# Sleep disruption in adolescents with Type 1 diabetes mellitus: relationships with adherence and diabetes control

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| Practice points |
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| • Adherence to diabetes care is particularly problematic during adolescence for young people with Type 1 diabetes mellitus (T1D). |
| • Difficulties with sleep have a known impact on cognitive and executive functioning, which is important for adherence. However, research has not yet examined relationships between sleep disturbance and adherence for adolescents with T1D. |
| • The current study aimed to examine relationships of sleep disturbance with adherence and glycemic control in adolescents with T1D. |
| • Participants included 72 adolescents between the ages of 10 and 18 years, who had poor diabetes control. |
| • Parents reported on adolescent sleep disturbance, self-report and frequency of blood glucose monitoring were used to assess adherence, and HbA1c and results of continuous glucose monitoring were used to assess glycemic control. |
| • Sleeping too much and trouble sleeping were associated with hyperglycemia. Sleeping too much was also associated with lower adherence and higher HbA1c. |
| • Sleep variables collectively explained 16% of the variance in adherence and 15% of the variance in average CGM glucose levels. |
| • Associations of sleep disturbance with adherence suggests the importance of assessing sleep and also highlights the need for future research on methods to improve sleep for adolescents with T1D. |

**SUMMARY** **Aim:** To examine the relationship of sleep disturbance with adherence and glycemic control in adolescents with Type 1 diabetes mellitus. **Materials & methods:** Participants included 72 adolescents in poor metabolic control. Parents reported on the frequency of the following sleep disturbances: sleeping too much, not sleeping enough, trouble sleeping and being overtired. Adherence was assessed via self-report and frequency of blood glucose monitoring. Glycemic control was assessed via hemoglobin A1c and continuous glucose monitoring data. **Results:** Sleeping more was associated with lower adherence and higher HbA1c. Sleeping more and trouble sleeping were associated with hyperglycemia as measured by continuous glucose monitoring. **Conclusion:** Sleep disturbance may negatively impact adherence and glycemic control. Additional research is needed to determine directionality of relationships.

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Management of Type 1 diabetes mellitus (T1D) requires adherence to multiple self-care tasks, including blood glucose monitoring, insulin administration and carbohydrate counting. Adherence to diabetes care is particularly low during adolescence [1,2]. A variety of factors have been supported as correlates of adherence, including adolescent depression [3], executive functioning [4] and family conflict [5]. Although sleep quality is known to impact cognitive functioning and motivation, to our knowledge, adolescent sleep disturbance has not yet been examined as a correlate of adherence for adolescents with T1D.

Consistent with national norms, data on children and adolescents with T1D suggest insufficient sleep, with 52% of school-age children and 76% of adolescents with T1D receiving less than the recommended amount of sleep [6]. In addition to not receiving enough sleep, specific sleep problems that disrupt consolidated sleep have been identified in children and adolescents with T1D. For example, in comparison to children without T1D, results of polysymography (PSG) indicated more frequent and longer night-time awakenings for children with T1D [7]. Changes in the structure and pattern of sleep may also compound the sleep problems of adolescents with T1D. In one study of adolescents with T1D, reduced slow wave sleep was related to worse glycemic control even though total sleep time and sleep efficiency did not relate to glucose control [8]. Further, a greater proportion of time in stage two of sleep was related to worse glycemic control. Additionally, sleep disruption and daytime sleepiness in adolescents with T1D has been associated with poorer quality of life, socioemotional outcomes and academic performance [8]. Hypoglycemic episodes at night represent an additional area of concern for children and adolescents with T1D [9,10]. First, nocturnal hypoglycemia can impact sleep quality or cause sleep disruption if it results in nocturnal waking. Further, individuals with T1D may be less likely to awaken during hypoglycemia than individuals without T1D [7,10], which could have fatal consequences. These findings suggest the importance of better understanding sleep quality in individuals with T1D. Given the significant negative sequelae of sleep problems on psychosocial outcomes and potentially glycemic control, additional research is needed to better understand the relationship between sleep disturbance and diabetes management.

The purpose of the current study was to examine sleep disturbance as a correlate of adherence and glycemic control in adolescents with T1D. The analyses for the current study represent a secondary analysis in a sample of adolescents with poorly controlled T1D who participated in an intervention study designed to improve glycemic control.

It was hypothesized that sleep disruption would be associated with lower levels of adherence and worse glycemic control. In addition, given that depression in adolescents is associated with sleep impairment as well as adherence difficulties in adolescents with T1D [3], relationships among adherence, sleep problems and depressed mood were examined.

## Patients & methods
### • Participants
In total, 167 adolescents with poorly controlled T1D and their parents were eligible for participation in the larger intervention study and 72 adolescents and parents (43% participation rate) agreed to participation. Demographic and disease characteristics have been reported previously [11]. The average hemoglobin A1c (HbA1c) of the adolescent participants was 10.2% (SD: 1.7; range: 7.8–16.8). It should be noted that participants were recruited for the baseline assessment based on point of care HbA1c levels at or above 8.5%. However, four participants had HbA1c that were below 8.5 after completing the baseline serum HbA1c. All HbA1c levels were still at or above 7.8%, thus representing poor control. There were 28 males (38.9%) and 44 females (61.1%), with a mean age of 14.24 years (SD: 2.94; range: 10–18). The ethnic/racial make-up was 68.1% Caucasian, 19.4% African–American, 11.1% biracial/multiracial and 1.4% Hispanic/Latino.

### • Procedure
Adolescents with HbA1c levels greater than 8.5% were recruited through pediatric endocrinology specialty clinics at a midwestern, urban hospital for a multidisciplinary intervention study aimed at improving diabetic control [Macleish SA *et al.* Unpublished Data]. All study procedures were approved by the Institutional Review Board and informed consent and assent were obtained prior to study enrollment. For the current study, baseline measures of sleep habits, adherence and glycemic control were examined. During the baseline assessment, adolescents and their parents completed questionnaires to assess adherence and socioemotional functioning. Baseline

glycemic control was measured with HbA1c and data from a blinded Continuous Glucose Monitor (CGM, Medtronic iPro), which was worn for 5 days.

• **Measures**

Sleep

Four items from the Child Behavior Checklist (CBCL) [12] were included to assess sleep disruption: 'overtired without good reason', 'sleeps less than most kids', 'sleeps more than most kids during the day and/or night' and 'trouble sleeping.' Preliminary support for using the sleep items on the CBCL has been identified by comparing sleep item responses to standard measures of sleep disruption including sleep diaries, actigraphy and polysomnography [13]. Specifically, Gregory et al. found that 'overtired' was related to sleep diary sleep latency and fewer arousals on polysomnography. 'Sleeps less' was related to less total sleep time on polysomnography. 'Sleeps more' was related to less total awake time by sleep diary, less ease of waking by sleep diary and shorter sleep latency on actigraphy. 'Trouble sleeping' was correlated with longer sleep latency as measured by both sleep diary and actigraphy. Although the sleep items on the CBCL have subsequently been used by researchers as a composite to examine sleep-related issues in specific pediatric populations [14–17], the current research follows the precedent of Gregory et al. [13] and examines each item separately.

Adolescent depression

The Withdrawn/Depressed scale of the CBCL was used to assess parent-report of depressive symptoms. This scale has been shown to have adequate reliability and validity [12]. Consistent with recommendations for use of the CBCL [12], the raw score from the Withdrawn/Depressed scale was used to capture the variability in depressive symptoms.

BMI

BMI was computed based on height and weight at the baseline assessment.

Adherence

The Self Care Inventory (SCI) [18] is a 14-item inventory that assesses the adolescent's perception of their adherence to their diabetes treatment regimen during the past month. Responses are coded on a 5-point Likert scale ranging from 1 (never do it) to 5 (always do this as recommended without fail), with higher scores indicating higher levels of adherence. A total score was computed to assess self-reported adherence. Internal consistency has been high [19–21], and validity of the SCI has been supported by correlations with metabolic control [21].

Frequency of blood glucose monitoring was also used as a measure of adherence. Specifically, average number of blood glucose tests/day was determined from meter downloads at the baseline assessment.

Glycemic control

HbA1c was the primary measure of glycemic control and was measured by high performance liquid chromatography with a Bio-Rad Variant 2 Turbo. The CGM was placed subcutaneously and measured interstitial glucose levels every 5 min. This information was sent to the attached transmitter; the participant was blinded to the monitor readings. CGM data used in the current study included average glucose level for the duration of the 5-day recording period, area below 70 mg/dl (reflecting both duration and severity of hypoglycemia) and area above 180 mg/dl (reflecting duration and severity of hyperglycemia). Cut-offs of 70 mg/dl and 180 mg/dl were chosen based on standard clinical cut-offs. In addition, counter-regulatory hormone responses of glucagon, epinephrine, growth hormone and cortisol begin at blood sugars just below 70 mg/dl [22]. Lower HbA1c, a lower average CGM glucose, and smaller areas above and below the curve indicated better glycemic control.

• **Statistical analysis**

Two-tailed Pearson correlation analyses were computed to investigate the associations among self-reported adherence, glycemic control, adolescent depressed mood and sleep problems. Due to previous literature suggesting lower adherence and glycemic control in older children and children from lower income households [23], age and family income were examined in relation to adherence and glycemic control to determine whether they should be controlled for in partial correlations. Additionally, due to previous reported associations between BMI and glycemic control [24] and between sleep disordered breathing and obesity [25], correlations were examined to determine whether BMI needed to be controlled for in analyses. Linear regressions were used to test whether the combination of the four

sleep variables would explain a significant portion of the variance in adherence and glycemic control. Multicollinearity diagnostics were computed for regression analyses and neither tolerance not variable inflation factor diagnostics suggested the presence of a problem with multicollinearity.

## Results

### • Descriptive statistics

Approximately 15% of parents reported that their children have trouble sleeping (6.9% sometimes, 8.3% often). In total, 22% of parents reported that their children are overtired without good reason (18.1% sometimes, 4.2% often). Variability in sleep was also relatively common, with 29% of parents indicating that their children sleep more than most kids during the day and/or night (25.0% sometimes, 4.2% often) and 18% of parents indicating that their children sleep less than most kids (15.3% sometimes, 2.8% often). It should be noted that the individual sleep items from the CBCL were not highly correlated with each other in the current study. Descriptive statistics for the glycemic control and adherence variables are displayed in Table 1.

### • Sleep habits & depressive symptoms

Higher levels of depressive symptoms, as reported by parents on the CBCL, were significantly correlated with sleeping more, being overtired and having trouble sleeping (see Table 2). Sleeping less was not significantly correlated with parent report of depressive symptoms.

### • Sleep habits & BMI

Correlations between BMI and sleep items on the CBCL are displayed in Table 2. None of the correlations were statistically significant.

### • Sleep habits, adherence & glycemic control

Age, family income, BMI and parent report of depressive symptoms were not significantly correlated with glycemic control ($p > 0.05$) and thus were not controlled for in analyses examining relationships between sleep and glycemic control. Parent-report of sleeping more than most children was correlated with higher HbA1c ($r = 0.24$; $p < 0.05$). Sleeping more was also correlated with greater area above the curve ($r = 0.28$: $p < 0.05$) and higher average CGM glucose ($r = 0.26$: $p < 0.05$; see Table 2). Trouble sleeping was significantly correlated with greater area above the curve ($r = 0.26$; $p < 0.05$). Sleeping less than most

children, being overtired without good reason and trouble sleeping were not significantly correlated with any of the measures of glycemic control.

Combined, the sleep variables explained a significant portion of the variance in both average CGM glucose ($R = 0.39$, $R^2 = 0.15$, $F = 2.56$, $p = 0.048$) and area above the curve ($R = 0.39$, $R^2 = 0.15$ $F = 2.53$, $p = 0.050$). Sleep variables did not explain a significant portion of the variance in HbA1c or area below the curve (see Table 3).

### • Sleep habits & adherence

Age, family income, BMI and parent report of depressive symptoms were not significantly correlated with adherence ($p < 0.05$) and were not controlled for in subsequent analyses. Sleeping more was significantly correlated with lower adolescent-reported adherence on the SCI and less frequent BG tests (see Table 2). Sleeping less than most children, trouble sleeping, and being overtired without good reason were not significantly correlated with adherence. When examining adherence as reported on the SCI, sleep variables significantly explained 16% of the variance (see Table 3). Sleep variables did not account for a statistically significant portion of the variance in average number of blood glucose checks.

### • Glycemic control & adherence

HbA1c was correlated with poorer self-reported adherence on the SCI and less frequent BG tests (see Table 4). Adherence was not significantly correlated with average CGM glucose, area above the curve, or area below the curve.

## Discussion & conclusion

The current study expands on previous research on sleep disruption in adolescents with T1D by examining how sleep difficulties and deviations in total sleep time relate to adherence to diabetes care. Results of the current study supported relationships between sleep difficulties/altered total sleep time and both adherence and glycemic control in adolescents with poorly controlled T1D. Specifically, parent report of their child sleeping too much was associated with worse metabolic control, higher average CGM glucose and lower adherence. Additionally, sleep difficulties collectively explained approximately 16% of the variance in self-reported adherence.

In the current study, parent report of adolescents sleeping more than other children was associated with multiple measures of adherence and glycemic control. Trouble sleeping was associated

| Table 1. Descriptive statistics for glycem/ic control and adherence variables. | | | |
|---|---|---|---|
| Adherence/glycemic control variable | Mean | Standard deviation | Range |
| HbA1c[†] | 10.2 | 1.7 | 7.8–16.8 |
| Average CGM glucose[‡] | 208.92 | 40.41 | 127–306 |
| % time in hypoglycemia[‡] | 6.4 | 7.26 | 0–28 |
| Area below the curve[‡] | 1.11 | 1.60 | 0–7 |
| % time in hyperglycemia[‡] | 57.29 | 18.20 | 9–98 |
| Area above the curve[‡] | 55.25 | 28.01 | 2–130 |
| Average # of BG tests/day[§] | 3.16 | 1.42 | 0–7 |
| Self-reported adherence[†] | 48.31 | 9.50 | 23–67 |
| [†]n = 72. | | | |
| [‡]n = 63. | | | |
| [§]n = 65. | | | |
| BG: Blood glucose; CGM: Continuous glucose monitor. | | | |

with a greater area above the curve. However, trouble sleeping, sleeping less, and being overtired were not associated with adherence. It is important to note that sleeping more than other children was the most frequently endorsed sleep item. The combination of the small sample size and limited variability on some of the other sleep items likely reduced statistical power. Nonetheless, the results suggest that sleep is important to consider when assessing adherence in adolescents with T1D.

One explanation for the relationship between sleeping too much and HbA1c may be that blood glucose levels impact sleep. There is some support for the relationship between glucose changes and sleep disruption in children [26]. However, it is also important to consider how sleep relates to adherence, as the impact of sleep on adherence may account for the relationship between sleep and glycemic control. For example, children who sleep too much may be sleeping at times when diabetes care behaviors are required, such as BG checks and insulin injections. In addition, given

that sleep difficulties are associated with problems with executive functioning [27], this may interfere with the management of the daily demands of diabetes care. It is important to acknowledge that the relationship between adherence and sleep disruption cannot be assumed to be causal. It may be that children who are less adherent with sleep recommendations are also less adherent to diabetes care.

It is noteworthy that parent-report of sleep difficulties was not correlated with hypoglycemia. One investigation of hypoglycemic episodes at night indicated that the overall sleep structure and pattern did not change for children who experienced hypoglycemia at night [7]. However, children spent significantly more time in slow wave sleep and less time in REM sleep during episodes of hypoglycemia [7]. The lack of findings related to hypoglycemia and sleep in the current study may be due to the absence of objective measures of sleep (e.g., PSG) and nocturnal hypoglycemia or the reliance on parent-report since parents are often not as aware of adolescent

| Table 2. Correlations among study variables. | | | | |
|---|---|---|---|---|
| Study variable | Sleeps more | Sleeps less | Overtired | Trouble sleeping |
| HbA1c[†] | 0.24** | 0.03 | -0.09 | 0.00 |
| Average CGM glucose[‡] | 0.26** | 0.18 | -0.02 | 0.24* |
| Area below the curve[‡] | -0.15 | -0.15 | 0.00 | -0.18 |
| Area above the curve[‡] | 0.28** | 0.15 | -0.01 | 0.26** |
| Average number of BG tests/day[§] | -0.30** | -0.03 | -0.09 | -0.07 |
| Self-reported adherence[†] | -0.34*** | 0.08 | 0.03 | -0.09 |
| Withdrawn/Depressed Scale (raw score) | 0.45*** | 0.20 | 0.57*** | 0.34*** |
| BMI | 0.15 | -0.05 | 0.14 | 0.08 |
| [†]n = 72. | | | | |
| [‡]n = 63. | | | | |
| [§]n = 65. | | | | |
| *p < 0.08. | | | | |
| **p < 0.05. | | | | |
| ***p < 0.01. | | | | |
| BG: Blood glucose; CGM: Continuous glucose monitor. | | | | |

nocturnal behaviors. Thus, further research is needed to examine sleep disruption and night-time hypoglycemia in a sample of adolescents with varying levels of glycemic control and with multiple sources of sleep information.

There are limitations of the current study that should be considered when interpreting results. Data were taken from a study that was not designed to assess the relationship between sleep and diabetes management. Thus, sleep-specific measures and assessment of specific sleep disorders were not included and assessment of sleep was based on parent-report. Although there is support for using the sleep items from the CBCL to assess sleep in secondary analyses [13], the sleep items used for the current study did not correct for age. Thus, additional research with adolescent and parent report sleep measures and objective sleep data (e.g., actigraphy, PSG) is needed to replicate the findings of the current study. Relatedly, parents may underestimate the difficulties their child experiences throughout the night due to not typically being present while their child is sleeping as well as inaccuracy in estimating the amount of sleep adolescents require per night [28]. Parents also overestimate the amount of sleep adolescents receive representing a more idealized pattern of sleep habits [29]. In general, adolescents tend to receive less than a sufficient amount of sleep at night [30] and previous research on adolescents with T1D suggests a similar tendency [6]. The current study did not collect data on total sleep time and research on how total sleep time relates to adherence is necessary. It is also noteworthy that

| Table 3. Linear regressions of sleep predicting adherence and glycemic control. | | | | | | |
|---|---|---|---|---|---|---|
| Adherence/glycemic control variable | Predictor | $R^2$ | F | Unstandardized beta | Standardized beta | t |
| Self-reported adherence | | 0.16 | 3.19** | | | |
| | Overtired | | | 4.14 | 0.23 | 1.84* |
| | Sleeps less | | | 2.46 | 0.12 | 0.90 |
| | Sleep more | | | -6.77 | -0.40 | -3.17*** |
| | Trouble sleeping | | | -2.18 | -0.14 | -0.99 |
| Average number of BG tests/day | | 0.10 | 1.65 | | | |
| | Overtired | | | 0.07 | 0.03 | 0.20 |
| | Sleeps less | | | -0.11 | -0.04 | -0.23 |
| | Sleep more | | | -0.86 | -0.32 | -2.40** |
| | Trouble sleeping | | | -0.08 | -0.03 | -0.20 |
| HbA1c | | 0.12 | 2.24* | | | |
| | Overtired | | | -0.73 | -0.23 | -1.79 |
| | Sleeps less | | | 0.30 | 0.08 | 0.60 |
| | Sleep more | | | 1.11 | 0.37 | 2.87*** |
| | Trouble sleeping | | | -0.10 | -0.04 | -0.26 |
| Average CGM glucose | | 0.15 | 2.56** | | | |
| | Overtired | | | -14.37 | -0.20 | -1.45 |
| | Sleeps less | | | 13.37 | 0.14 | 1.01 |
| | Sleep more | | | 21.54 | 0.31 | 2.27** |
| | Trouble sleeping | | | 12.58 | 0.16 | 1.16 |
| Area below the curve | | 0.06 | 0.98 | | | |
| | Overtired | | | 0.30 | 0.10 | 0.72 |
| | Sleeps less | | | -0.45 | -0.12 | -0.82 |
| | Sleep more | | | -0.47 | -0.17 | -1.19 |
| | Trouble sleeping | | | -0.36 | -0.12 | -0.79 |
| Area above the curve | | 0.15 | 2.52* | | | |
| | Overtired | | | -9.57 | -0.19 | -1.39 |
| | Sleeps less | | | 6.04 | 0.09 | 0.66 |
| | Sleep more | | | 14.88 | 0.31 | 2.26 |
| | Trouble sleeping | | | 10.27 | 0.19 | 1.37 |

*p < 0.08,
**p < 0.05.
***p < 0.01.
BG: Blood glucose; CGM: Continuous glucose monitor.

| Table 4. Correlations between glycemic control and adherence. | | |
|---|---|---|
| Adherence/glycemic control variable | Self-reported adherence | Average number of BG tests/day |
| HbA1c | -0.29* | -0.31* |
| Average CGM glucose | -0.10 | -0.02 |
| Area below the curve | 0.10 | 0.03 |
| Area below the curve | -0.12 | -0.06 |
| *p < 0.05. | | |
| BG: Blood glucose; CGM: Continuous glucose monitor. | | |

the current sample consisted of adolescents in poor control who had agreed to participate in an intervention study. Therefore, it is not known whether the current results would generalize to samples of children in adequate control. An additional limitation is that a comparison group of adolescents without T1D was not included. Finally, given that all data is cross-sectional, conclusions about the directions of the relationship between sleep, adherence and glycemic control cannot be made.

Future research on sleep in children with T1D would benefit from the inclusion of multiple methods of assessment of sleep as well as measurement of other medical and psychosocial variables that may impact sleep and adherence (e.g., depression, hypoglycemic episodes at night). Sleep disorders such as sleep disordered breathing, night eating and circadian rhythm disorders should also be examined in future studies. There are many factors that are known to impact sleep and it may be that other aspects of functioning, such as mood, may impact sleep, adherence and glycemic control and relationships among these variables. Although the current results did not support a relationship between parent report of withdrawal/depressive symptoms and sleep difficulties, additional research with adolescent report of depressive symptoms is needed, as adolescents are typically better than parents at reporting on depressive symptoms [31]. It is also likely that the directionality of the relationships among sleep, adherence and glycemic control may vary across individuals. Longitudinal data would be beneficial in better understanding these relationships.

Results of the current study support the need for routine assessment of sleep for adolescents with T1D who present to pediatric endocrinologists. Typical adolescent changes in sleep patterns on the weekend or during summer months are likely to disrupt diabetes routines and negatively impact adherence to diabetes care. Routine assessment of sleep would provide the needed monitoring of sleep habits and practices during adolescence. Additionally, taken together with results of previous studies on disturbed sleep in adolescents [7–8,26] and adults [32] with T1D, results suggest the need for research on interventions to improve sleep for adolescents with T1D.

## Future perspective
Although future research with objective measures of sleep is needed to better understand relationships among sleep, adherence and glycemic control, communication with endocrine providers about the importance of adequate sleep is likely to be beneficial for adolescents' functioning. It is important to consider whether standard recommendations about sleep should be given to adolescents with T1D, as recommendations often vary across providers. Recommendations may include an emphasis on sleep hygiene and education regarding the importance of sleep for general and disease specific functioning. The integration of sleep interventions within standard diabetes care is likely to be a promising area of focus for the future.

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