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Daily Variations in Sleep and Glucose in Adolescents with Type 1 Diabetes

Stephanie Griggs, PhD, RN,
Instructor of Nursing, Frances Payne Bolton School of Nursing, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, Ohio 44106

Nancy S. Redeker, PhD, RN, FAAN,
Beatrice Renfield Term Professor of Nursing & Professor of Medicine, Yale University, School of Nursing and School of Medicine, West Haven, Connecticut, USA 06477

Sangchoon Jeon, PhD,
Research Scientist, Yale University, School of Nursing, West Haven, Connecticut, USA 06477

Margaret Grey, DrPH, RN, FAAN
Annie Goodrich Professor of Nursing and Professor of Pediatrics, Yale University, School of Nursing and School of Medicine, West Haven, Connecticut, USA 06477

Abstract

Objective—We used multilevel models (MLMs) to determine person (between-persons) and day level (within-person) associations between glucose variability indices and sleep characteristics in adolescents with type 1 diabetes (T1D).

Methods—Adolescents with T1D (Mean age 13.4 ± 1.8 years; 37.8% male; mean HbA1c 8.2 ± 1.2%, 66 mmol/mol) monitored their sleep and glucose patterns concurrently for 3–7 days with a wrist actigraph on their nondominant wrist and a continuous glucose monitor (CGM) (their own or a provided, blinded CGM). Glucose variability indices included J index, coefficient of variation, low and high blood glucose risk indices (LBGI and HBGI), time in range, and sleep characteristics, including bedtime, wake time, total sleep time, sleep efficiency, wake after sleep onset, awakenings, and sleep fragmentation index.

Results—More overall glucose variability was associated within person, more sleep disruptions (more awakenings and more fragmentation) or poorer sleep in our study (earlier wake time or longer wake after sleep onset). Also, more time spent in hypoglycemia <70mg/dL and a higher

Corresponding Author: Stephanie Griggs, Ph.D., R.N., Instructor of Nursing, Frances Payne Bolton School of Nursing, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, Ohio 44106, stephanie.griggs@case.edu.

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LBGI was associated within person with earlier wake time indicating poorer sleep. However, a lower LBGI was associated with a later between-persons wake time.

Conclusions—Monitoring over a longer period of time in subsequent studies would allow researchers to determine the within person association between habitual short sleep duration and glucose variability. Providers should regularly assess sleep habits in adolescents as a way to improve glycemic control. Targeting a euglycemic range overnight is also important to promote better sleep and to decrease sleep disruptions.

Keywords

adolescence; sleep; type 1 diabetes; glucose variability

Habitual short sleep duration, defined as less than 7.5 hours per night for ages 14–17 and less than 8.5 hours for ages 10–13 years, is a major public health concern affecting more than two-thirds of adolescents (68–83%) ages 10 to 16 years in the United States.[1] Meeting the recommended sleep duration of 8–10 hours per night for ages 14–17 and 9–11 hours for ages 10–13 years[2] is difficult due to the interaction of biological (e.g., puberty, circadian, or homeostatic changes) and environmental factors (e.g., early school start times, social pressure, and academic workload).[3]

Adolescents with type 1 diabetes (T1D) have an additional layer of responsibility in managing an intensive regimen including frequent or continuous glucose monitoring, dietary management, insulin administration, and engaging in regular physical activity. Further, fear of hypoglycemia, hypoglycemia, hyperglycemia with associated symptoms (e.g., nocturia, polyphagia, polydipsia), and device alarms often delay bedtimes and disrupt sleep overnight.[4] Subsequently, adolescents with T1D get significantly less sleep, with more day-to-day variability in their sleep duration than those without diabetes.[4,5] Sleep variability is associated with more stress, more depressive symptoms, and more glucose variability in adolescents with T1D.[4,5]

The role of short sleep duration in glucoregulation has been examined extensively both in adults without chronic conditions[6] and in children and adults with T1D.[7] Short sleep duration and more awakenings overnight lead to increases in cortisol and thyroid stimulating hormone and poorer glucose metabolism.[8] Adolescents with T1D have a more pronounced sleep extension on weekends compared to controls without diabetes.[4]

There are only a few studies where the direct effect of glucose fluctuations on sleep was examined among adults with T1D.[7,9] This is likely due to the heavy reliance on HbA1c levels for glycemic control and/or intermittent glucose monitoring[4] with the inability to detect patterns overnight. HbA1c is the gold standard for determining glycemic control in research and practice, yet it does not account for glycemic variability or hypoglycemia in those with T1D. Glycemic variability, fluctuations outside of range, is also associated with premature micro- and macrovascular complications,[10] and has gained attention in research, particularly with the advent of continuous glucose monitors (CGMs) to detect these fluctuations. These fluctuations are significant because they contribute to endothelial damage and the onset or progression of atherosclerosis.[11]

On the other hand, there has been minimal research on the experimental manipulation of sleep, especially in adolescents. The impact of sleep restriction (only 4 to 5 hours of sleep per night, for a period ranging from a single night to several weeks) on impaired glucose tolerance and insulin sensitivity has been demonstrated in adults without chronic conditions[12] and in one study of adults with T1D.[13] In people without chronic conditions, extending sleep over 6 weeks to 12 months in natural environments is feasible and contributes to improved insulin sensitivity and glucose levels,[14] improved neurocognition in adults and adolescents,[15] and improved psychological symptoms in adolescents.[16] Extending sleep in adolescents with T1D led to more time in range (7.4% improvement in mean glucose levels) measured via CGM in mg/dL based on preliminary results (N = 111 adolescents).[17]

It is critical to examine both within-person and between-persons associations between sleep and glucose levels to inform our understanding of how these parameters interact in adolescents with T1D. These analyses may help to identify key modifiable sleep targets to improve glucose variability and glycemic control in adolescents with T1D, who are at a high risk of premature micro- and macrovascular complications. The aim of this analysis was to determine person (between-persons) and day level (within-person) associations among glucose variability indices (J index, coefficient of variation, low and high blood glucose risk indices [LBGI and HBGI], time in range) and sleep characteristics (bedtime, wake time, total sleep time, sleep efficiency, wake after sleep onset, awakenings, and sleep fragmentation index) in adolescents with T1D. We hypothesized that more glucose variability would be associated with more sleep disruptions (more awakenings, higher fragmentation index) and poorer sleep (longer wake after sleep onset, later bedtimes, earlier wake times, poorer sleep efficiency, shorter total sleep time).

Methods

This study was a secondary analysis of a pilot study where data on sleep (objective and self-report), coping, adherence, and adjustment were collected from adolescents using a between-persons descriptive design with variables averaged across all days of monitoring.[5] Full details of the study procedure have been reported previously,[5] and details pertinent to this report are summarized below:

Adolescents monitored their sleep and glucose patterns concurrently for 3–7 days with a sleep-wake activity monitor on their nondominant wrist (Philips Respironics Actiwatch 2) and either their own CGM or a provided, blinded Medtronic iPro CGM. Within-person and between-persons variations in sleep and glucose patterns using the actigraphy and CGM data were analyzed. The study followed the World Medical Association Declaration of Helsinki for research involving human subjects,[18] and it was approved by the Yale University Human Investigation Committee (#1507016174).

Procedures

Adolescents with T1D and their caregivers were recruited from the Yale Children's Type 1 Diabetes Program. Adolescents between the ages of 10–16 years, diagnosed with T1D for at least 6 months, without any other major health problem (e.g., other chronic medical

condition or major psychiatric illness), not currently participating in other intervention studies, and able to read/speak English fluently were eligible to participate. The age range was chosen to capture the period of deteriorating glycemic control during the transition to adolescence.

Trained research assistants (RAs) approached adolescents and their caregivers during regularly scheduled clinic visits. After informed consent and verbal assent were obtained, adolescents and caregivers completed questionnaires, and the adolescents completed a test of executive function (Trail Making Test A and B). Adolescents were given the Philips Respironics Actiwatch 2,™ a wrist-worn actigraph, to wear continuously on their nondominant wrist for 1 week, removing it only for bathing. They were instructed to depress the event marker at “lights out” and “lights on” times to demarcate time in bed. Adolescents were asked to record bedtimes and wake times in a paper sleep diary. Adolescents wore the CGM concurrently with the Actiwatch. Adolescents and caregivers received a small incentive for their time to complete questionnaires and received an additional incentive for returning the watch and sleep diary.

Participants

A total of 68 participants (65% response rate) consented and completed baseline questionnaires. Of these, 40 wore the CGM and Actiwatch concurrently for 3 to 7 continuous days/nights (mean = 6.4 ± 1.1 days/nights), and 38 were included in this analysis. Two were excluded because the sleep and glucose data dates/times did not align. Some of the provided and blinded CGMs came back without data. Participants were offered a chance to re-wear the CGM and Actigraph and four successfully completed this request. The data presented in this article represent a total of 229 reports of daily CGM and sleep actigraphy data. A sample size of 38 and 229 reports is comparable to previously published studies using daily actigraphy and/or glucose data among adolescents/young adults.[7]

Measures

Demographics and Clinical Characteristics—Age, duration of diabetes, most recent HbA1c level, and medical history data were collected from the electronic medical record. Parents completed the following via a self-report paper questionnaire: family demographics, including income, race/ethnicity, parent education level, marital status, and adolescent/young adult’s gender.

Objective Sleep Characteristics—Adolescents wore the Philips Respironics Actiwatch 2™ actigraphy devices, which are used to estimate sleep and wake intervals. Actigraphs are valid and reliable instruments to estimate sleep activity.[19] Actigraph data were collected in 30-second epochs.[20] The following objective sleep outcomes were derived: bedtime, wake time, total sleep time, sleep efficiency (%), wake after sleep onset (minutes), awakenings (number), and sleep fragmentation index (% movement index + % fragmentation index). Daily scores of each of these variables were used for this analysis. Actigraphs provide the greatest agreement and least bias compared with Polysomnography (PSG) in T1D for sleep parameters (ICC 0.38 to 0.78) with nonsignificant associations ($p > 0.65$) for all sleep parameters (e.g., total sleep time, sleep efficiency, wake after sleep onset, and sleep

fragmentation index), except for sleep onset latency (p = 0.04).[21] Sleep onset latency is considered a less precise measure compared to PSG.[21]

Self-Report Sleep Characteristics—The Pittsburgh Sleep Quality Index (PSQI) was used to measure self-reported sleep characteristics.[22] The PSQI is a 19-item self-report measure that is used to assess sleep duration and quality during the past month.[22] Each item is grouped into 1 of 7 components and each component yields a score from 0–3, with 3 indicating poor quality. [22] Component scores are summed and range from 0–21, with a higher score indicating poorer sleep quality.[22] The total PSQI score was used to describe the sample. Cronbach's alpha in this sample was 0.87.

Glucose Variability—CGM data from the time the wrist actigraph was worn were downloaded directly from each adolescent's existing or provided, blinded CGM to capture day level glucose patterns. Participants inserted a small sensor wire just under their skin using an automatic inserter.[23] CGMs are accurate across a wide range of levels.[24] CGM systems provide real-time, dynamic glucose information every five minutes—up to 288 readings in a 24-hour period, and values are measured in mg/dL.[24] Glucose variability was calculated from CGM with the following indices: Mean ± SD, J index—overall glucose variability (calculated as 0.001 * $(\bar{x} + SD)^2$, low and high blood glucose risk indices (LBGI and HBGI),[24] and time in range (calculated as % in target range 70–180 mg/dL, hypoglycemia <70 mg/dL & severe hypoglycemia <54 mg/dL, hyperglycemia > 180, and severe hyperglycemia >250 mg/dL).[24] J index represents the overall quality of glucose variability excluding severe and persistent hypoglycemia. LBGI and HBGI represent the degree of clinical severity risk scores, mean amplitude of glucose excursion (MAGE), which is the average amplitude of upstrokes or downstrokes with magnitude >1 SD, and mean of daily differences.[24] The coefficient of variation (CV) is the ratio of the SD to the mean, and this was examined continuously and ≥ 36%.[24] The daily score was computed for the following glucose variability variables: (J index, CV, time in range, LBGI, and HBGI). The other glucose indices were used to describe the sample.

Data Management

Actigraph data were scored with Actiware version 5 software. Actigraph rest intervals for bedtime and wake time were hand scored from a combination of the event marker and a diary, with preference given to the event marker. CGM data were calculated with GlyCulator version 2.0 software.[25] GlyCulator 2.0 was created to calculate glycemic variability indices from raw CGM data following guidelines for CGM reporting specified in the International Consensus on Use of Continuous Glucose Monitoring.[26] Questionnaires and diary forms, collected in a scannable format, were examined for improperly filled-in items and missing data, scanned and exported into to an MS Access database. Data were screened for missing or out-of-range values and distributions of continuous variables. Descriptive statistics were calculated for all variables and analyzed using SPSS version 26 for Mac (IBM Corp: Armonk, NY) and SAS 9.4 (SAS Institute, Inc., Cary, NC, USA). Skewed variables were log-transformed, and all variables were standardized for 0 (mean) and 1 (standard deviation) before analyses. The intraclass correlation coefficient (ICC) was computed to measure the relative individual variability in daily glucose and sleep outcomes defined as the ratio of

variability between individuals to total variability (individual variability + daily variability). Greater ICCs, ranged 0 to 1, indicate relatively less daily variability.

Data Analysis

We assessed bivariate associations among sleep characteristics with glucose variability indices at the person level using Pearson correlation coefficients. A series of multilevel models (MLMs) were performed to examine the effects of glucose variability on sleep characteristics at both the day and person level. Day level glucose reports were level 1 variables (N= 292) nested within person at level 2 (N = 38 individuals). To address missing data, in bivariate analyses we used the individual score averaging day-to-day scores; therefore, there are no missing data presented in Table 2. MLM uses maximum likelihood (ML) to handle missing data points; therefore, all 38 participants were included in the MLMs. The MLMs were set with a random intercept for individual variability, and the sleep characteristics were predicted by day and person average glucose variability indices. This approach places the fewest restrictions on the models and allows variances and covariances to be freely estimated from the data. The person level represents how the average glucose variability index (between persons) is associated with sleep characteristics, and the day level represents how the daily level of glucose (within person) is associated with sleep characteristics.

Results

Descriptive Analyses

Adolescents in the study had a mean age of 13.4 (SD = 1.8) years, were 37.8% male, 84.4% White non-Hispanic, and 28.1% of their parents reported an income < $80,000/year. The mean diabetes duration was 7.5 years (SD = 4.4), mean HbA1c was 8.2% (SD = 1.2, 66 mmol/mol), and most used an insulin pump (97.3%) and CGM (60%) for treatment. For CGM systems, participants used either Dexcom (68.4%, n = 26) or were provided with iPro (31.6%, n = 12). The mean glucose was 170.9 (SD = 41.3) mg/dL, mean CV was 32.5 (SD = 12.5), and mean MAGE was 168.6 (SD = 31.9) measured via CGM across the 7 days.

We present the descriptive statistics of the sleep characteristics and glucose variability indices, including the daily average means and standard deviations, daily variability means and standard deviations, and ICCs in Table 1. The majority of our sample slept less than 8 hours on average (78.9%, n = 30), with a range from 5.05 hours to 8.63 hours across the days of monitoring. Adolescents reported a mean PSQI global sleep quality score of 6.9 (±1.5), which is above the clinical cutoff for poor sleep quality.[5]

Participants ranged from 3 to 7 days of concurrent monitoring (mean duration = 6.4 ± 1.1 days/nights). We present the bivariate associations between sleep characteristics and glucose variability indices at the daily level in Table 2. The bivariate associations between sleep characteristics and glucose variability indices at the person level were not significant. Participants slept slightly, but not significantly longer on the weekends compared to weekdays (451 minutes vs. 437 minutes), therefore we did not control for weekday vs. weekend differences in the models.

Multilevel Models of Glucose Variability and Sleep Indices

As shown in Table 3, glucose variability was significantly associated with sleep characteristics (wake after sleep onset, awakenings, and wake time) mostly at the day level (within-person). Specifically, a significantly earlier wake time occurred on days when adolescents had a higher LBGI ($\beta = -0.13$, $p = .020$) and spent more time in the hypoglycemic range (<70 mg/dL, $\beta = -0.17$, $p = .037$). However, a lower LBGI was significantly associated with later wake time at the person level (between-persons) ($\beta = 0.28$, $p = .005$). The associations among other glucose variability indices (J index, HBGI, time in range) and wake time were not significant at the person or day level.

A significantly longer wake after sleep onset occurred on days with more overall glucose variability (J index) ($\beta = 0.20$, $p = .013$), higher HBGI ($\beta = 0.17$, $p = .040$), lower LBGI ($\beta = -0.19$, $p = .019$), and less time spent in hypoglycemia (<70 mg/dL, $\beta = -0.26$, $p = .006$). The associations were not significant for glucose variability indices and wake after sleep onset at the person level.

More awakenings were seen on days with more overall glucose variability ($\beta = 0.16$, p = .039) and with less time spent in hypoglycemia (<70 mg/dL, $\beta = -0.24$, $p = .014$). More sleep fragmentation was seen on days with lower LBGI ($\beta = -0.18$, $p = .02$). Neither awakenings nor sleep fragmentation were significantly associated with any of the glucose variability indices at the person level. Also, the person or day level associations between glucose variability indices and bedtime, total sleep time, or sleep efficiency were not significant in our sample.

Discussion

More overall glucose variability was associated within person with more sleep disruptions (more awakenings and more fragmentation) or poorer sleep in our study (earlier wake time or longer wake after sleep onset). Also, more time spent in hypoglycemia <70 mg/dL and a higher LBGI was associated within person with earlier wake time, indicating poorer sleep. Our findings were similar to previous studies where naturally occurring rapid decreases in glucose or periods of nocturnal hypoglycemia were associated with more frequent awakenings or movements during sleep in adolescents with T1D [27] and rapid glucose variations were associated with more movements in young adults with T1D.[7] Specifically, in a study of 15 adolescents with T1D (mean age 12.6 ± 2.9 years), rapid decreases in glucose measured via CGM were associated with more frequent awakenings measured via PSG over 1 night of sleep.[28] We were unable to corroborate our finding that more time spent in hypoglycemia (<70 mg/dL) and higher LBGI were associated with an earlier wake time, but this is likely due to the short concurrent monitoring of sleep and glucose in previous studies (1 night to 60 hours).

Most researchers have focused on the between-persons level of analysis, and they indicate that, at a group level, adolescents with T1D with shorter sleep duration or more variability in sleep duration have poorer glycemic control and more glucose variability,[4] and those with poor glycemic control tend to be at a greater risk for shorter sleep duration.[29] These researchers have not addressed whether adolescents with more glucose variability or less

time in range experience poorer sleep or have more sleep disruptions within-person. We provide a systematic evaluation of the person and day level associations between glucose variability and sleep characteristics for multiple days in adolescents with T1D in their natural home environments. We found significant associations between glucose variability, wake time, wake after sleep onset, awakenings, and sleep fragmentation mostly at the day level (within-person), with one significant association at the person-level (between-persons). Day level glucose variability indices may be more useful in determining daily sleep characteristics rather than person level glucose variability. We provide insight into the extent to which glucose fluctuations, both high and low, disrupt sleep in adolescents with T1D.

The association between total sleep time and glucose variability was not significant in our study at the person or day level. This finding has been supported in previous studies of adolescents with T1D.[4] The methods in those studies were different, with researchers in one study relying on intermittent glucometer testing to determine glucose variability,[4] and other studies focusing on self-reported sleep duration.[30] Also, in all of these studies, total sleep time was averaged across the monitoring period, and associations reported were between-persons.

Adolescents may maintain a higher glucose level at bedtime to avoid hypoglycemia overnight (e.g., fear of hypoglycemia). This higher glucose level likely leads to more awakenings due to the symptoms associated with or need to manage hyperglycemia or hypoglycemia.[31] In a study of 18 adolescents ages 10–16 years with T1D, hypoglycemia was significantly associated with more motor activity detected by actigraphy over 1 night.[27] In two studies, it was reported that emerging adults with T1D exhibit an impaired awakening response to induced hypoglycemia compared to matched controls without diabetes.[32] This failure to awaken from sleep increases the risk for those with T1D to suffer prolonged and potentially fatal hypoglycemia.[33] Sleep disturbances for caregivers and adolescents with T1D have been reduced in pilot studies of hybrid closed-loop systems with computer-based algorithms for insulin therapy;[34] however in a study of 16 middle aged adults and 12 adolescents with T1D, no differences were noted in self-reported sleep quality for those with T1D using a closed-loop system or insulin pump.[35] Although these devices have shown improvements in glycemic control,[35] more research is needed to determine the effect of these technologies on sleep quantity and quality.

Conclusions

Given the observational nature of the current study, the specific mechanisms for the associations between glucose variability and more wake after sleep onset/more awakenings among adolescents with T1D remain unclear. Sleep fragmentation from multiple arousals results in decreased insulin sensitivity in individuals without chronic conditions.[36] Hormones secreted during sleep and wake states can impact glucose levels. Specifically, growth hormone secreted during sleep reduces insulin sensitivity,[37] and increased glucose levels are seen with increased levels of growth hormone and cortisol.[14] Other factors, such as age, diet, exercise, and insulin-dosing regimen influence time-varying glucose levels. We did not collect data about whether the adolescents in the present study were in school, so we cannot determine if any differences in sleep or glucose characteristics are related to school

vs. summer schedule differences. Despite not controlling for these other factors in the natural setting in the present study, our findings are novel in demonstrating these associations over a longer period of time in the natural setting than previous studies. Our participants ranged from 3 to 7 days of concurrent monitoring; however, only one participant monitored for 3 days (mean duration = 6.4 ± 1.1 days/nights). While this duration may not fully capture habitual sleep patterns, 72 hours is adequate for monitoring sleep based on current recommendations for actigraphy.[38] Future studies that control for hormonal, dietary, and insulin treatment effects and over a longer period of time (e.g., over two weeks) can provide further insight into the findings we report here.

Sleep is an unappreciated target to improve glucose variability and glycemic control in diabetes care and research. Extending sleep is both feasible and led to an improvement in target range for adolescents with T1D based on previous studies.[17] Given the growing body of literature on the detrimental impact of sleep deprivation on glucoregulation in adults without chronic conditions and the role of poor sleep in poorer glycemic control in adolescents with T1D, practitioners should aim to optimize sleep in this population. Providers should assess sleep habits in adolescents regularly as a way to improve diabetes management, glucose variability, and glycemic control. Targeting a euglycemic range overnight is also important to promote better sleep and to decrease sleep disruptions. Monitoring over a longer period of time in subsequent studies would allow researchers to determine the within person association between habitual short sleep duration and glucose variability. Understanding glucose variability and addressing barriers to sleep may allow for improved management and clinical outcomes for adolescents with T1D.

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Table 1.

Descriptive Statistics of Sleep Characteristics and Glucose Variability Indices (N=38)

Variables	Daily Average (Individual Means)		Daily Variability (Individual Standard Deviations)		Intraclass Correlation Coefficient (ICC)
	Mean	(SD)	Mean	(SD)	
Sleep Characteristics					
Bedtime (hh:mm)	23:24	(1:10)	00:57	(0:39)	0.463
Wake time (hh:mm)	6:54	(1:51)	1:34	(1:44)	0.326
Total Sleep Time (min)	433.1	(45.6)	72.4	(46.1)	0.152
Sleep Efficiency (%)	85.3	(5.3)	4.9	(3.8)	0.373
WASO (min)	41.8	(14.8)	15.1	(11.4)	0.297
Awakenings*	33.7	(8.4)	8.8	(5.1)	0.352
Sleep Fragmentation Index	17.1	(4.9)	5.6	(3.3)	0.260
Glucose Indices					
J Index	58.3	(23.3)	20.5	(12.77)	0.409
CV	32.1	(8.4)	10.0	(4.9)	0.193
Low Blood Glucose Index	1.5	(2.73)	1.7	(2.86)	0.262
High Blood Glucose Index	11.0	(6.04)	5.2	(3.01)	0.444
Time in Range of 70–180mg/dL %	50.6	(17.20)	19.2	(6.52)	0.343
Hypoglycemia (<70mg/dL) %	4.2	(5.03)	6.1	(9.24)	0.002
Hypoglycemia (Time <54mg/dL) %	3.4	(11.29)	3.8	(8.53)	0.569
Hyperglycemia (Time >180mg/dL) %	45.2	(18.25)	19.8	(7.15)	0.335
Hyperglycemia (Time >250mg/dL) %	17.8	(15.67)	13.4	(8.99)	0.444

Note. Awakenings is the number of wake bouts. The ICC represents the associations within subject.

Table 2.

Bivariate Associations between Sleep Characteristics and Glucose Variability Indices – Person Level (N=38)

	Bedtime β±StdErr (p-value)	Wake Time β ±StdErr (p-value)	Total Sleep Time β ±StdErr (p-value)	Sleep Efficiency β ±StdErr (p-value)	WASO β±StdErr (p-value)	Awakenings β ±StdErr (p-value)	Sleep Fragmentation Index β±StdErr (p-value)
Index	−0.04±0.16 (.814)	0.13±0.16 (.439)	0.12±0.16 (.482)	−0.04±0.16 (.809)	0.02±0.16 (.881)	0.08±0.16 (.633)	0.07±0.16 (.692)
CV	−0.18±0.16 (.164)	0.26±0.16 (.121)	0.21±0.16 (.203)	−0.09±0.16 (.604)	0.16±0.16 (.340)	0.28±0.16 (.087)	0.18±0.16 (.283)
Proportion of CV>36	−0.44±0.60 (.468)	1.09±0.58 (.066)	0.34±0.60 (.570)	−0.46±0.60 (.448)	0.87±0.59 (.145)	0.01±0.60 (.987)	0.89±0.59 (.139)
Low Blood Glucose Index[a]	−0.07±0.18 (.676)	0.18±0.17 (.297)	0.11±0.17 (.523)	−0.02±0.17 (.918)	0.09±0.16 (.579)	−0.20±0.16 (.195)	−0.08±0.16 (.620)
High Blood Glucose Index	0.05±0.16 (.783)	0.04±0.16 (.827)	0.05±0.16 (.779)	−0.03±0.16 (.859)	0.03±0.16 (.851)	−0.07±0.16 (.681)	−0.01±0.16 (.970)
Time in Range of 70–180mg/dL %	−0.10±0.16 (.564)	0.05±0.16 (.766)	0.04±0.16 (.796)	0.08±0.16 (.607)	−0.12±0.16 (.474)	0.17±0.16 (.287)	0.01±0.16 (.941)
Hypoglycemia <70mg/dL %	−0.20±0.17 (.911)	0.05±0.17 (.795)	0.04±0.17 (.829)	−0.00±0.18 (.980)	−0.03±0.17 (.848)	−0.07±0.16 (.658)	−0.07±0.17 (.711)
Hypoglycemia <54mg/dL %	0.05±0.21 (.828)	0.11±0.22 (.634)	0.13±0.19 (.502)	−0.05±0.22 (.829)	0.23±0.20 (.264)	0.4±0.18 (.811)	0.05±0.19 (.797)
Hyperglycemia >180mg/dL %	0.10±0.16 (.556)	−0.10±0.16 (.551)	−0.07±0.16 (.678)	−0.07±0.16 (.677)	0.09±0.16 (.604)	−0.19±0.16 (.249)	−0.01±0.16 (.948)
Hyperglycemia >250mg/dL %	−0.07±0.17 (.696)	−0.14±0.17 (.427)	0.11±0.17 (.534)	0.04±0.17 (.808)	0.07±0.17 (.697)	−0.11±0.17 (.499)	−0.11±0.17 (.514)

Note.βs are equivalent with Pearson correlation coefficients and obtained in multilevel models with standardized variables with zero mean and one standard deviation.

[a]indicates log-transformed variables. P values are rounded.

Table 3.

Person- and Day-Level Effects of Glucose Variability on Sleep Characteristics – Multilevel Models (N=38)

		Bedtime β±StdErr (p-value)	Wake Time β±StdErr (p-value)	Total Sleep Time β±StdErr (p-value)	Sleep Efficiency β±StdErr (p-value)
Index	Person Level	−0.01±0.13 (.955)	−0.03±0.10 (.774)	0.05±0.11 (.622)	−0.00±0.12 (.987)
	Day Level	0.02±0.07 (.797)	0.08±0.06 (.159)	0.05±0.08 (.571)	−0.03±0.08 (.741)
CV	Person Level	−0.16±0.13 (.233)	0.04±0.10 (.703)	0.15±0.11 (.155)	−0.03±0.12 (.812)
	Day Level	0.10±0.06 (.123)	0.01±0.05 (.900)	−0.05±0.07 (.453)	−0.04±0.07 (.571)
Proportion of CV>36	Person Level	−0.44±0.47 (.346)	0.42±0.33 (.203)	0.35±0.37 (.343)	−0.20±0.43 (.643)
	Day Level	0.20±0.12 (.116)	0.01±0.10 (.914)	−0.21±0.15 (.151)	−0.12±0.13 (.358)
Low Blood Glucose Index	Person Level	−0.06±0.14 (.641)	**0.28±0.10 (<.005)**	0.09±0.11 (.447)	−0.03±0.13 (.836)
	Day Level	0.03±0.07 (.609)	**−0.13±0.06 (.020)**	−0.04±0.08 (.623)	0.01±0.07 (.893)
High Blood Glucose Index	Person Level	0.06±0.13 (.678)	−0.01i0.10 (.897)	0.01±0.11 (.932)	−0.02±0.12 (.852)
	Day Level	−0.02±0.07 (.820)	0.07±0.06 (.243)	0.05±0.09 (.563)	0.00±0.08 (.986)
Time in Range 70–180mg/dL %	Person Level	−0.12±0.13 (.354)	−0.05±0.09 (.582)	0.01±0.11 (.888)	0.11±0.12 (.345)
	Day Level	0.10±0.07 (.153)	0.02±0.06 (.756)	0.02±0.08 (.810)	−0.05±0.07 (.470)
Hypoglycemia <70mg/dL %	Person Level	−0.16±0.18 (.380)	0.04±0.17 (.807)	0.10±0.18 (.600)	−0.07±0.17 (.667)
	Day Level	−0.04±0.10 (.704)	**−0.17±0.08 (.037)**	−0.17±0.13 (.195)	0.09±0.12 (.466)
Hypoglycemia <54mg/dL %	Person Level	−0.45±0.38 (.250)	0.07±0.28 (.810)	0.19±0.43 (.662)	−0.08±0.42 (.845)
	Day Level	0.48±0.33 (.154)	0.01±0.19 (.945)	−0.42±0.39 (.295)	0.01±0.37 (.985)
Hyperglycemia >180mg/dL %	Person Level	0.08±0.13 (.521)	−0.03±0.10 (.723)	−0.07±0.11 (.508)	−0.09±0.12 (.459)
	Day Level	−0.04±0.07 (.544)	0.08±0.06 (.165)	0.06±0.08 (.482)	0.04±0.07 (.610)
Hyperglycemia >250mg/dL %	Person Level	−0.08±0.15 (.618)	−0.04±0.11 (.748)	0.09±0.12 (.448)	−0.03±0.14 (.836)
	Day Level	0.05±0.08 (.525)	0.07±0.06 (.231)	0.03±0.09 (.778)	0.08±0.09 (.380)

Note. βs are standardized coefficients in multilevel model of repeatedly measured sleep characteristic with glucose variability index as predictor. The person level represents how the average glucose variability index is associated with sleep characteristics (between persons) and day level represents how the daily level of glucose is associated with sleep characteristics (within person). **Bolded values are significant.** P values are rounded.