Inadequate sleep as a contributor to obesity and type 2 diabetes

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Abstract:

Epidemiological studies suggest that adults and children who are habitual short sleepers tend to have a higher body mass index, fat percentage and abdominal circumference when compared to average-duration sleepers. Reduced or disturbed sleep is also associated with certain predictors of type 2 diabetes, such as glucose intolerance, insulin resistance, reduced insulin response to glucose and a reduction in the disposition index. Current experimental evidence suggests that sleep restriction may lead to increased food intake but does not appear to result in decreased energy expenditure. Furthermore, sleep restriction has been reported to increase evening cortisol levels, which may decrease insulin sensitivity the next morning. This notion was further supported by studies, which noted decreases in the effectiveness of insulin-mediated glucose uptake the following morning. Further evidence suggests that short sleepers have glucose responses that are similar to average-duration sleepers, but at the cost of an increase in insulin release, which may be the result of decreased insulin sensitivity over time. Recent studies also provide evidence that sleep restriction enhances susceptibility to food stimuli, especially for energy-dense, high-carbohydrate foods. In summary, inadequate sleep, in both quality and quantity, should be regarded as a plausible risk factor for the development of obesity and type 2 diabetes. In addition to other health promotion measures, a good night's sleep should be seen as a critical health component by clinicians in the prevention and treatment of obesity and type 2 diabetes.

Les études épidémiologiques montrent que les adultes et les enfants qui sont habituellement des petits dormeurs ont tendance à avoir un indice de masse corporelle, un pourcentage de graisse et un périmètre abdominal élevés comparativement aux dormeurs avec une durée de sommeil adéquat. La perturbation ou la réduction du sommeil sont également associées à certains prédicteurs du diabète de type 2 tels que l'intolérance au glucose, l'insulinorésistance, la diminution de la réponse insulinique au glucose et la diminution de l'indice de prédisposition. Les preuves expérimentales actuelles montrent que le manque de sommeil peut mener à l'augmentation de l'apport alimentaire, mais qu'il ne semble pas entraîner la diminution de la dépense énergétique. De plus, il a été signalé que le manque de sommeil augmente les taux de cortisol en soirée, ce qui peut diminuer l'insulinosensibilité le lendemain matin. Cette notion est aussi corroborée par des études, qui ont noté des diminutions de l'efficacité de l'absorption de glucose par l'action de l'insuline le matin suivant. D'autres preuves montrent que les petits

dormeurs ont des réponses glycémiques similaires aux dormeurs avec une durée de sommeil adéquat, mais au prix d'une augmentation de la libération de l'insuline, qui peut entraîner une diminution de l'insulinosensibilité avec le temps. Les récentes études fournissent également des preuves que le manque de sommeil augmente la vulnérabilité quant aux stimuli alimentaires, particulièrement pour les aliments énergétiques et à forte teneur en glucides. En résumé, un sommeil inadéquat, tant sur le plan de la qualité que de la quantité, devrait être considéré comme un facteur de risque plausible du développement de l'obésité et du diabète de type 2. En plus des autres mesures de promotion de la santé, un bon sommeil nocturne devrait être vu par les cliniciens comme une composante de santé importante dans la prévention et le traitement de l'obésité et du diabète de type 2.

Keywords: obesity | poor sleep quality | short sleep duration | type 2 diabetes

Article:

Introduction

The increase in the prevalence of obesity and type 2 diabetes mellitus, concurrent with the decreases in sleep duration (1) has led some to believe that short sleep duration may be a possible risk factor for the development of obesity and type 2 diabetes (2, 3).

Short sleep duration has been suggested to play an important role in promoting obesity (4), and was further associated to an increased risk of weight and fat mass gains over time in adults (5), with odds ratio exceeding other well-known contributors (e.g. high lipid intake and the nonparticipation in high-intensity physical activity, with odds ratios of 1.64 and 2.03, respectively, vs. 3.81 for short sleep duration) (4). Similar results were observed in children aged between 5 and 10 years, where short sleep duration was found to be the most important risk factor for overweight and obesity when compared to other well-known contributors (e.g. parental obesity, ≥3 hours of television viewing and physical inactivity, with odds ratios of 2.39, 2.08 and 1.45, respectively, vs. 3.45 for short sleep duration in boys and girls combined) (6). Spiegel et al. (7) noted that disturbed or reduced sleep was associated with glucose intolerance, insulin resistance, reduced acute insulin response to glucose, and a reduction in the disposition index, thus suggesting that individuals who reported a poor sleep quality and/or short sleep time may be predisposed to developing type 2 diabetes. Additionally, patients with type 2 diabetes reported sleeping less and sleeping more poorly (8). These results thus suggest that short sleep duration and/or poor sleep quality, even after adjusting for body mass index (BMI) and waist-to-hip ratio, is associated with the development of type 2 diabetes.

This narrative review discusses the associations between short sleep duration and sleep restriction with obesity and type 2 diabetes. Furthermore, the potential factors by which habitual short sleep duration, sleep restriction and poor sleep quality may predispose to weight gain and the development of type 2 diabetes are discussed. Although long sleep duration (≥9 hours of sleep/night in adults) has also been previously associated with an increased risk of developing obesity and/or type 2 diabetes (9), this article concentrates on the effects of inadequate sleep, in both quality and duration, as a potential risk factor for the development of obesity and/or type 2 diabetes.

Association between Short Sleep Duration and Obesity

Epidemiological studies have noted that adults (5) and children (10) who are short sleepers (<6 hours of sleep/night in adults and <10 hours of sleep/night in children) tend to have greater body weight, BMI, body fat percentage and abdominal circumference when compared to average-duration sleepers (7–8 hours of sleep/night in adults and ≥10 hours of sleep/night in children). Furthermore, the association between short sleep duration and body weight appears to be stronger in children, and seems to decrease with age (11). These results suggest that children may be more vulnerable to the negative effects of short sleep duration on body weight. However, this effect may be due to greater sleep duration requirements in children (i.e. recommendation of 10 or more hours of sleep in children vs. 7 or more hours of sleep in adults) (11). Furthermore, the stronger association between sleep duration and body weight in children may be subject to bias, because children gain more weight over time due to natural growth and development (12).

Chaput et al. (13) recently observed that short sleep duration (≤6 hours of sleep/night) is associated with a preferential increase in abdominal adiposity in adults, when compared to those who sleep on average ≥7 hours/night, over a 6-year follow-up period. Similarly, the association between sleep duration and waist circumference in children remained significant after adjusting for BMI, thus suggesting that short sleep duration (<10 hours of sleep/night) may be an important predictor of abdominal adiposity in children that is independent from total adiposity (14). These findings are of particular concern because abdominal adiposity is correlated with a number of metabolic anomalies, which include type 2 diabetes (15).

Sleep timing seems to also be an important predictor of weight gain. A recent study in adults (16) noted that those who went to bed later consumed more calories after 8 p.m. when compared to those who went to bed earlier, which was a positive predictor of BMI after controlling for sleep duration and sleep timing. Furthermore, Olds et al. (17) reported that morning-type children (i.e. those who wake up earlier) were less likely to be obese when compared to evening-type children (i.e. those who go to bed later), despite similar sleep durations. This study also mentioned that evening-type children were almost twice as likely to have low levels of moderate-to-vigorous physical activity levels and were 2.9 times more likely to watch television and play video games for more hours than those recommended in guidelines. It may thus be suggested that later bedtimes may lead to weight gain by decreasing moderate-to-vigorous physical activity participation and increasing time spent partaking in sedentary activities, such as screen time, an activity that also generally promotes snacking and overeating.

Taken together, the current evidence suggests that short sleep duration has an effect on body weight and body weight gain, with this effect being stronger in children when compared to adults. However, the results of epidemiological studies must make allowance for limitations. Causality cannot be inferred based on these studies, because it is unknown whether short sleep duration preceded body weight gains (3). Furthermore, habitual sleep duration is often self-reported with one question, which does not take into consideration daytime napping, sleep fragmentation, night-to-night variability in sleep durations, as well as differences between weekday and weekend sleep durations (3). Lastly, the adoption of a chronic short sleep duration pattern in regard to the time of data collection in epidemiological studies may falsify results (12).

More specifically, short sleep duration may lead to weight gain if the participant adopted a short sleep duration pattern during data collection, or slightly before the start of data collection. However, if the adoption of a short sleep duration pattern had been already maintained for many years before the start of data collection, then weight gain would have most likely already occurred. This may in part explain the discrepancy in the short sleep-weight gain relationship, where certain studies noted a clear increase in body weight in short sleepers over time 5, 18, whereas others did not 19, 20.

Association between Short Sleep Duration and Type 2 Diabetes

Both sleep duration and sleep quality seem to affect the prevalence, development and control of type 2 diabetes (8). Chaput et al. (21) noted adjusted odds ratio of 2.09 for the prevalence of type 2 diabetes and impaired glucose tolerance in individuals who reported sleeping 5–6 hours/night, in comparison to those who reported sleeping 7–8 hours/night. This association did not weaken after the adjustment for several confounders, such as energy intake, physical activity level, age, heart disease and waist circumference. Additionally, substituting BMI or body fat percentage for waist circumference as a confounder did not alter this relationship. This positive association may be explained by significantly greater fasting plasma glucose and insulin concentrations, total insulin area under the curve values, and homeostasis model assessment of insulin resistance (HOMA-IR) index in short sleepers when compared to average- and long-duration sleepers (21). A different study by Chaput et al. (22) assessed the development of type 2 diabetes in the same individuals over a 6-year follow-up period and observed that age, obesity, sleep duration and glucose/insulin homeostasis indicators were significantly and independently associated with new cases of type 2 diabetes and impaired glucose tolerance. Furthermore, the adjusted relative risk of developing type 2 diabetes and impaired glucose tolerance was 2.42 after adjusting for waist circumference. Similar results were noted in another epidemiological study, where the odds ratio of developing type 2 diabetes was significantly greater (1.57) in those sleeping less than 5 hours/night, when compared to those who slept 7 hours/night (23).

Studies that assessed sleep quality noted that participants who reported having difficulty falling asleep or remaining asleep were at greater risk of developing type 2 diabetes (24, 25). More specifically, Kawakami et al. (24) noted greater age-adjusted risks of developing type 2 diabetes in individuals who reported difficulty falling asleep or remaining asleep (hazard ratios of 2.98 and 2.23, respectively). Additionally, Meisinger et al. (25) noted that men and women who reported difficulty remaining asleep had hazard ratios of developing type 2 diabetes of 1.6 and 1.98, respectively, after adjusting for other diabetes risk factors such as age, physical activity, BMI and parental history of diabetes among others. Lastly, a meta-analysis by Cappuccio et al. (9) noted a clear and consistent risk of developing type 2 diabetes in individuals with short sleep durations and disturbed sleep qualities. More specifically, the risk of developing type 2 diabetes were 28%, 57% and 84% greater in short sleepers (≤6 hours of sleep/night), individuals who reported difficulty in initiating sleep and in those with difficult maintaining sleep, respectively, when compared to the reference group of average-duration sleepers (>8 hours of sleep/night). The tool used for sleep assessment (e.g. questionnaires, interview), the definition of short sleep duration and the populations tested did not affect these results. These effects did, however, tend to increase with the duration of follow-up, thus suggesting that studies with longer

follow-up periods reported greater relative risks of developing type 2 diabetes in individuals with short sleep durations and/or disturbed sleep qualities.

Taken together, disturbed sleep quality and short sleep duration should be considered as plausible risk factors in the prevalence and development of type 2 diabetes. Furthermore, the associations between short sleep duration, inadequate sleep quality and the risk of developing type 2 diabetes seem to be consistent among different populations and studies.

Possible Mechanisms by Which Short Sleep Duration and Sleep Restriction May Predispose to Obesity and Type 2 Diabetes

Effects of short sleep duration on energy intake

Short sleepers (≤6 hours of sleep/night in adults) are more likely to have irregular eating habits, to snack between meals, to use an excessive amount of food seasoning and to consume less vegetables when compared to average-duration sleepers (26, 27). These results are in part supported by a study in adolescent short sleepers (<8 hours of sleep/night) who reported consuming relatively higher energy intake from lipids (28). A significant difference in BMI was also noted between short-sleepers (<8 hours of sleep/night) and the reference group (>8 hours of sleep/night); however, adjustments for BMI only lead to a modest attenuation in the association between short sleep duration and fat intake. Certain controlled intervention studies have found no significant effect of sleep restriction (5.5 hours of sleep/night for 14 nights; 4 hours of sleep/night for 2 nights) (29, 30) on energy and macronutrient intake when measured inside the laboratory setting. However, Nedeltcheva et al. (29) reported an increase in snack intake between 7 p.m.–7 a.m., despite no significant increase in total energy and macronutrient intake during 14 days of sleep restriction (5.5 hours of sleep/night). Additionally, a study that measured energy and macronutrient intake inside the laboratory (breakfast and lunch) and under free-living conditions (afternoon snacks and dinner) showed greater total energy and fat intake after 2 days of sleep restriction (4 hours of sleep/night), when compared to the control condition (2 days of 8 hours of sleep/night) (31). This increase was mainly characterized by greater total energy intake during breakfast (+45%) and dinner (+56%), as well as greater fat intake during dinner (+98%). A controlled intervention study also noted significantly greater energy intake using dietary records over 4 days of increasing sleep restriction (1 night of 7 hours, 2 nights of 6 hours and 1 night of 4 hours of sleep/night) when compared to baseline (2 nights of more than 8 hours of sleep/night) (32). Taken together, there is some evidence suggesting that sleep restriction, especially when measured under free-living conditions, may lead to greater energy and fat intake.

Effects of short sleep duration on energy expenditure

Current evidence suggests that sleep restriction does not alter total energy expenditure, nor resting energy expenditure (5, 29, 32). Furthermore, a 6-year prospective cohort study noted no significant difference in resting energy expenditure between short- (<6 hours of sleep/night), average- (7–8 hours of sleep/night) and long-duration (>9 hours of sleep/night) sleepers (5). As for physical activity energy expenditure (PAEE), 2 studies saw no significant difference in this variable when assessed inside the laboratory (29) and under free-living conditions (32) after

sleep restriction. Conversely, a study noted greater PAEE under free-living conditions after sleep restriction (31), whereas another reported a decrease in PAEE and moderate-to-vigorous physical activity participation after 4 p.m. after sleep restriction (30). Based on these results, sleep restriction may impact PAEE in some individuals but a better characterization of those more likely to change their physical activity pattern as a result of sleep restriction is needed.

Effects of short sleep duration on neuroendocrine hormones

It has been previously suggested that the downregulation of the hypothalamic-pituitary-adrenal (HPA) axis may fail to occur after sleep restriction, which results in greater evening cortisol levels (3). Many studies have noted a slower decline in cortisol levels throughout the day after sleep restriction, which leads to greater cortisol levels during the afternoon and evening post-sleep restriction (33, 34). Visceral adipose tissue, when compared to subcutaneous adipose tissue, is also more prone to the effects of cortisol, due to more cells per unit of mass, greater blood flow and more glucocorticoid receptors located in this region (3, 23). These results may in part explain the preferential increases in abdominal adiposity in habitual short sleepers (13, 14). Increased cortisol levels in the evening have also been suggested to be associated to decreased insulin sensitivity the following morning (35, 36). Furthermore, increases in sympathetic nervous system activation in response to sleep restriction (7) has been shown to inhibit the secretion of leptin and insulin (37). The increase in sympathetic nervous system activity in response to a stressor, such as sleep restriction, induces a short-term "fight or flight" response, which inhibits many long-term functions related to the maintenance of energy balance, such as the release of leptin (37). This inhibition in leptin release may then increase hunger levels and decrease feelings of satiety (38). Some studies have noted lower mean leptin levels in short sleepers than that predicted by their fat mass (39), and after 2 nights of imposed sleep restriction (4 hours sleep/night for 2 nights) (38). Thus, greater sympathetic nervous system activity and evening cortisol levels induced by sleep restriction may cause disturbances in glucose metabolism and alter the release of certain metabolic hormones (e.g. leptin and insulin). These neuroendocrine and metabolic hormone variations due to sleep restriction are presented in Figure 1.

Participants subjected to sleep restriction generally have an increase in their glucose levels after a standardized breakfast without an adequate, subsequent rise in insulin, thus leading to a decrease in the effectiveness of insulin-mediated glucose uptake (7). This lack in insulin response to increased glucose levels after sleep restriction may be related to a decrease in the autonomic regulation of beta cells, or increased sympathetic nervous system activity (41). However, the response of insulin to the rise in glucose levels after midday and evening meals has been shown to be the same between the sleep restriction and control conditions in these studies. Further evidence suggests that 5 days of sleep restriction (4 hours of sleep/night) lead to an increase in the fasting (i.e. measurement before breakfast) insulin-to-glucose ratio (42), thus suggesting that a decrease in insulin sensitivity may have transpired. Additionally, a study by Broussard et al. (43) observed an approximate 30% reduction in cellular insulin sensitivity in adipocytes after 4 nights of sleep restriction (4.5 hours of sleep/night), which suggests that sleep may also play an important role in peripheral energy metabolism and cellular insulin signaling. Lastly, decreases in slow-wave sleep, an important marker of sleep quality, for 3 days lead to decreases in insulin sensitivity (44), which suggests that an adequate amount of slow-wave sleep, in addition to total sleep duration, is needed to maintain proper glucose metabolism.

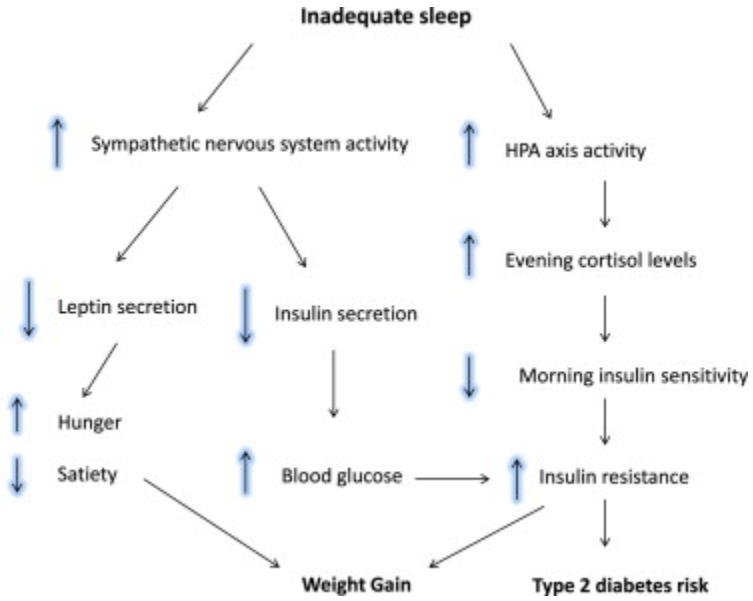

Figure 1. The neuroendocrine and metabolic hormone variations induced by insufficient sleep, which may lead to weight gain and increased type 2 diabetes risk. This figure illustrates the effects of sleep restriction/short sleep duration on the neuroendocrine system, thus leading to alterations in cortisol and certain metabolic hormones in a way that may induce weight gain and increase the risk of developing type 2 diabetes. *HPA*, hypothalamic-pituitary-adrenal. Adapted from Zimberg et al. (40).

Similar outcomes were noted in habitual short sleepers. For instance, a study showed that non-obese short sleepers (<6.5 hours of sleep) had glucose responses to an intravenous glucose tolerance test that were similar to non-obese average-duration sleepers (7.5–8.5 hours of sleep/night), but at the cost of a significantly greater increase in insulin release (45), which may be the product of decreased insulin sensitivity over time. This study further confirmed that insulin sensitivity in short sleepers was almost 40% lower when compared to average-duration sleepers, even though participants in each group were carefully matched for sex and ethnic differences, as well as exercise habits. On the other hand, Chaput et al. (21) noted that short sleepers had greater insulin levels and a more pronounced decline in blood glucose (i.e. greater difference between minimal and maximal blood glucose levels) during a 3 hour oral glucose tolerance test (OGTT), as well as a greater glucose area below fasting glucose levels immediately after the OGTT. Based on the glucostatic theory (46), a more pronounced reactive hypoglycemia at the end of an OGTT in short sleepers may in part explain the relationship between sleep duration and the risk of weight gain (21). The glucostatic theory states that a pattern of dynamic changes in glucose levels sensed in critical glucosensitive sites (e.g. brain) in part controls food intake; an increase in hunger and a decrease in satiety are expressed when glucose use is decreased, whereas an increase in glucose use in these same glucosensitive sites has the opposite effect on these appetite markers (46). And so, according to this theory, it may be hypothesized that lower glucose concentrations observed immediately after an OGTT in short sleepers may lead to an increase in hunger, food intake and eventual weight gain in this population. To restore glucose homeostasis, an increase in food intake and weight gain in chronic short sleepers might be a normal physiological adaptation (46).

In summary, greater cortisol levels during the evening as a result of sleep restriction may alter insulin sensitivity, which may then negatively affect glucose uptake and potentially lead to the development of insulin resistance over time, independently of changes in BMI and/or body weight. Furthermore, based on the glucostatic theory, it may be speculated that reductions in glucose levels in habitual short sleepers immediately after an OGTT may lead to greater hunger sensations and food intake, which may eventually lead to the development of obesity in this population. Lastly, preferential increases in abdominal adiposity, which has been previously associated with habitual short sleep duration (13, 14), may be a possible consequence of greater evening cortisol levels and altered insulin sensitivity.

Effects of sleep duration on the non-homeostatic drive to eat

The explanation of an increase in the homeostatic drive to eat as a result of sleep restriction is not as widely accepted as it once was (3), because many studies do not observe a decrease in leptin and/or an increase in ghrelin after sleep restriction interventions (29, 30, 32). Another possibility is that sleep perturbations may lead to an increase in the non-homeostatic drive to eat (i.e. motivation to eat in the absence of hunger; related to certain cognitive, hedonic, social and environmental factors), rather than the homeostatic drive to eat, and may in part explain the shift in food selection previously noted after sleep restriction (29, 38). In an environment in which energy-dense food is highly palatable and readily available, caloric intake may be directly proportional to the time spent awake, especially if this wakefulness is spent doing sedentary activities where snacking is common.

To date, few studies have looked at the possible relationship between reward-driven eating behaviour and sleep restriction. Functional magnetic resonance imaging (MRI) results from Holm et al. (47) showed a decreased reactivity in the ventral striatum, a primary reward center of the brain, in adolescents with short sleep durations, decreased sleep qualities and later sleep onset times when anticipating and receiving a monetary reward. St-Onge et al. (48) also noted greater neuronal activation in the orbitofrontal cortex, an area of the brain related to motivation, in response to food cues when compared to non-food cues after sleep restriction (4 hours of sleep/night for 6 nights). Similar results were noted after 1 night of total sleep deprivation, where a greater activation of the right anterior cingulate cortex, which plays a key role in perception, was observed when participants were presented with images of foods with different caloric (high vs. low) content (49). These participants also rated high calorie foods as being 24% more appetizing after the 24-hour sleep deprivation session. Lastly, sleep restriction (4 hours of sleep/night) for 2 nights led to a 24% and 23% increase in hunger and appetite ratings respectively, which tended to be greatest for energy dense foods that were high in carbohydrates, whereas appetite for fruits and vegetables increased to a lesser extent (38). Future studies are needed to address potential alterations in the nonhomeostatic drive to eat in habitual short sleepers, as well as the potential cause-and-effect relationship between sleep restriction and reward-driven eating behavior.

Conclusion

Despite the inability to draw firm cause-and-effect associations between inadequate sleep duration and poor sleep quality with the prevalence and development of obesity and type 2

diabetes, the evidence presented in this article, as a whole, suggests that inadequate sleep, both in quality and quantity, should be regarded as a plausible risk factor for the development of obesity and type 2 diabetes. Thus, in addition to other health promotion measures, a good night's sleep should be seen as a critical health component tool in the prevention and treatment of obesity and type 2 diabetes. Lastly, it is important for clinicians to target the root causes of habitual short sleep duration and/or poor sleep quality (e.g. insomnia, anxiety, shift work, late-night TV viewing) because the reasons for adopting habitual short sleep duration and/or suffering from poor sleep quality can be very different between individuals.

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The authors declare no conflict of interest.

Author Contributions

JMcN compiled articles, drafted the article and gave final approval of the version to be published. ÉD revised the article for scientific content and gave final approval of the version to be published. J-PC compiled articles, revised the article for scientific content and gave final approval of the version to be published.

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