleep, assessed by the Pittsburgh sleep quality index (PSQI), is associated with an increased risk of obesity and T2DM [33,34]. However, it does not speak to specific mechanisms, which requires some analysis and speculation. One possibility involves disrupted sleep patterns. Insomnia and obstructive sleep apnea (OSA) – constituting major sleep disorder categories – are manifested with impaired nocturnal sleep quality, including single or recurrent long-lasting wake episodes after sleep onset, frequent awakenings after sleep onset, light sleep, extended sleep onset, low sleep efficiency (typically defined as time asleep divided by time in bed), and excessive daytime sleepiness. Given that especially sleep loss (also known as slow-wave sleep, SWS or sleep stage N3) has been proposed to be restorative and also to reduce sleep pressure [35], light and fragmented sleep may not sufficiently reduce sleep pressure generated during daytime wakefulness, and could therefore result in prolonged habitual sleep duration.

Noteworthy, compared to sleepers who report normal sleep duration (i.e., between 7 and 8 h), long-duration sleepers more frequently use pharmaceutical sleep aids [3] – indicating problems to fall and stay asleep –, more often snore [36], have a higher risk to be diagnosed with moderate to severe OSA (apnea hypopnea index > 15 events/h) [37], and more frequently suffer from insomnia symptoms, such as increased sleep fragmentation, wake after sleep onset and sleep latency [38,39]. Finally, time in bed has been positively correlated with the abundance of light sleep (stages other than SWS) in insomnia patients [40]. Hence, it could be hypothesized that prolonged time in bed is an attempt of long-duration sleepers to cope with and compensate for poor sleep quality. In this context it must, however, be noted that there is no available evidence to suggest that traditional treatment for insomnia and OSA, such as cognitive behavioral therapy and continuous positive airway pressure, normalize sleep duration in long-duration sleepers. Moreover, a considerable portion of people with insomnia and OSA report habitual short sleep duration rather than long sleep duration, which would also argue against this hypothesis. There are, however, possible explanations for why most short-duration sleepers with insomnia and OSA might not show a compensatory increased time in bed. For instance, they may have early morning obligations such as school or work. By this theory long sleep duration patients who suffer

from OSA or insomnia would be less likely to have such obligations. Finally, it could be that compensatory increases in sleep duration are more likely to occur in those who chronically experience symptoms of insomnia and sleep-disordered breathing.

Given the possibility that long sleep duration is a result of poor quality sleep, an important question is how it promotes the development of obesity and T2DM. Studies have shown that light sleep (induced by subtle acoustic stimulation whenever SWS occurred without awakening subjects), fragmented sleep (using auditory and mechanical stimuli), and sleep-disordered breathing (in T2DM patients), without any change in total bedtime, all can impair insulin-mediated glucose disposal from the circulation\(^4\)\(^4\). Nocturnal increases in sympathetic nervous system activity, adrenocortical activity, and sleep apnea-related hypoxia (notably those occurring during rapid-eye movement, REM sleep) may thereby mediate the adverse effects of poor sleep quality on insulin sensitivity\(^4\)\(^2\)\(^4\). The effects of poor sleep quality on body weight control, however, is not so well-studied. To our best knowledge, there is only one published article involving twelve healthy young adult men showing that sleep fragmentation (not conducted in the context of long sleep duration), induced by wake-up calls occurring approximately every 90 min, lowered circulating concentrations of the satiety-enhancing gut hormone glucagon-like peptide 1 (GLP-1) and decreased fullness scores\(^4\). This and similar mechanisms may induce increased daytime and nighttime food intake and snacking in long-duration sleepers suffering from poor sleep quality, thus contributing to a positive energy balance and finally, weight gain.

The long sleep—sedentary behavior relationship

Sedentary lifestyle hallmarked by prolonged sitting or lie-down time while awake is often mentioned as a possible explanation for the association between long sleep duration and the risk of obesity and T2DM\(^7\)\(^2\)\(^1\). A recent population-based study among European adults (\(n = 6037;\) mean age of 52 y) showed that long sleepers (defined as >8 h per night) spent a higher proportion (3.2%) of their wake period in sedentary behaviors than normal sleepers (defined as 6–8 h per night; sleep duration was estimated by questionnaires)\(^4\). Moreover, as observed in two different cohort studies (including 7224 Finnish participants and 113,138 Chinese participants, respectively), adults with self-reported sleep duration \(<8\ h\ per\ day\)\(^5\) or \(\geq 10\ h\ per\ day\)\(^5\) appear to be less engaged in leisure time physical activity, such as regular exercise. Thus, a sedentary lifestyle combined with less moderate to vigorous physical activity may contribute to obesity and T2DM among long sleepers. One explanation why sedentary behaviors are found in long sleepers could be that this group suffers from tiredness and sleepiness more frequently\(^4\), which could be one of the primary causes of their inactive behaviors.

With these findings in mind, the question arises which mechanisms related to the sedentary lifestyle drive the association between long sleep duration and the risk of obesity and T2DM? Physical exercise has been shown to induce a spectrum of beneficial effects. This includes increased glucose effectiveness, namely the ability of glucose to stimulate its own disposal from the bloodstream and to suppress its own production independent of insulin\(^4\), improved peripheral tissue insulin sensitivity\(^4\), and better pancreatic \(\beta\)-cell insulin secretory function\(^5\). Physical exercise has also been shown to enhance the transcription of mitochondrial and glucose regulatory genes\(^5\), such as proliferator-activated receptor gamma coactivator 1-alpha which is known to facilitate glucose entry into skeletal muscle\(^5\). Finally, studies have demonstrated that myokines such as interleukin-6 (IL-6), which is found increased in blood upon acute exercise in humans, affect whole-body energy homeostasis\(^5\)\(^4\), and enhance systemic...
insulin-stimulated glucose disposal [55]. Specifically, at the peripheral level, IL-6 has been shown to increase the secretion of the satiety-promoting hormone GLP-1 from intestinal L cells [56]. Moreover, centrally acting IL-6, which is also released from the brain during prolonged exercise [57], appears to play a role in the regulation of appetite, energy expenditure, and body composition, possibly as a result of enhanced central nervous system action of the anorexigenic adipokine leptin [58]. The other candidate myokine named irisin, putatively having obesity-preventive property, is released into blood following exercise and causes an increase in energy expenditure in mice with no changes in movement or food intake [59]. Adding further evidence to the hypothesis that sedentary behavior contributes to the association between long sleep duration and obesity and T2DM, recent studies involving healthy young adults demonstrated that a few hours of uninterrupted sitting resulted in higher postprandial blood concentrations of glucose and insulin [60,61]. Collectively, these findings suggest that sedentary lifestyle, in addition to its main effect of reducing activity energy expenditure, may predispose long-duration sleepers to gain weight and develop T2DM through mechanisms at multiple peripheral and central nervous system sites.

**Dietary choices and timing of consumption in long-duration sleepers**

There are several connections tying diet to long sleep duration and metabolic disorder. Questionnaire-based data from the US National health and nutrition examination survey (NHANES; n = 15,199; aged ≥20 y) have shown that long-sleepers (defined as ≥9 h), in comparison with normal sleepers (defined as 7–8 h), ate less dietary fiber [62]. This could represent a potential dietary mechanism through which long sleep duration increases the risk of metabolic pathologies, as prospective studies show a reduced risk of T2DM and weight gain with high fiber intake [63]. Moreover, in the same analysis long-duration sleepers consumed a lower proportion of 24-h energy intake from primary meals, thus receiving a higher proportion from snacks [62]. This is consistent with an earlier study (n = 28,000 women, aged 35–74 y) in which very long self-reported sleep duration (defined as ≥10 h) was associated with a greater proportion of snacks in relation to meals, and a reduced tendency for eating during conventional eating hours [64]. While the optimal meal pattern for weight maintenance and metabolic control is still under debate, some researchers propose that regular eating habits might facilitate weight balance, while sporadic snacking as well as consuming the major part of the energy intake at the end of the day seems to be unfavorable [65]. Finally, another study based on NHANES (n = 5,587, aged ≥18 y) found that long sleepers (defined as ≥9 h) exhibited greater alcohol consumption compared to those with more optimal sleep duration (defined as 7–8 h; both sleep duration categories relied on questionnaire data) [66]. Alcohol is a well-known risk factor for upper airway collapse, thereby favoring the occurrence of sleep apneas, which may not only compromise sleep quality but also lead to oxygen desaturation [67,68], both of which have been shown to increase the risk of obesity and T2DM [69].

**Link between long sleep duration and risk of obesity and T2DM as a consequence of phase incoherence**

Circadian clocks that regulate the circa 24-h expression of key metabolic genes are found in almost all somatic cells [70]. In order to keep peripheral clocks synchronized to the 24-h day, the photosensitive circadian pacemaker neurons found in the hypothalamic suprachiasmatic nuclei, together with other hypothalamic regions, utilize primary ambient light as Zeitgeber (timing cue). This is to regulate downstream oscillators in peripheral tissues by daily rhythmic neuronal activity and release of a variety of hormones, including but not limited to glucocorticoids and melatonin [71]. In combination with direct signals to cell-autonomous, tissuespecific circadian clocks, the activities of key metabolic pathways (e.g., glycolysis, tricarboxylic acid cycle) can be kept aligned with daily adjustments in behavioral (sleep/wake) and nutritional (fasting/feeding) states [72]. Importantly, the preferred phase of the organismal sleep-wake behavior (also called chronotype) can exhibit large differences due to inter-individual (e.g., genes or gender) and intra-individual factors (e.g., aging or seasonal fluctuations in ambient light) [73,74]. It is worth noting that persons with evening chronotype more frequently report long sleep duration than those with morning chronotype [75–77]. For instance, in about 100,000 participants from the UK biobank cohort, a positive association was found between later chronotype and sleep duration [77]. In support of these epidemiological findings, individual timing of factors such as sleepiness, nadir in core body temperature, production of cortisol, and dim-light onset of melatonin have all been shown to be phase-delayed in habitual long sleepers (defined as ≥9 h) compared to short sleepers (defined as ≤6 h) [78]. Collectively, this may suggest that long sleepers with evening chronotype have greater difficulties in realigning their endogenous circadian rhythms with the day-night rhythm imposed by the 24-h day and interlinked societal norms.

But how can having an evening chronotype increase the risk of long sleepers to develop obesity and T2DM? One mechanism could relate to cumulative exposure to daylight and evening artificial light (see also Fig. 2), which differentially strongly influence the activity and downstream hormonal output of the central master clock [79]. For instance, having a majority of the average daily light exposure at an earlier timepoint during the day — which would be expected to be highly prevalent among persons with morning preference — has been related to lower BMI [80]. This could be possibly as a result of phase coherence between endogenous (e.g., expression of clock-regulated energy metabolism-regulating genes in tissues) and behavioral rhythms (e.g., meal timing and physical activity). On the contrary, shifting the majority of the average daily light exposure toward evening hours may cause the energy metabolism to be out of sync with behavioral rhythms. This could be proposed to increase the risk for weight gain and impaired systemic glucose disposal. In support of this proposed association, it has been demonstrated that late timing of meals results in greater weight gain among healthy adults [81]. Contrarily, restricting food intake to a shorter period of time during the day reduces body weight [82].

Increased artificial light exposure in individuals with evening preference could represent an additional explanation for the association between long sleep duration and the risk of obesity and T2DM. Evening exposure to blue-enriched light (typically generated by light-emitting diode display devices or first-generation energy-saving lamps) has been demonstrated by some studies to delay circadian phase and sleep onset, possibly as a result of inhibiting the sleep-hormone melatonin [83,84]. Moreover, serum cortisol levels are significantly elevated by artificial light exposure at night [85]. Thus, impaired sleep quality and activation of stress hormones elicited by evening and night exposures to artificial light may lead individuals with late chronotype to sleep longer and be more vulnerable to metabolic perturbations. Furthermore, it has been demonstrated in mice that light exposure at night disrupts the timing of food intake and impairs glucose tolerance, leading to excess weight gain and disturbed glucose metabolism [86]. Collectively, interventions aiming to improve evening light hygiene and to increase light exposure in morning hours may help long sleepers with evening chronotype to reduce their risk of obesity and T2DM.
Long sleep duration as a consequence rather than cause of obesity and T2DM

Obesity and T2DM increase the risk of several comorbidities, including depression [87,88], hypertension [89,90], and low-grade inflammation [91], all of which have been shown, with varying degrees, to be associated with long sleep duration. Individuals with depression are frequently reported with prolonged sleep [3], possibly as a result of various sleep problems including difficulty falling asleep (sleep onset insomnia), difficulty staying asleep (sleep maintenance insomnia), and non-restorative sleep [92]. Questionnaire-based long sleep duration (defined as ≥9 h) has also been linked to an increased prevalence of hypertension (30% greater compared to reports of 7–8 h sleep per day) [93]. This association appears to be primarily driven by sleep-disordered breathing, since it has been estimated that nearly half of the individuals with hypertension are comorbid with OSA [94]. Finally, chronic low-grade inflammation hallmarked by increased blood concentrations of cytokines such as tumor necrosis factor alpha (TNFα) has been found in obese and T2DM patients, as well as in people with long sleep duration [95]. Noteworthy, TNFα has been shown to enhance sleep duration and sleepiness in different species including humans [96]. Altogether it could be speculated that long sleep duration may partially be driven by obesity and T2DM and their co-morbidities, rather than that its occurrence would precede these conditions. In this context, long sleep duration could be hypothesized to represent an endogenously driven mechanism to cope with obesity and T2DM. A recent study demonstrated that two nights of recovery sleep averaging nearly 10 h per night following four nights of sleep restriction in healthy men was sufficient to improve insulin sensitivity and restore their disposition index (a marker of diabetes risk) to the levels observed after normal sleep [97]. In another study involving healthy adults, it has further been shown that following sleep restriction, recovery sleep decreased nighttime post-dinner food intake and total food intake to the levels seen under normal sleep conditions [98]. Finally, the glymphatic system, which has been proposed to be a functional waste clearance pathway for the vertebrate central nervous system by clearing brain extracellular solutes especially during sleep [99,100], has been shown to be less effective in T2DM rats compared to non-T2DM rats [101]. If this also holds true for humans, long sleep duration in people with T2DM (and possibly obesity) could constitute a homeostatic mechanism attempting to compensate for the reduced efficacy of the glymphatic system to clear out neurotoxic and other waste substances that accumulate during wakefulness.

Conclusion

Long sleep duration is proposed to impair whole-body energy metabolism and thereby increase the risk of obesity and T2DM through multiple possible compounding mechanisms, including poor sleep quality, sedentary lifestyle, unhealthy dietary choices, and desynchrony between circadian and behavioral states. On the other hand, there is additional evidence suggesting that habitual long sleep duration — as a trait — could also partially arise due to comorbidities of obesity and T2DM, such as depression and hypertension, both of which have been shown to impair sleep quality. Thus, there appears to be a bidirectional relationship between habitual long sleep duration and obesity and T2DM, respectively. Notwithstanding the direction of the relation, our review clearly highlights that long sleepers suffer many similar metabolic consequences to short sleepers, and it would be dangerous to overlook this when developing public health strategies that aim to improve metabolic health in the general population. The association between long sleep duration and the risk of obesity and T2DM has

---

**Fig. 2.** Proposed mechanisms through which phase incoherence in long sleepers raise the risk for metabolic perturbations. Upper panel: In comparison with normal-duration sleepers (in this scheme defined as 7 h), the 24-h behavior of long-duration sleepers with evening chronotype are characterized by postponed in-bed and wake-up time points, reduced access to natural daylight, and extended exposure period to artificial light, especially during evening hours. Bottom panel: Restricted daylight exposure in long sleepers may lead to desynchrony between external (e.g., light) and internal (e.g., meals) Zeitgebers (timing cues), causing peripheral clocks to be out of sync with the master clock in the brain. Such conditions have been linked to both obesity and T2DM [66]. On the other hand, poor sleep and activation of stress hormones elicited by evening and/or night exposure to artificial light (e.g., due to the prolonged use of cell phones and ceiling lights) may make long sleepers more vulnerable to metabolic perturbations. In the long run, both pathways could raise the risk of obesity and T2DM in long-duration sleepers. **Abbreviations:** SCN, suprachiasmatic nucleus; T2DM, type 2 diabetes mellitus.
mainly been established by observational studies with a lack of objectively defined sleep. Thus, experiments manipulating sleep duration will help to further examine the role of long sleep duration in the development of obesity and T2DM.

### Practice points

Long sleep duration may be associated with an increased risk of obesity and type 2 diabetes mellitus (T2DM) through several mechanisms:

1. Observational studies suggest that long-duration sleepers more often complain about sleep apnea and insomnia symptoms, i.e., sleep disruptions that have previously been shown to tip the energy balance in favor of weight gain and reduce systemic insulin-induced glucose disposal.
2. Sedentary behavior and poor dietary choices are more prevalent in long-duration sleepers compared to normal sleepers. Exercise deprivation and unhealthy dietary choices have been associated with impaired insulin sensitivity and positive energy balance, which may predispose long-duration sleepers to gain weight and become diabetic in the long run.
3. Long sleep duration combined with habitual late sleep onset may lead to desynchrony between external and internal Zeitgebers (timing cues), causing peripheral clocks (e.g., in the adipose tissue and skeletal muscle) to be out of sync with the master clock in the brain. Such conditions have been linked to both obesity and T2DM.
4. Since studies have shown that short-term sleep extension can restore insulin metabolism and hunger control, sleep extension may represent an attempt of the body and the brain to slow the development of obesity and T2DM. In other words, some long sleepers may have acquired the need for long sleep duration during life because of their metabolic condition, i.e., the drive to sleep long may not be inherent.

### Research agenda

Future research should address the following questions with regards to long sleep and metabolic disorders:

1. At what point do the metabolic benefits of sleep duration extension start and where do they turn to be metabolically detrimental?
2. Do multifaceted lifestyle interventions, including dietary education and exercise programs, help long-duration sleepers in the prevention of obesity and T2DM?
3. Should timing of meals be adjusted to a metabolically more beneficial circadian phase in long sleepers to minimize risk of obesity and T2DM?
4. Could controlled light intervention (e.g., strong light stimuli after morning awakening) which has been shown to advance the phase of circadian rhythm help long sleepers who also exhibit evening chronotypes to align their endogenous metabolic activities with societally driven behavioral rhythms?

### Conflicts of interest

The authors have no conflicts of interest to report. This work was funded by the Novo Nordisk Foundation. The Foundation had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

### Acknowledgments

This work was funded by the Novo Nordisk Foundation (NNF14OC0009349); the Swedish Brain Foundation (FO2016-0092); and the Swedish Research Council (2015-03100). The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. We would also like to thank the anonymous academic peer reviewers who provided helpful and detailed comments on earlier drafts of this review manuscript. We apologize to the many researchers who have contributed to the field and who because of space constraints have not been cited herein.

### References


* The most important references are denoted by an asterisk.


Chaput JP, Després JP, Bouchard C, Tremblay A. Short sleep duration is associated with reduced leptin levels and increased adiposity: results from the Quebec family study. Obesity (Silver Spring) 2007;15:253–61.


