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REGULAR ARTICLE

Associations Between Objective Sleep Behaviors and Blood Glucose Variability in Young Children With Type 1 Diabetes

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Abstract

Background Young children with Type 1 diabetes (T1D) are at risk for extreme blood glucose variability, a risk factor for suboptimal glycated hemoglobin A1c (HbA1c) and long-term health complications. We know that a reciprocal relationship exists between sleep and glycemic outcomes in older youth with T1D; however, little research has examined objective sleep in young children (<7 years) with T1D.

Purpose This study examines bidirectional associations between sleep behaviors and glycemic variability in young children with T1D.

Methods Thirty-nine young children with T1D (*M*age 4.33 ± 1.46 years; *M*HbA1c 8.10 ± 1.06%) provided accelerometry data to objectively measure sleep onset latency, number of nighttime awakenings, and total sleep time. We also assessed HbA1c, average blood glucose, and glycemic variability (i.e., standard deviation of blood glucose from device downloads). We evaluated bidirectional relationships using multilevel modeling in SAS, with weekday/weekend as a Level 2 moderator.

Results Children averaged 8.5 ± 1.44 hr of sleep per night, but only 12.8% met current sleep recommendations. Children experienced more nighttime awakenings, higher blood glucose, and more glycemic variability on weekends. Sleep onset latency and nighttime awakenings predicted greater glycemic variability on weekends, and weekend glycemic variability predicted increased nighttime awakenings.

Conclusions Most young children with T1D did not meet sleep recommendations. Young children experienced more nighttime awakenings, higher blood glucose, and increased glycemic variability on weekends only, when routines may be less predictable. Findings suggest that one way families of young children with T1D may be able to decrease glycemic variability is to keep consistent routines on weekdays and weekends.

Keywords: Type 1 diabetes · Glycemic variability · Sleep · Nighttime awakenings · Child

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Introduction

The American Academy of Sleep Medicine (AASM [1]) currently recommends that toddlers (i.e., 1–2 years old) receive 11–14 hr of sleep, preschoolers (i.e., 3–5 years old) receive 10–13 hr of sleep, and school-aged children (i.e., 6–12 years old) receive 9–12 hr of sleep. Unfortunately, many children do not meet current sleep recommendations, with behavioral sleep issues and nighttime awakenings occurring in 20%–30% of healthy toddlers and preschoolers [2]. Poor sleep is associated with increased emotional and behavioral problems [3, 4], as well as disruptions to the development of executive functioning skills in young children [5]. Youth with Type 1 diabetes mellitus (T1D) experience more sleep disruptions, shorter sleep durations, and poorer sleep quality than their same-aged peers without T1D [6, 7]. Importantly, research suggests that sleep disturbances, measured subjectively in older children and adolescents with T1D, relate to suboptimal glycemic outcomes,

decreased insulin sensitivity, behavioral and executive functioning problems, and suboptimal diabetes management (e.g., reduced blood glucose monitoring), and these potentially negative outcomes may increase the risk of both acute and long-term health complications [8–11]. Emerging research in adolescents and adults with T1D demonstrates that sleep and blood glucose potentially interact during the day and night through a 24 hr recursive cycle [12]. Unfortunately, the majority of this research relied on parent- or self-reported sleep data and cross-sectional analyses. Therefore, the aim of the current study is to address several gaps in the literature associating sleep and glycemic levels by providing new data examining these associations longitudinally and using objective sleep and glucose data.

To date, evidence in young adults with T1D suggest a link between higher glycemic variability (i.e., standard deviation (*SD*) of continuous glucose data and changes in glucose concentration) and greater difficulty falling asleep [13]. There is also evidence from a study in school-age youth with T1D suggesting a link between higher glycemic variability and more nighttime awakenings [14]. Combined, these studies provide support for a link between fluctuating glucose levels and fragmented sleep and lower sleep quality in persons with T1D or the potential for glucose levels to influence sleep outcomes. Yet, a review completed by Barone and Menna-Barreto [8] provide evidence suggesting the inverse relationship, with poor sleep (i.e., decreased sleep duration, increased nighttime awakenings, and decreased sleep quality), greater insulin resistance, and glucose intolerance leading to suboptimal glycemic control. Indeed, there is one study in youth with T1D showing an association between poorer sleep quality and higher next day blood glucose values [15], while another study suggests an association between shorter sleep durations and fewer next day blood glucose checks in youth [11]. Interestingly, there is also recent evidence suggesting that differences in sleep patterns between weekdays and weekend days may associate with increased insulin needs for adolescents with T1D [16], which adds additional complexity to the association between sleep and glucose levels.

Another potential gap in the literature relates to sleep in young children with T1D. There are only a few studies in young children (<7 years) with T1D that have used objective measures to examine sleep behaviors. As a matter of fact, one existing study, completed by Jaser et al. [17], reported that young children with T1D can experience elevated sleep disturbances and may not meet sleep recommendations. However, because this study did not link young children's sleep behavior to their routine glucose levels, it remains unknown if there is also an association between sleep and glycemic levels in young children with T1D. We would assert that there is a need for longitudinal research examining objectively measured sleep and glucose levels in young children with T1D because it is highly likely that an association exists. Moreover, it may be important to conduct this research in young children because it is possible that the association could include glucose variability in addition to above-target glucose levels. It is known that young children with T1D are at risk for extreme blood glucose variability due to several developmentally related risk factors, including a greater sensitivity to insulin [18], variable and unpredictable physical activity and food intake patterns [19–22], and difficulty recognizing and communicating the symptoms of a high or low blood glucose level [23]. Unfortunately, in research conducted with older children with T1D, there is also evidence linking glycemic variability to high glycated hemoglobin A1c (HbA1c) levels and long-term health complications [24]. Thus, there may be important clinical implications to understanding if an association exists between sleep behavior and glycemic variability in young children with T1D. Sleep behaviors are potentially modifiable and could offer families another strategy to help them reduce glycemic variability and achieve more optimal glycemic levels in their young child.

The present study builds upon the existing sleep literature in young children with T1D by beginning to fill the knowledge gap specific to how objectively measured sleep behaviors relate to glucose levels in young children. In this study, we measured sleep behaviors using actigraphy to examine possible recursive associations between child sleep behaviors and their blood glucose variability. Specifically, we examined total sleep time (TST), sleep onset latency, and number of nighttime awakenings independently as proxies for sleep behavior in multilevel models of glycemic variability and we hypothesized that greater glycemic variability would lead to poorer sleep outcomes, such as (a) shorter TST, (b) longer onset latency, and (c) more frequent nighttime awakenings. Additionally, as an exploratory hypothesis, we tested the inverse relationship to examine how these sleep behaviors influence child blood glucose variability and we included a dichotomous weekday/weekend variable as moderator in our analyses to examine the differences in these relationships between weekday and weekend days.

Methods

Participants

We recruited families of young children with T1D from a large Midwestern children's hospital's two-state clinic network to participate in a larger intervention that aimed to reduce parental fear of hypoglycemia [25]. Data for this study were collected at the initial study visit and prior to the start of the intervention (ClinicalTrials.gov

#NCT03879642). To be eligible for study participation, children had to be between the ages of 1 and 6 years old, diagnosed with T1D for at least 6 months, on intensive insulin therapy (e.g., multiple daily injections or continuous subcutaneous insulin infusion), and English speaking. Study procedures excluded children who were not currently living with a legal guardian. We approached eligible families during their regularly scheduled diabetes clinic visit or informed families of the study via telephone. A parent/legal guardian provided written informed consent for their child prior to study participation. The hospital institutional review board approved all study procedures prior to study initiation.

Procedures

We collected data during the child's preintervention assessment visit. We met with the family in-clinic or at their home to gather child demographic information, collect a finger-prick HbA1c, and place an accelerometer on the child. We retrieved the accelerometer or provided parents with a prepaid envelope to return the device at the end of the wear period (i.e., 7 days). Parents used a hospital-accessible electronic data integration system (e.g., Medtronic Carelink, Glooko/Diasend) to upload their child's glucometer data from the past 14 days (including days when the child wore the accelerometer). Children received a toy ($10 value) for participating in this phase of the study, while parents could earn up to $85 for completing the larger intervention.

Accelerometry

Children wore the Actiwatch 2 (Philips Respironics, Bend, OR) accelerometer on their nondominant wrist for seven consecutive days and nights based on previous recommendations [26]. Objective measures included: sleep onset latency (e.g., minutes between going to bed and falling asleep), number of nighttime awakenings (e.g., number of bouts or continuous blocks of one or more epochs, where activity level was above the rest threshold during night), and total sleep time (TST; e.g., minutes between sleep onset and wake time minus time spent above the rest threshold during the night). We calculated these proxy measures of sleep behavior for each day using preset algorithms in Actiware version 5 (Philips Respironics) as validated in previous research [27]. Further, using previously published procedures [28], we carefully reviewed young children's actigrahy data to discriminate between sleep and nonwear time and used the epochs surrounding typical sleep onset and wake times to identify obvious artifacts in the data (e.g., lack of physical activity or changes in activity) that may help to improve data accuracy. To calculate child sleep variables, we did not include time spent asleep during the day (i.e., naps). We also did not attempt to limit data collection to "school months" because the majority of young children in our sample were not yet attending primary school, so we observed very little variation in children's days and nights based on the calendar year. However, in line with procedures for the larger study, we did make an effort to avoid data collection during major U.S. holidays as we thought these might cause a temporary change in young children's days and nights.

Blood glucose

Parents uploaded 14 days of blood glucose data from their child's glucometer, as part of the larger intervention study, and the 7 days during which the child also wore the accelerometer were included in the current analyses. We calculated daily blood glucose by averaging all blood glucose values per day, glycemic variability from the *SD* of blood glucose levels per day, and frequency of blood glucose monitoring from the number of blood glucose values recorded per day. We also calculated the coefficient of variation by dividing daily blood glucose variance by the central tendency as an additional measure of glycemic variability. Of note, the larger intervention study from which we extracted our current data did not require that young children use a personal continuous glucose monitor (CGM) as a study inclusion criterion and did not loan CGMs to young children who did not use a personal CGM. Therefore, all blood glucose data were based on manual blood glucose checks as this was available for all participants.

Hemoglobin A1c

As a proxy measure of average glycemic control over the past 3 months, we collected a finger-prick HbA1c from the child using standardized procedures. The hospital central laboratory analyzed all blood samples using automated high-performance liquid chromatography with measurement methods reliable to Diabetes Control and Complications Trial standards (reference range 4.0%–6.0%; Tosoh 2.2, Tosoh Corporation, San Francisco, CA) [29].

Demographics

Parents entered basic demographic and medical history information for their child into an electronic survey using REDCap electronic data capture tools [30]. Demographics included child's date of birth, age at T1D diagnosis, sex, race/ethnicity, family income, socioeconomic status, treatment regimen (e.g., multiple daily injections or continuous subcutaneous insulin infusion), CGM use, parent-reported child sleep duration, and diabetes-related adverse events (e.g., severe hypoglycemia and seizure).

Data Analysis

We estimated multilevel models using SAS PROC MIXED to evaluate the bidirectional relationship between blood glucose variability and sleep behaviors at the "day" level (i.e., Level 1) and "participant" level (i.e., Level 2). To permit interpretation of beta weights, we centered each independent variable at 0 by subtracting the grand mean of that variable from each observation. We then tested the influence of time by entering time as a linear, random linear, quadratic, and random quadratic predictor in four separate models and compared nested models to determine which effect of time was most representative of the data. We defined "time" as a 1 day wave, or 24 hr period, in each of the estimated models. Therefore, each young child had up to seven "waves" of both sleep and blood glucose data that corresponded to each day in the study period (coded 0–6, 0 being the first day of the study period when the child first wore the device). We modeled the effect of time for each outcome to better understand how each variable changed over each 24 hr period with regards to fixed and random effects. Our intent was to understand if: (a) there was a general effect of time and (b) the average effect of time varied across young children. Additionally, we estimated both random and fixed effects of time to establish whether sleep or blood glucose varied systematically as a function of time. If significant, we would then retain time in subsequent models as an additional predictor.

We centered each predictor variable to represent each young child's daily deviation from his or her average predictor value. We then reverse-lagged data included in each model to (a) examine how blood glucose metrics predict nighttime sleep the next day and (b) examine how nighttime sleep predicts blood glucose the following day. In order to address collinearity among glycemic metrics, we examined both the *SD* of blood glucose values and the coefficient of variation as measures of glycemic variability. We fit separate models to examine TST, sleep onset latency, and the number of nighttime awakenings as predictors of glycemic variability. To evaluate bidirectional relationships, we examined glycemic variability as a predictor of sleep behavior variables and added a dichotomous weekday/weekend variable in the model as a Level 2 moderator to examine differences between weekday and weekend days. For the "Weekday" variable, we coded weekdays (Monday, Tuesday, Wednesday, and so forth) as 1 and weekend days (i.e., Sunday and Saturday) as 0. We also entered child age, number of blood glucose checks, number of minutes of moderate-to-vigorous physical activity (MVPA), and HbA1c value as control variables in the models. We decided to control for the number of child blood glucose checks because we used these values to calculate child glucose variability and glycemic control, and we expected that families who checked their child's blood glucose more frequently would have greater opportunity to observe glycemic variability. Furthermore, we decided to control for child MVPA each day since this variable may also relate to child glucose. We placed our covariates in the intercept as a Level 2 variable, with the exception of MVPA, which was a Level 1 variable. For our analyses, we used full information maximum likelihood estimation (FIML) to handle missing data, with the assumption that data were missing at random [31]. In FIML, data missing at random requires that missing values on a given variable be dependent on the other observed variables in the data set and, thus, expects that the model could obtain parameters using likelihood-based estimation that reflect the parameters that would have been estimated had the data been complete. During model estimation, FIML skips the missing responses and assumes the actual responses to be representative of the overall shape of each parameter. Therefore, the FIML estimator does not impute, or fill in, missing values for each variable but, instead, estimates the model parameters and standard errors (*SE*s) using all available raw data. We selected FIML to handle any missing data because this method introduces less bias when estimating the model parameters and *SE*s; FIML does this by using all available data to indicate probable values for vectors of partially complete data. Specific to the rate of missing data for our primary variables, in the current analyses, we had 88% of young children's actigraphy data and 79% of their blood glucose data available to use in our models.

Results

Of the eligible families screened for the larger intervention study, 26 declined to participate and we enrolled 43 families, yielding a recruitment rate of 62.3%. Of the 43 families enrolled in the study, 39 children completed their preintervention study visit. On average, children were 4.33 (*SD* = 1.46) years old, 59% male, and 95% Non-Hispanic White. Children were diagnosed with T1D at 2.47 (*SD* = 1.18) years on average. Children's average HbA1c was 8.14% (65 mmol/mol; *SD* = 1.01%) and 20.5% achieved American Diabetes Association glycemic control targets <7.5% (58 mmol/mol). For T1D management, 79.5% reported using insulin pumps and 43.6% reported using a personal CGM. Parents reported checking blood glucose 7.54 (*SD* = 2.94) times per day on average. All parents checked their child's blood glucose at least 75% of the nights during the study window. One parent endorsed a history of child hypoglycemic seizures and 97% of parents reported at least weekly child hypoglycemic episodes. Parents reported that their child slept

8–10 hr per night on average. Additional demographics are listed in Table 1.

Children averaged 8.5 hr (*SD* = 1.44 hr, range= 4.2–13.7 hr) of TST over the study period and only 12.8% of young children met current sleep recommendations for their age group. Since some research suggests very young children (<4 years) may not have stable sleep patterns [32], we examined sleep differences between children aged 1–4 years (n = 18) and those aged 5–7 years (n = 21). The results of these comparisons revealed no significant differences between age groups for TST or onset latency. We did detect a significant difference for the number of nighttime awakenings ($\beta = -0.16$, $p < .05$), which suggests that young children in the 1–4 years age group experienced more nighttime awakenings than children in the 5–7 years age group.

We report the means and *SD* of each objective sleep variable, overall and separately for weekdays and weekends, in Table 2. We calculated two measures of glycemic variability: the coefficient of variation and the *SD* of blood glucose values. For each model, we examined both of these variability measures separately and found no differences. Therefore, to simplify reporting of our models here, we presented glycemic variability as the *SD* of blood glucose values (alternative models can be found in Supplementary Materials).

Table 1. Descriptive characteristics of study sample (N = 39)

	M ± *SD* or % (*n*)
Age (years)	4.33 ± 1.46
Age at T1D diagnosis (years)	2.47 ± 1.18
Sex (male)	59.0% (n = 23)
Race (Caucasian)	94.9% (n = 37)
Ethnicity (non-Hispanic)	89.7% (n = 35, 3 not reported)
HbA1c (%)	8.14 ± 1.01%
HbA1c in-target (<7.5%)	20.5% (n = 8)
Average blood glucose (mmol/mol)	197.11 ± 62.44
SD blood glucose (mmol/mol)	83.08 ± 22.83
Coefficient of variation (%)	0.43 ± 0.15
SMBG (checks per day)	7.54 ± 2.94
Family income (>$70,000 annually)	59.0% (n = 23)
Treatment regimen (pump therapy)	79.5% (n = 31)
Continuous glucose monitoring (yes)	43.6% (n = 17)
Hypoglycemic episodes (once a day)	15.4% (n = 6)
3–5 times per week	35.9% (n = 14)
1–2 times per week	46.2% (n = 18)
Once a month	2.6% (n = 1)
Hypoglycemic seizure (lifetime)	2.6% (n = 1)
Parent-reported sleep (8–10 hr/night)	97.4% (n = 38)

HBA1c hemoglobin A1c; *M* mean; *SD* standard deviation; *SMBG* self-monitoring blood glucose; *T1D* Type 1 diabetes.

Blood Glucose and Weekday/Weekend

There was a significant difference between blood glucose values across weekdays and weekends such that blood glucose values ($\beta = -22.47$, $p < .05$) and glycemic variability ($\beta = -13.10$, $p < .05$) were lower on weekdays. Intraclass correlations for average blood glucose values indicated that 41.2% of the variability was between person and 58.8% of the variability was within person. The parameter estimates and *SE*s of each sleep variable predicting glycemic outcomes are presented in Table 3. The parameter estimates and *SE*s of blood glucose predicting each sleep variable are presented in Table 4.

TST and Blood Glucose

Intraclass correlations for TST indicated that 30.4% of the variability was between person and 69.6% of the variability was within person. We established a random linear effect of time for both variables. Results of the multilevel models did not reveal a significant relationship between blood glucose variability predicting TST, nor TST predicting blood glucose variability. Neither model revealed significant interactions between weekdays and weekend days.

Onset Latency and Blood Glucose

Intraclass correlations for onset latency indicated that 19.9% of the variability was between person and 80.1% of the variability was within person. We established a random linear effect of time for both variables. The model for onset latency predicting glycemic variability revealed a main effect of within-person onset latency significantly ($\beta = 1.46$, $p < .05$). This effect indicated that, when children experienced a longer period of time between going to bed and falling asleep than typical for themselves, they were more likely to have increased glycemic variability. The model for onset latency predicting glycemic variability further revealed a two-way interaction of sleep onset latency by the weekday/weekend variable ($\beta = 1.35$, $p < .05$). Probing this significant interaction to interpret the conditional effects indicated that children who experienced longer onset latency on weekend nights were more likely to have higher glycemic variability on the weekend days ($\beta = 1.46$, $p < .05$). Lastly, the model for blood glucose variability predicting onset latency revealed a significant main effect ($\beta = 0.13$, $p < .05$) indicating that higher glucose variability related to longer onset latency. There were no additional significant main effects or interactions for this model.

Table 2. Descriptive information of each objective sleep variable during full study period

Outcome measures	Overall *M* ± *SD* (range)	Weekdays *M* ± *SD* (range)	Weekends *M* ± *SD* (range)
TST	514.62 ± 86.50 min (253.00–820.00)	515.40 ± 81.87 min (294.50–800.00)	512.60 ± 98.19 min (253.00–820.00)
# Nighttime awakenings	37.81 ± 14.45 (0.00–83.00)	37.74 ± 14.56 (0.00–76.00)	38.00 ± 14.23 (0.00–83.00)
Onset latency	13.32 ± 16.04 min (0.00–106.00)	13.36 ± 15.82 min (0.00–84.50)	13.22 ± 16.72 min (0.00–106.00)
Blood glucose	197.11 ± 62.44 (80.67–428.33)	194.87 ± 61.14 (80.67–428.33)	215.16 ± 63.98 (95.20–432.00)

TST is the number of minutes between sleep onset and wake time minus time spent above the rest threshold during the night, onset latency is the minutes between going to bed and falling asleep, and number of nighttime awakenings indicate the number of bouts (i.e., continuous blocks of one or more epochs) where activity level was above the rest threshold during night. Information presented in this table describe each measurement during the full 7 day study period.

M mean; *SD* standard deviation; *TST* total sleep time.

Table 3. Associations of predictors and covariates with blood glucose as the dependent variable

	Glycemic variability		Average blood glucose	
	β (*SE*)	*p*	β (*SE*)	*p*
TST				
Intercept	91.78 (15.28)	.76	212.26 (30.12)	.77
BP	0.06 (0.06)	.39	0.19 (0.12)	.12
WP	0.01 (0.06)	.81	0.03 (0.08)	.73
Weekday	**−13.98 (5.03)**	**<.01**	**−22.41 (7.67)**	**<.01**
WP TST × Weekday	−0.01 (0.07)	.96	−0.08 (0.11)	.49
Onset latency				
Intercept	87.03 (14.77)	.76	215.43 (30.25)	.68
BP	−0.14 (0.51)	.79	−0.86 (0.95)	.37
WP	**1.46 (0.55)**	**.01**	−1.53 (0.81)	.06
Weekday	−10.01 (5.9)	.09	**−20.78 (7.75)**	**<.01**
WP onset latency × Weekday	**1.35 (0.62)**	**.03**	1.22 (0.90)	.18
Nighttime awakenings				
Intercept	92.06 (14.62)	.57	219.95 (30.41)	.67
BP	0.21 (0.52)	.69	−0.80 (1.03)	.44
WP	0.71 (0.39)	.07	−1.01 (0.67)	.14
Weekday	**−13.62 (4.94)**	**<.01**	**−22.04 (7.69)**	**<.01**
WP awakenings × Weekday	**−1.20 (0.47)**	**.03**	1.03 (0.84)	.22

Bolded values indicate beta weights with $p < .05$. All models controlled for age, number of blood glucose checks, hemoglobin A1c, and the number of minutes each child engaged in moderate-to-vigorous physical activity. The variable "Weekday" was coded as a dichotomous variable such that weekdays (Monday, Tuesday, Wednesday, and so forth) were coded as 1 and weekend days (i.e., Sunday and Saturday) were coded as 0.

BP between person; *SE* standard error; TST total sleep time; *WP* within person.

Nighttime Awakenings and Blood Glucose

Intraclass correlations for nighttime awakenings indicated that 32.8% of the variability was between person and 67.2% of the variability was within person. We established a random linear effect of time for both variables. The model for nighttime awakenings predicting glycemic variability revealed a significant two-way interaction of nighttime awakenings by the weekday/weekend variable ($\beta = 1.35$, $p < .05$). Probing this significant interaction to interpret the conditional effects indicated that children who experienced more nighttime awakenings on

Table 4. Associations of predictors and covariates with proxies of sleep behavior as the dependent variable

	TST		Onset latency		Nighttime awakenings	
	β (*SE*)	*p*	β (*SE*)	*p*	β (*SE*)	*p*
Glycemic variability						
Intercept	540.42 (82.94)	<.0001	31.19 (15.50)	.05	42.25 (14.77)	.01
GV	0.53 (0.31)	.09	**0.13 (0.06)**	**.03**	0.08 (0.05)	.16
Weekday	63.98 (36.21)	.08	−8.83 (6.71)	.19	9.34 (5.96)	.12
GV × Weekday	−0.65 (0.37)	.08	0.13 (0.07)	.07	**1.72 (0.94)**	**.01**
Average blood glucose						
Intercept	614.47 (96.04)	<.0001	10.88 (17.77)	.55	52.36 (17.14)	.01
BP	0.07 (0.29)	.81	−0.06 (0.05)	.32	0.01 (0.05)	.98
WP	−0.09 (0.24)	.71	−0.06 (0.04)	.18	−0.06 (0.04)	.13
Weekday	0.81 (12.61)	.95	2.19 (2.33)	.35	−0.26 (0.22)	.91
WP avg BG × Weekday	−0.02 (0.29)	.95	0.04 (0.06)	.48	0.06 (0.05)	.26

Bolded values indicate beta weights with $p < .05$. All models controlled for age, number of blood glucose checks, hemoglobin A1c, and the number of minutes each child engaged in moderate-to-vigorous physical activity. The variable "Weekday" was coded as a dichotomous variable such that weekdays (Monday, Tuesday, Wednesday, and so forth) were coded as 1 and weekend days (i.e., Sunday and Saturday) were coded as 0.

BP between person; *GV* glycemic variability; *TST* total sleep time; *WP* within person.

weekend nights were more likely to have higher glycemic variability on the weekend days (β = 0.57, $p < .05$). We observed a reciprocal interaction of glycemic variability by weekdays/weekends in the model between glycemic variability predicting nighttime awakenings (β = 1.72, $p < .05$). Probing this significant interaction to interpret the conditional effects indicated that children who experienced more glycemic variability on weekend days were more likely to have increased nighttime awakenings on weekend nights (β = 1.14, $p < .05$).

Discussion

The aim of the present study was to examine the reciprocal associations between objective sleep behaviors and glycemic variability in young children with T1D. The majority of children in the current sample (i.e., 79.5%) were not meeting the American Diabetes Association glycemic control targets of <7.5% (58 mmol/mol). The average HbA1c observed in the current sample is consistent with average HbA1c observed in 5 year olds with T1D in the T1D Exchange [33]. The results demonstrated that most young children in the sample did not, on average, meet the AASM sleep recommendations of 11–13 hr of sleep duration each night based on their age group [1]. This aligns with results from a previous study demonstrating that young children with T1D may not obtain adequate sleep [17]. Meeting sleep recommendations may be particularly important for young children because some research suggests associations between shorter sleep durations (i.e., <10 hr) and a variety of negative outcomes, including hypotension and low systolic blood pressure [34], increased risk of accidental falls [35], more externalizing problems, and lower cognitive performance [36]. Moreover, in research conducted in older youth and adolescents with T1D, there is evidence associating poor sleep with suboptimal glycemic outcomes, decreased insulin sensitivity, and less frequent blood glucose monitoring [8, 10, 11]. Since we observed inadequate sleep in the majority of the sample, we believe it may be important for diabetes teams to assess sleep in young children and to counsel families on how to alter their child's sleep routine in cases where children are obtaining insufficient sleep. We also believe our results support a need for additional research to identify any other health consequences that may be associated with poor sleep in young children with T1D.

While existing evidence suggests that adolescents with T1D typically obtain significantly more sleep on weekend nights than school nights and frequently alternate between periods of insufficient sleep and sleep compensation [37–39], ours is the first study to objectively assess for weekday or weekend sleep patterns in young children with T1D. In our results, young children experienced more nighttime awakenings, longer onset latency, higher blood glucose, and increased glycemic variability on weekends. We speculate that one reason for these associations may be that families followed a less structured bedtime routine for their child on weekends than on weekdays. We can apply at least indirect support for our speculation with evidence gathered from studies conducted in older youth with T1D that link more optimal child glycemic control to increased family

organization, use of child routines, and consistent structured mealtimes [40–42]. Moving forward, there is a need for additional research to formally assess how differences in young children's bedtime routines on weekdays versus weekends relate to their sleep and T1D outcomes. Until then, we would assert that our results can guide research methodology by underscoring the importance of differentiating weekday versus weekend sleep data in young children with T1D. Clinically speaking, our study results offer at least preliminary evidence of how valuable it may be for diabetes teams to ask families of young children about their child's sleep routines on weekend versus weekdays and to counsel families on the potential sleep and health benefits of maintaining a more consistent child bedtime routine on weekends.

The bidirectional association we observed between children's glycemic variability and nighttime awakenings on weekends suggests that: (a) young children with T1D may be more likely to experience nighttime awakenings following weekend days when their blood glucose is more variable and (b) young children who have more nighttime awakenings on weekend nights may experience increased glycemic variability on the following days. Drawing from the literature, it is possible that both physiological and behavioral factors could explain this bidirectional association. Speaking first to potential physiological factors, several existing studies suggest that there are differences in the sleep architecture of youth with T1D (namely less time in deep sleep stages [43] and more episodes of wakefulness [6]) versus youth without T1D, which may be a result of diabetes physiology [44]. Moreover, Pillar et al. [14] found a link between rapid declines in glucose concentration and more nighttime awakenings and an association between severe nocturnal hypoglycemia and fewer nighttime awakenings in a sample of adolescents with T1D, which may identify some of the mechanisms underlying how youth glycemia relates to their sleep. With respect to behavioral factors, we know that parents of young children frequently monitor their child's blood glucose throughout the night and that parents who experience high anxiety, stress, and fear of hypoglycemia are more likely to engage in nighttime glucose checks, which could introduce additional sleep disturbance if children typically wake up when their parent checks their blood glucose [45, 46]. Moreover, even if children do not wake up when their parents check their blood glucose, it is likely children that will experience sleep disturbances when they require treatment for an out of range blood glucose value. Unfortunately, due to our study design, we cannot determine if the bidirectional association we observed between young children's sleep and glycemic variability could be explained by either physiological or behavioral factors. Therefore, future research studies may consider the role of both physiology and behavioral correlates in the association between family sleep behaviors and child glycemic outcomes in order to help explain this bidirectional association.

One last finding of significance is the association we observed between young children's sleep latency on weekend nights and their glycemic variability on weekend days. Specifically, our results suggested that young children's blood glucose levels may be more difficult to manage following nights when they experienced longer sleep latency. This finding aligns with a previous study by Barone et al. [13], who reported an association between more difficulty falling asleep (i.e., longer onset latency) and higher glycemic variability in a small sample of adults with T1D compared to healthy controls. The only existing research specific to young children with T1D that may relate to our findings is a study in which mothers of young children with T1D report frequent behavioral insomnia and child bedtime resistance as a result of children's T1D treatment regimen [47]. Notably, T1D management may delay child sleep onset if parents increase their glucose monitoring when their child requires nighttime treatment or has an out of range glucose value at bedtime. In our study, we did not ask parents about their child's sleep routine, so we cannot determine why some children may have experienced longer sleep latency. However, we believe our results lend further support for why diabetes care teams may consider routinely assessing children's sleep quality and the occurrence of sleep disturbances at regularly scheduled clinic visits. Sleep is potentially modifiable and there are several evidence-based strategies that diabetes care teams could share with families if their child is experiencing significant sleep onset difficulties on weekend nights [2, 48, 49]. Further, some evidence suggests that psychological variables (i.e., stress, mood) could impact sleep onset and blood glucose outcomes in youth with T1D and is an area in need of additional research in young children [12].

Strengths

The present study provides novel data regarding the bidirectional association between objectively measured child sleep behaviors and blood glucose variability. Further, the present study is one of only a few studies [17] to use an objective sleep measure in youth with T1D rather than solely relying on parent-reported sleep data. We believe our study is rigorous because we examined interindividual glycemic variability to test for a bidirectional association between children's daytime glucose and their sleep behaviors. We also believe our study is rigorous because we did not aggregate our sleep data to create an average sleep variable for analysis. Our study used multilevel modeling

and one benefit of this technique is the ability to retain nested data and analyze interindividual and intraindividual data with appropriate power, longitudinally. Furthermore, our results demonstrate the importance of differentiating between weekdays and weekends when examining objective sleep behaviors and glycemic outcomes. Few studies in the literature make this distinction and, therefore, may miss important variability between child sleep behaviors and glycemic outcomes on weekday and weekend days.

Limitations

There are also some limitations to consider when evaluating our results. First, our study did not include a sleep log for parents to complete while children wore the accelerometer. A sleep log is typically included alongside an objective assessment of sleep for increased validity and accuracy for determining bedtimes and waketimes. We elected not to include a sleep log in an effort to limit family burden with respect to the larger study. Thus, we used published procedures to help us to determine children's bedtimes and waketimes based on their actigraphy data but acknowledge that it may be helpful to collect sleep logs to confirm data accuracy in future studies. Second, there are several important factors we were unable to include in the current study. For example, we did not include a record of food intake to examine how the consumption of macronutrients influences glycemic variability during the day. Furthermore, we did not assess for child weight or sleep disorders (e.g., obstructive sleep apnea), which are two additional factors that can impact sleep behavior and may warrant future investigation in youth with T1D. Third, the dichotomous variable of weekday/weekend is a weak proxy for structured and unstructured days. It is possible that future research could uncover stronger associations if researchers can characterize this variable in a more robust way. Fourth, our sample was small and largely homogeneous with regard to family income, race, and ethnicity. While our sample's demographics are typical of the families who receive their child's diabetes care from the participating clinic [50, 51] and for youth with T1D in the USA [33], this may limit the generalizability of our findings. Lastly, our measure of glycemic variability was based on glucometer data and not on CGM data. As a result, it is possible that our data do not provide a complete picture of young children's glycemic levels. Therefore, future studies should consider examining similar relationships in young children with T1D and using CGM devices in order to see if the observed associations between young children's sleep behavior and glycemic variability remain.

Conclusions

Our results suggest that young children with T1D are not meeting current sleep recommendations and young children experienced more nighttime awakenings, higher blood glucose, and increased glycemic variability on weekends. Additional technology to increase monitoring, such as CGM, the use of closed-loop systems, and maintaining a more consistent bedtime routines on weekend days may help young children with T1D to achieve lower glycemic variability and fewer sleep disruptions and, thereby, potentially experience better T1D outcomes. Furthermore, in order to better understand relationships between child glycemia and sleep behaviors, diabetes providers should consider integrating measures of sleep quality into routine T1D care and may counsel families how to follow healthy sleep behaviors across weekdays and weekend days. Diabetes care teams often stress the importance of routines when discussing diabetes management and currently assess other child health factors (i.e., diet and physical activity). Thus, we believe it may be feasible and practical for diabetes care teams to also consider measuring child sleep with a brief self-report measure [12] or by inquiring about children's sleep quality when routinely collecting health information during clinic visits.

Supplementary Material

Supplementary material is available at *Annals of Behavioral Medicine* online.

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Compliance With Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards No competing financial interests exist for authors A.D.M., A.M.M., A.E.N., and S.R.P. MAC is the chief medical officer for Glooko, has consulted with Medtronic Diabetes, Eli Lilly, and receives research support from Abbott Diabetes. All procedures in the present study were performed in accordance with the ethical standards of the institutional research committee.

Authors' Contributions S.R.P. and M.A.C. developed the initial concept for the study and obtained funding. A.D.M., A.M.M., and A.E.N. collected the data. A.D.M. and S.R.P. ran the analyses and wrote the first draft of the manuscript. All authors reviewed and commented on subsequent drafts of the manuscript.

Ethical Approval The protocol of the study was approved by the Institutional Review Board at Children's Mercy Hospital.

Informed Consent Caregivers provided written consent for their participation and consent for their child's participation.

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