

Type 1 Diabetes and Sleep

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■ **IN BRIEF** In people with type 1 diabetes, sleep may be disrupted as a result of both behavioral and physiological aspects of diabetes and its management. This sleep disruption may negatively affect disease progression and development of complications. This review highlights key research findings regarding sleep in people with type 1 diabetes.

Recent research has increasingly identified sleep as a key process for the maintenance of good cardiovascular and metabolic health. Disturbed sleep patterns (i.e., restriction, deprivation, and fragmentation) in healthy young adults produce alterations in both metabolism and cardiovascular disease risk markers. Sleep restriction refers to reduced amount of total sleep (i.e., sleeping 5 hours instead of 8 hours); sleep deprivation refers to total sleep loss or prevention of sleep; and sleep fragmentation refers to sleep periods that are broken up by multiple awakenings throughout the night. Conditions that accompany type 1 diabetes (e.g., hyperglycemia, glucose variability, and hypoglycemia) may result in sleep disruption. Sleep disruption in people with type 1 diabetes may negatively affect disease progression and the development of complications. Thus, the purpose of this review is to summarize the relevant recent research on sleep in people with type 1 diabetes.

Sleep Quality and Sleep Architecture (Structure of Sleep) Children (1) and adults (2) with type 1 diabetes subjectively report poorer sleep quality than healthy control subjects. Objective measures based on polysomnography (PSG)

demonstrate that children with type 1 diabetes spend more time in stage 2 (lighter) sleep and less time in stage 3 (deep) sleep compared to healthy children (3). Young adults with type 1 diabetes also exhibit more stage 2 sleep and tend to have less deep sleep during the first half of the night compared to healthy control subjects (4). Differences in neuroendocrine correlates of sleep were also reported; growth hormone and epinephrine levels were elevated throughout the night and adrenocorticotrophic hormone levels were higher during the first 4 hours of the night in young adults with type 1 diabetes (4). It is apparent that important differences may exist in sleep patterns of people with type 1 diabetes compared to those of people without diabetes. However, larger studies including a wider clinical and age spectrum are needed to fully characterize sleep derangements and their impact on health and disease progression.

Effects of Disrupted Sleep on Glucose Control

Several studies have reported a relationship between A1C and sleep disturbances. Mean A1C was significantly higher in children aged 3–18 years with type 1 diabetes who self-reported problems with sleep initiation (5) and was positively associated with self-

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reported sleeping difficulties in young adults aged 18–21 years (6). Moreover, a positive association was reported between the number of full awakenings from sleep, measured by PSG, and A1C levels in 20- to 38-year-old adults with type 1 diabetes (7).

Sleep duration also appears to affect glycemic control. Adults with type 1 diabetes who slept <6.5 hours per night had higher A1C levels than those who slept >6.5 hours per night (8). Moreover, higher A1C was associated with less time spent in slow-wave sleep (i.e., deep sleep) in 10- to 17-year-olds (3) and 19- to 61-year-olds (9) with type 1 diabetes.

These studies are all descriptive. Few studies have been developed to determine the underlying mechanisms for the observed associations between sleep and glycemic control. Insulin sensitivity was decreased after a single night of partial sleep restriction compared to a normal night of sleep (4 vs. 8.5 hours) in normal-weight adults (mean age 44.3 ± 6.6 years, mean BMI 23.5 ± 0.9 kg/m²) with type 1 diabetes (10). This finding suggests that sleep restriction, a common behavior in the population, may negatively influence glycemic control. However, more interventional studies are needed to fully determine the mechanisms underlying reported associations between sleep disturbance and glucose regulation. Such research will help to inform clinical management strategies for type 1 diabetes.

Sleep Disorders

Sleep-disordered breathing is one of the most prevalent sleep disorders. Obstructive sleep apnea (OSA) and type 2 diabetes frequently occur together, and there is strong evidence to suggest the two pathologies are linked. Few studies have investigated the prevalence of sleep apnea in type 1 diabetes. The apnea index (number of apnea episodes/hour) during sleep was higher in normal weight (BMI 18.74 ± 3.58 kg/m²) 5- to 11-year-olds with type 1 diabetes than in healthy age- and BMI-matched children, and, in

the group with type 1 diabetes, the apnea index was higher in children with poorer glycemic control (A1C $\geq 8.0\%$) than those with good glycemic control (11). In another study of 556 adults with diabetes (58 with type 1 diabetes), 37.4% had OSA. However, only 1.1% of the subjects who were positive for OSA had type 1 diabetes (12). In a pilot study of 37 adults with type 1 diabetes, 40% of the subjects were found to have OSA. Subjects who had OSA were older, had a longer duration of diabetes, and were more likely to have retinopathy than those who did not have OSA (13). Sleep apnea and excessive daytime sleepiness were more prevalent in normal-weight (BMI <25 kg/m²) young adults with type 1 diabetes than in healthy control subjects (14). Within the group with type 1 diabetes, sleep apnea was more prevalent in those with cardiovascular autonomic neuropathy than in those without (23 and 67%, respectively) (14). OSA was common in a group of normal-weight (mean BMI 25.8 ± 4.7 kg/m²) adults with type 1 diabetes (46% of the 67 subjects), and the presence of OSA was independently associated with macrovascular complications, as well as with retinopathy (15). This study also reported that those with OSA had a longer duration of diabetes by ~9 years (15). Although limited, these studies demonstrate that OSA is more common among individuals with type 1 diabetes than among those without diabetes, and the presence and severity of OSA are linked to glycemic control in both children and adults with type 1 diabetes. Larger-scale studies are needed to confirm these findings.

Studies investigating the incidence of other sleep disorders such as insomnia and narcolepsy in type 1 diabetes have not been reported in the literature. One study found that restless legs syndrome, a problem that is common in adulthood but of unknown prevalence in childhood, was not more common among

children with type 1 diabetes than among healthy control subjects (5).

Impact of Diabetes Pathophysiology and Treatment on Sleep

Hypoglycemia

Research has shown that individuals with type 1 diabetes have a decreased awakening response to hypoglycemia during sleep (16,17), which could be the result of decreased counterregulatory response (18–20). Unfortunately, nocturnal hypoglycemia is a common occurrence in both children and adults with type 1 diabetes (21–24). Adults subjectively report that non-severe hypoglycemic events disrupt their sleep, and many have difficulty falling back to sleep after treating their hypoglycemia (25,26).

The impact of hypoglycemia on sleep architecture has been minimally investigated. Spontaneous hypoglycemia (<45 mg/dL) in teenagers with type 1 diabetes did not result in a change in sleep architecture compared to those who did not become hypoglycemic. However, only 6 of the total 20 subjects experienced hypoglycemia in this study, in which blood glucose was obtained via intravenous catheter every 30 minutes (27). In another study, the number of full awakenings was significantly higher in children with type 1 diabetes, but there was no relationship between awakenings and the occurrence of hypoglycemia measured by continuous glucose monitoring (28). In the same study, slow-wave sleep (stages 3 and 4) was significantly more prevalent during episodes of hypoglycemia. Using actigraphy to discriminate between sleep and wakefulness, hypoglycemia during sleep was associated with increased motor activity in adolescents with type 1 diabetes (29). In children, episodes of profound hypoglycemia were associated with increased slow-wave activity (deep sleep), but rapid declines in glucose (≥ 25 mg/dL per hour) were associated with increased awakenings from sleep (30). Few studies have addressed the

impact of hypoglycemia on sleep architecture in adults with type 1 diabetes. Still, the prevalence of nocturnal hypoglycemia combined with anecdotal subjective reports of sleep disruption from hypoglycemia highlight the need for future studies designed to fully characterize the impact of hypoglycemia-related sleep disruption. Interestingly, it has been reported that hypoglycemia does not alter the acoustic arousal threshold in adolescents with type 1 diabetes (17), indicating that alarms may be helpful in alerting individuals when hypoglycemia occurs during sleep.

Hyperglycemia

Investigators have reported that adults with type 1 diabetes who had a mean glucose >154 mg/dL had lower overnight urinary melatonin excretion than healthy control subjects (31). Melatonin is an important regulator of the sleep-wake cycle. These results suggest that hyperglycemia may negatively affect maintenance of a normal circadian cycle. Minimal research has been done investigating the direct impacts of hyperglycemia on sleep. As reviewed previously, there is a strong connection between disrupted sleep and poorer glycemic control; however, these studies were unable to determine causality. As noted above, one study found that sleep restriction led to impaired insulin sensitivity the next day in individuals with type 1 diabetes, which would disrupt glycemic control (10). It also is possible that sleep may be disrupted by the symptoms of hyperglycemia. Hyperglycemia leads to osmotic diuresis, resulting in the need to urinate more frequently, which may lead to sleep disruption, although no studies investigating this phenomenon have been reported. Studies comparing the effects of hyperglycemia versus euglycemia on sleep architecture in both children and adults are needed to determine whether hyperglycemia has a detrimental effect on sleep architecture.

Glucose Variability

Increased glycemic variability has been positively correlated with subjectively reported mean sleep latency (7). Pillar et al. (30) reported that rapid changes in glucose were associated with increased awakenings from sleep in children with type 1 diabetes. This finding raises the possibility that the rate of change in glucose levels may affect sleep architecture. These results highlight a need for more studies to investigate the influence of glucose variability, a common feature of type 1 diabetes, on sleep.

Blood Pressure and Sleep in Type 1 Diabetes

Blood pressure normally declines during sleep; loss of this decline is associated with increased risk for sustained hypertension, as well as an accelerated rate of development of complications (32). In two separate studies that did not include a control group, adults with type 1 diabetes who were “non-dippers” (i.e., who did not exhibit a decline in blood pressure during sleep) had shorter sleep durations as measured by PSG and wrist actigraphy (8,33). Larger studies that include a control group are needed to confirm whether short sleep duration increases the risk of or accelerates the development of cardiovascular and microvascular complications and whether this is specific to type 1 diabetes.

Conclusion

Evidence from the literature supports the likelihood that adults and children with type 1 diabetes have altered sleep architecture and reduced sleep quality relative to individuals without diabetes. Alterations in sleep architecture may be the result of both behavioral and physiological aspects of diabetes and its management. Sleep apnea may be more prevalent in people with type 1 diabetes, and presence of OSA has been linked to impaired glycemic control. Furthermore, lack of the normal decline in blood pressure during sleep may be linked to short sleep duration in people with type 1

diabetes, and this may accelerate the development of cardiovascular and microvascular disease. Additional research is needed to better understand the mechanisms determining why and how sleep is disrupted in individuals with type 1 diabetes and what impact sleep disruption may have on diabetes management and control.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

References

- Caruso NC, Radovanovic B, Kennedy JD, et al. Sleep, executive functioning and behaviour in children and adolescents with type 1 diabetes. *Sleep Med* 2014;15:1490–1499
- van Dijk M, Donga E, van Dijk JG, et al. Disturbed subjective sleep characteristics in adult patients with long-standing type 1 diabetes mellitus. *Diabetologia* 2011;54:1967–1976
- Perfect MM, Patel PG, Scott RE, et al. Sleep, glucose, and daytime functioning in youth with type 1 diabetes. *Sleep* 2012;35:81–88
- Jauch-Chara K, Schmid SM, Hallschmid M, Born J, Schultes B. Altered neuroendocrine sleep architecture in patients with type 1 diabetes. *Diabetes Care* 2008;31:1183–1188
- Happe S, Treptau N, Ziegler R, Harms E. Restless legs syndrome and sleep problems in children and adolescents with insulin-dependent diabetes mellitus type 1. *Neuropediatrics* 2005;36:98–103
- Bächle C, Lange K, Stahl-Peche A, et al. Associations between HbA1c and depressive symptoms in young adults with early-onset type 1 diabetes. *Psychoneuroendocrinology* 2015;55:48–58
- Barone MTU, Wey D, Schorr F, et al. Sleep and glycemic control in type 1 diabetes. *Arch Endocrinol Metab* 2015;59:71–78
- Borel A-L, Pépin J-L, Nasse L, Baguet J-P, Netter S, Benhamou P-Y. Short sleep duration measured by wrist actimetry is associated with deteriorated glycemic control in type 1 diabetes. *Diabetes Care* 2013;36:2902–2908
- Feupe SF, Frias PF, Mednick SC, McDevitt EA, Heintzman ND. Nocturnal continuous glucose and sleep stage data in adults with type 1 diabetes in real-world conditions. *J Diabetes Sci Technol* 2013;7:1337–1345
- Donga E, van Dijk M, van Dijk JG, et al. Partial sleep restriction decreases insulin sensitivity in type 1 diabetes. *Diabetes Care* 2010;33:1573–1577

11. Villa MP, Multari G, Montesano M, et al. Sleep apnoea in children with diabetes mellitus: effect of glycaemic control. *Diabetologia* 2000;43:696–702
12. Schober A-K, Neurath MF, Harsch IA. Prevalence of sleep apnoea in diabetic patients. *Clin Respir J* 2011;5:165–172
13. Borel A-L, Benhamou P-Y, Baguet J-P, et al. High prevalence of obstructive sleep apnoea syndrome in a type 1 diabetic adult population: a pilot study. *Diabet Med* 2010;27:1328–1329
14. Janovsky CC, Rolim LC, de Sá JR, et al. Cardiovascular autonomic neuropathy contributes to sleep apnea in young and lean type 1 diabetes mellitus patients. *Front Endocrinol (Lausanne)* 2014;5:119
15. Manin G, Pons A, Baltzinger P, et al. Obstructive sleep apnoea in people with type 1 diabetes: prevalence and association with micro- and macrovascular complications. *Diabet Med* 2015;32:90–96
16. Schultes B, Jauch-Chara K, Gais S, et al. Defective awakening response to nocturnal hypoglycemia in patients with type 1 diabetes mellitus. *PLoS Med* 2007;4:e69
17. Ly TT, Jones TW, Griffiths A, et al. Hypoglycemia does not change the threshold for arousal from sleep in adolescents with type 1 diabetes. *Diabetes Technol Ther* 2012;14:101–104
18. Banarar S, Cryer PE. Sleep-related hypoglycemia-associated autonomic failure in type 1 diabetes reduced awakening from sleep during hypoglycemia. *Diabetes* 2003;52:1195–1203
19. Jones TW, Porter P, Sherwin RS, et al. Decreased epinephrine responses to hypoglycemia during sleep. *N Engl J Med* 1998;338:1657–1662
20. Diabetes Research in Children Network Study Group. Impaired overnight counterregulatory hormone responses to spontaneous hypoglycemia in children with type 1 diabetes. *Pediatr Diabetes* 2007;8:199–205
21. JDRF Continuous Glucose Monitoring Study Group. Prolonged nocturnal hypoglycemia is common during 12 months of continuous glucose monitoring in children and adults with type 1 diabetes. *Diabetes Care* 2010;33:1004–1008
22. Ahmet A, Dagenais S, Barrowman NJ, Collins CJ, Lawson ML. Prevalence of nocturnal hypoglycemia in pediatric type 1 diabetes: a pilot study using continuous glucose monitoring. *J Pediatr* 2011;159:297–302.e1
23. Woodward A, Weston P, Casson IF, Gill GV. Nocturnal hypoglycaemia in type 1 diabetes: frequency and predictive factors. *Q J Med* 2009;102:603–607
24. Kaufman FR, Austin J, Neinstein A, et al. Nocturnal hypoglycemia detected with the continuous glucose monitoring system in pediatric patients with type 1 diabetes. *J Pediatr* 2002;141:625–630
25. Brod M, Pohlman B, Wolden M, Christensen T. Non-severe nocturnal hypoglycemic events: experience and impacts on patient functioning and well-being. *Qual Life Res* 2013;22:997–1004
26. Brod M, Christensen T, Bushnell DM. Impact of nocturnal hypoglycemic events on diabetes management, sleep quality, and next-day function: results from a four-country survey. *J Med Econ* 2012;15:77–86
27. Porter PA, Byrne G, Stick S, Jones TW. Nocturnal hypoglycaemia and sleep disturbances in young teenagers with insulin dependent diabetes mellitus. *Arch Dis Child* 1996;75:120–123
28. Matyka KA, Crawford C, Wiggs L, Dunger DB, Stores G. Alterations in sleep physiology in young children with insulin-dependent diabetes mellitus: relationship to nocturnal hypoglycemia. *J Pediatr* 2000;137:233–238
29. Radan I, Rajer E, Ursic Bratina N, Neubauer D, Krzysnik C, Battelino T. Motor activity during asymptomatic nocturnal hypoglycemia in adolescents with type 1 diabetes mellitus. *Acta Diabetol* 2004;41:33–37
30. Pillar G, Schuscheim G, Weiss R, et al. Interactions between hypoglycemia and sleep architecture in children with type 1 diabetes mellitus. *J Pediatr* 2003;142:163–168
31. Amaral FG, Turati AO, Barone M, et al. Melatonin synthesis impairment as a new deleterious outcome of diabetes-derived hyperglycemia. *J Pineal Res* 2014;57:67–79
32. Dost A, Klinkert C, Kapellen T, et al. Arterial hypertension determined by ambulatory blood pressure profiles: contribution to microalbuminuria risk in a multicenter investigation in 2,105 children and adolescents with type 1 diabetes. *Diabetes Care* 2008;31:720–725
33. Borel A-L, Benhamou P-Y, Baguet J-P, et al. Short sleep duration is associated with a blood pressure nondipping pattern in type 1 diabetes: the DIAPASOM study. *Diabetes Care* 2009;32:1713–1715