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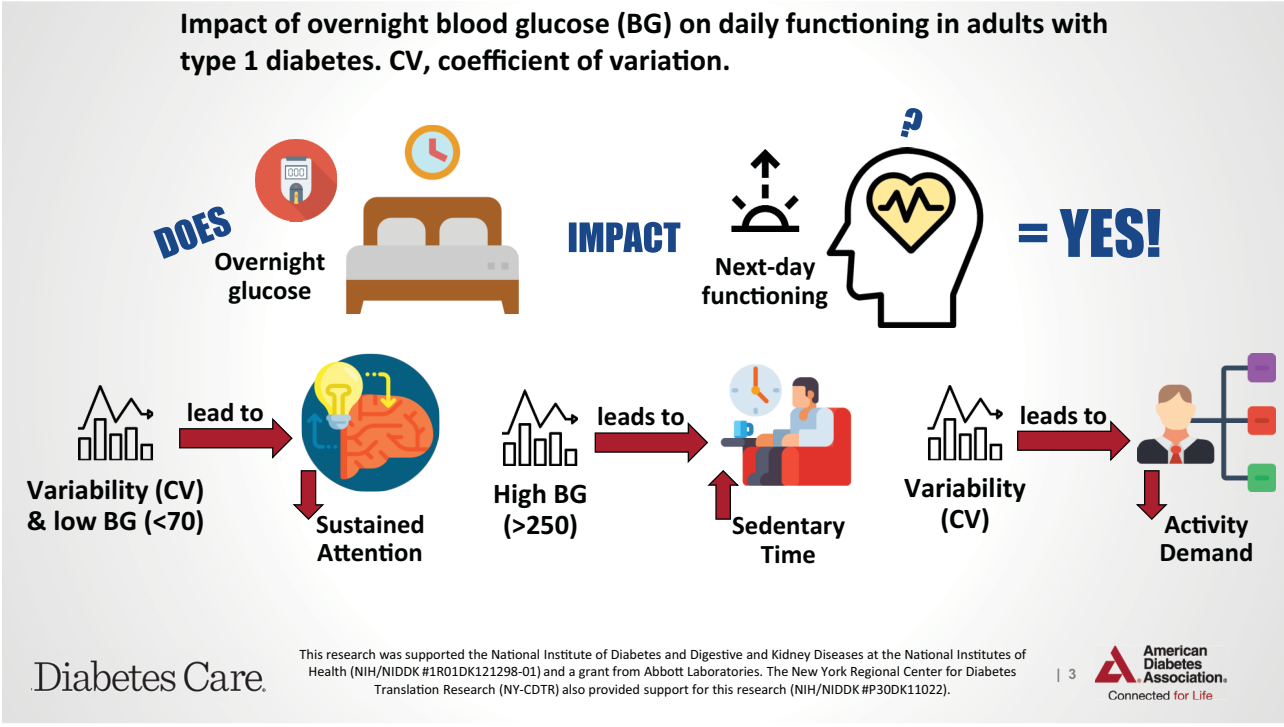

ARTICLE HIGHLIGHTS

- Although people with diabetes have indicated that glucose fluctuations impact their daily lives, little research has been done to understand what areas of functioning are impacted by which glucose parameters.
- This study investigates how various aspects of glucose regulation overnight predict cognitive, physical, and global functioning the following day, as measured by ambulatory cognitive testing, accelerometry, and self-report.
- Relationships between glucose and functioning are complex, with greater variability, time below range, and time above range having different associations with aspects of functioning.

Impact of Overnight Glucose on Next-Day Functioning in Adults With Type 1 Diabetes: An Exploratory Intensive Longitudinal Study

Elizabeth A. Pyatak,[1] Donna Spruijt-Metz,[2,3,4] Stefan Schneider,[2,4,5] Raymond Hernandez,[1,2] Loree T. Pham,[1] Claire J. Hoogendoorn,[6,7] Anne L. Peters,[3] Jill Crandall,[7] Haomiao Jin,[2,8] Pey-Jiuan Lee,[1,2] and Jeffrey S. Gonzalez[6,7]

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ORIGINAL ARTICLE

OBJECTIVE

While there is evidence that functioning, or ability to perform daily life activities, can be adversely influenced by type 1 diabetes, the impact of acute fluctuations in glucose levels on functioning is poorly understood.

RESEARCH DESIGN AND METHODS

Using dynamic structural equation modeling, we examined whether overnight glucose (coefficient of variation[CV], percent time <70 mg/dL, percent time >250 mg/dL) predicted seven next-day functioning outcomes (mobile cognitive tasks, accelerometry-derived physical activity, self-reported activity participation) in adults with type 1 diabetes. We examined mediation, moderation, and whether short-term relationships were predictive of global patient-reported outcomes.

RESULTS

Overall next-day functioning was significantly predicted from overnight CV (P = 0.017) and percent time >250 mg/dL (P = 0.037). Pairwise tests indicate that higher CV is associated with poorer sustained attention (P = 0.028) and lower engagement in demanding activities (P = 0.028), time <70 mg/dL is associated with poorer sustained attention (P = 0.007), and time >250 mg/dL is associated with more sedentary time (P = 0.024). The impact of CV on sustained attention is partially mediated by sleep fragmentation. Individual differences in the effect of overnight time <70 mg/dL on sustained attention predict global illness intrusiveness (P = 0.016) and diabetes-related quality of life (P = 0.036).

CONCLUSIONS

Overnight glucose predicts problems with objective and self-reported next-day functioning and can adversely impact global patient-reported outcomes. These findings across diverse outcomes highlight the wide-ranging effects of glucose fluctuations on functioning in adults with type 1 diabetes.

Human functioning, or the ability to perform necessary and valued daily life activities (1), is critical for well-being and quality of life. Functioning is a complex, multidimensional construct emerging from interactions among personal factors (e.g., sensory, cognitive, motor, socioemotional capacities), task demands, and environmental

[1]Chan Division of Occupational Science and Occupational Therapy, University of Southern California, Los Angeles, CA
[2]Center for Economic and Social Research, University of Southern California, Los Angeles, CA
[3]Keck School of Medicine, University of Southern California, Los Angeles, CA
[4]Department of Psychology, University of Southern California, Los Angeles, CA
[5]Leonard Davis School of Gerontology, University of Southern California, Los Angeles, CA
[6]Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, NY
[7]Fleischer Institute for Diabetes and Metabolism, Division of Endocrinology, Department of Medicine, Albert Einstein College of Medicine, Bronx, NY
[8]Faculty of Health and Medical Sciences, School of Health Sciences, University of Surrey, Guildford, U.K.

Corresponding author: Elizabeth A. Pyatak, beth.pyatak@usc.edu

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affordances and constraints (2). Full participation in daily activities is predicated on adequate function to perform these activities and has been highlighted by people with type 1 diabetes as a critically important outcome of diabetes care (3). Some evidence suggests that type 1 diabetes may adversely affect daily activities. For example, adults with type 1 diabetes have reduced engagement in sports (4) and leisure activities (5) and experience lower labor participation rates and self-rated work ability than the general population (6,7). The impact of type 1 diabetes on function, however, has not been studied comprehensively.

The ability to interpret existing research in this area is hampered by varying definitions of function (including physical, cognition, health-related quality of life, and participation in life roles and activities) and inclusion of populations with varying conditions without subgroup analyses specific to type 1 diabetes. For example, a population-based study found that children with chronic complex conditions (including type 1 diabetes) have greater functional limitations (defined as difficulty with mobility, self-care, communication, or learning behavior) than those without medical impairments (8) but did not differentiate between type 1 diabetes and other conditions. Similarly, older adults with diabetes experience greater functional limitations (defined as challenges in rising from a chair, standing balance, and walking) than those without diabetes (9), yet this analysis did not differentiate between type 1 and type 2 diabetes and used a narrow definition of function focused on mobility.

Another limitation is that, to date, most research has examined type 1 diabetes's impact on function over long-term time horizons, often resulting from chronic complications (e.g., 10,11). In contrast, few studies have examined how short-term fluctuations in glucose may influence day-to-day functioning. Recent efforts have capitalized on the use of more real-time, ecologically valid measures to capture short-term variation in function and other constructs, mirroring the advantage of continuous glucose monitoring (CGM)–derived glucose metrics over more static measures, such as HbA_{1c} (12,13). Similarly, the Function and Emotion in Everyday Life With Type 1 Diabetes (FEEL-T1D) study is investigating relationships between glucose, functioning, and emotional well-being in adults with type 1 diabetes using CGM, accelerometry, ecological momentary assessment (EMA), and mobile cognitive tasks.

Although literature in this area is relatively sparse, several studies have identified relationships between short-term glucose and functioning. Acute hypo- and hyperglycemia have been shown to adversely affect cognition in adults with type 1 diabetes (14). Work performance may also be affected, as hypoglycemia (particularly overnight) predicts decreased productivity (15). In a laboratory setting, inducing overnight hypoglycemia in adults with type 1 diabetes worsened subjective well-being and fatigue the next day but not objective cognitive or physical function (16). People with type 1 diabetes also note the impact of overnight glucose on function; for example, Brown (17) noted, "The more dramatic or prolonged [overnight highs and lows] are, the worse I end up feeling the following morning." Given this prior literature and the potential for new treatments (i.e., automated insulin delivery [AID] systems) to be particularly efficacious at managing glucose during sleep, we targeted overnight glucose as our primary predictor. This approach also allows for a logical temporal ordering, wherein glucose predictors always precede functioning outcomes. Thus, we sought to answer the following research questions: *1*) At an individual level, what aspects of daily functioning are predicted by glucose fluctuations the previous night? *2*) Is the relationship between overnight glucose and next-day functioning mediated by sleep quality, pain, or fatigue? *3*) Do relationships between overnight glucose and next-day functioning differ among various population subgroups? *4*) Is the strength of relationships between overnight glucose and next-day functioning predictive of global patient-reported outcomes?

RESEARCH DESIGN AND METHODS

The full protocol for the FEEL-T1D study was previously published (18); a summary of design aspects pertaining to the current analysis are presented here. All procedures were approved by the University of Southern California and Albert Einstein College of Medicine institutional review boards, and all participants provided informed consent prior to completing study procedures. The study was completed remotely because of the coronavirus 2019 public health emergency. Participants were recruited between June 2020 and February 2022 from the patient populations of two large health systems in Los Angeles, California, and the Bronx borough of New York City, New York, via direct solicitations (phone, mail, e-mail) from research coordinators. Participants were English- or Spanish-speaking adults aged 18 years or older and had type 1 diabetes for at least 1 year, were on a stable treatment regimen for diabetes and any other medical conditions, and had sufficient visual, cognitive, and fine motor abilities to perform the study protocol. All written materials not previously validated in Spanish underwent certified translation, and bilingual/bicultural research coordinators conducted study procedures with Spanish-speaking participants.

After enrollment, participants completed demographic, clinical, and psychosocial questionnaires via Research Electronic Data Capture (REDCap) (19). They were then mailed study materials, including a wrist-worn ActiGraph wGT3X-BT accelerometer, blinded CGM (FreeStyle Libre Pro Flash Glucose Monitoring System; Abbott), and smartphone (Xiaomi Mi A1) preloaded with an EMA survey application (Ilumivu) and mobile cognitive tasks (20). During a videoconference call, participants applied the study CGM and received in-depth training on completing EMA surveys and mobile cognitive tasks. They subsequently underwent 14 days of data collection, taking EMA surveys and cognitive tasks five to six times per day at 3-h intervals. Upon completing EMA data collection, participants returned the study devices and completed additional questionnaires via REDCap. Participants received up to $200 for completing all study procedures.

Measures

Sleep and wake times were derived from *1*) self-report as part of the first (i.e., morning) EMA prompt of each day and *2*) accelerometry data processed with ActiLife version 6.13.4 software using Tudor-Locke auto sleep period detection calculated by the Cole-Kripke algorithm (21). Because each of these sources can carry measurement error, we used an algorithm to combine information from both sources, creating a weighted average

of self-reported and accelerometry-derived data for each individual, which gives more weight to the empirically more likely value (22).

Glucose metrics were calculated during the time asleep as defined above, and included coefficient of variance (CV), percent time <70 mg/dL, and percent time >250 mg/dL. All glucose metrics were derived from raw data files, which recorded interstitial glucose values every 15 min converted via algorithm to estimated blood glucose values. Data files were obtained from Abbott Diabetes Scientific Research Group, who processed the Libre Pro sensors using the Libre 2 algorithm.

Physical activity levels were derived from accelerometer data by calculating *1*) daily step counts and *2*) the proportion of wake time in sedentary behaviors. Accelerometer data were collected at a frequency of 30 Hz. Daily step counts were calculated in 60-s epochs using ActiLife software. Sedentary behaviors were defined as vector magnitude counts <2,860 per minute, following recommended cut points for the wrist-worn ActiGraph (23).

Cognitive functioning was assessed with two mobile cognitive tasks administered on smartphones at each EMA survey, selected in consultation with neuropsychologists experienced in type 1 diabetes research and mobile cognitive assessment (L. Germine, N. Chaytor, personal communication, 12 September 2019). Sustained attention was measured with a gradual-onset continuous performance test, a go/no-go task in which participants responded to city images (go) and withheld responses to mountain images (no-go) for 75 trials (24,25). The task was scored using the d' metric (reliability 0.34 within-person and 0.97 between-person) based on the proportions of hits (correct omissions to mountains) and false alarms (incorrect omissions to cities) after removing slow outlier (>1,600 ms) responses (25). Perceptual speed was measured with a symbol search task in which participants decided, as quickly as possible, which of two figures shown at the bottom of the screen matched one of three figures at the top of the screen (20 trials). We calculated the median response time of accurate trials (reliability 0.57 within-person and 0.98 between-person) after removing premature (<200 ms) and slow outlier (>5,000 ms) responses (20). Each test was scored with higher scores indicating better performance. Momentary scores for each test were averaged into daily scores.

Activity participation was captured with three self-report measures. The first measure was self-reported functioning, which was assessed with two momentary items: "how well were you able to do the current activity" and "how satisfied were you with the way you did the activity" (rated on 1–100 slider scales), administered at each EMA survey (26). A daily function composite was computed by averaging the two items over all momentary assessments each day. The measure showed high internal consistency (Cronbach $\alpha = 0.90$ within-person and 0.98 between-person) in this sample (27). The second measure was the net demand of daily activities, which was measured as the percentage of strenuous activities (e.g., work, caregiving) minus the percentage of restful activities (e.g., resting/chilling) each day, following procedures outlined by Hernandez et al. (28). The third measure was task load using the daily diary version of the six-item National Aeronautics and Space Administration Task Load Index (29) administered at the end of each day ($\alpha = 0.64$ within-person and 0.78 between-person).

Mediators

The total sleep fragmentation index was derived from accelerometry data using a validated algorithm (30), with higher scores indicating more disrupted sleep. When multiple sleep periods were detected overnight, sleep fragmentation was calculated using a sleep-time weighted average of the index. Sleep quality, fatigue, and pain were each assessed with a single self-report item administered in the first daily EMA prompt ("how well-rested do you feel," "how tired do you feel," and "how much bodily pain do you have" rated on a 1–100 slider scale).

Moderators

Self-identified race, ethnicity, sex, language, education level, and treatment regimen were assessed via a study-specific demographic questionnaire. In accordance with literature indicating that CGM and AID have a greater impact on outcomes than insulin delivery mechanisms, treatment regimen was trichotomized into non-CGM users, CGM users without AID, and AID users. Average glucose level was calculated using the mean of all CGM-derived glucose values recorded during the 14-day data collection period.

Global Patient-Reported Outcomes

We examined whether relationships between overnight glucose and next-day functioning were predictive of global functioning as assessed by the following: illness intrusiveness, as evaluated with the Adapted Illness Intrusiveness Rating Scale (average score of five subscales, with α ranging from 0.65 to 0.77 [31]); diabetes-specific quality of life, as assessed with the Type 1 Diabetes and Life measure (overall mean score of age-group–specific items, with α ranging from 0.86 to 0.90 [32]); and physical function, as measured with the 36-item Short Form survey physical component score (sum of subscale *z* scores weighted by factor scoring coefficients, with subscale α ranging from 0.74 to 0.92 [33]).

Data Analysis

Overall Analysis Framework

To be included in analyses, we required that participants had both continuous glucose readings and EMA surveys for at least 7 of the 14 days. We also required a minimum of 20 CGM observations to calculate overnight glucose metrics. The study was designed to have 80% power to detect an effect size of 0.10 for within-person dynamics between glucose and function (18). Data were analyzed using multilevel dynamic structural equation modeling (DSEM). Figure 1*A* illustrates the model structure. DSEM decomposes intensive longitudinal data into time-varying (within-person) and time-invariant (between-person) parts, each of which have their own submodel (34,35). The within-person level (level 1) estimates lagged (or dynamic) relationships within each individual over time. A glucose metric during a given night t served as predictor of a functioning variable at the following day $t + 1$ while controlling for autoregressive effects (each variable at time t regressed on itself at lag $t - 1$) and for lagged effects of functioning at day $t - 1$ on the glucose metric at night t. At the between-person level (level 2), the intercepts of the functioning and glucose measures were estimated as (correlated) random effects, which account for the clustered data (multiple time points nested within each participant). While DSEM is typically applied

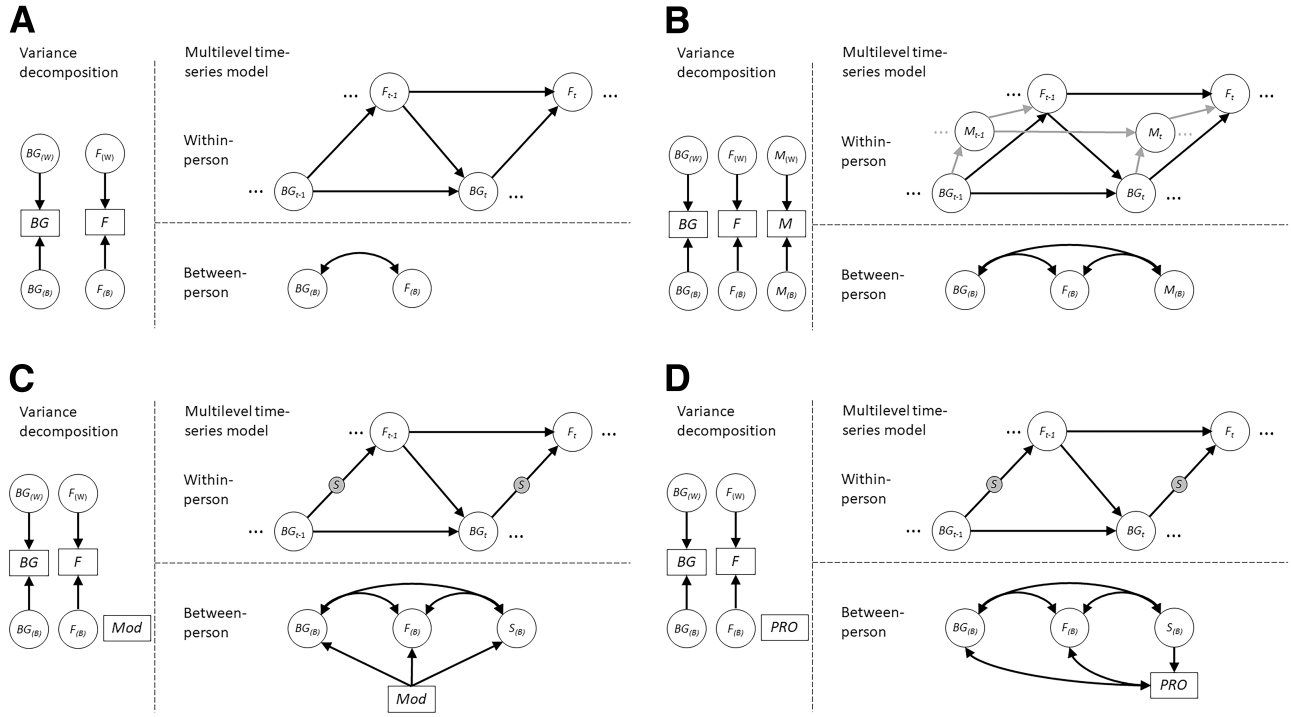

Figure 1—Schematic representation of the estimated DSEMs. *A*: Model examining lagged within-person relationships between an overnight glucose metric and a next-day functioning measure. *B*: Model examining a putative within-person mediator of a glucose-functioning relationship. *C*: Model examining a between-person moderator of the glucose-functioning relationship. *D*: Model examining a global patient-reported outcome (PRO) predicted by individual differences in the glucose-functioning relationship. The left part in each panel shows the decomposition of the observed variables into within-person (time-varying) and between-person (time-invariant) variance components. The right part in each panel shows the multilevel time series model. B, between person; BG, blood glucose; F, functioning measure; M, putative mediator variable; Mod, moderator variable; s, random regression slope; t, time point; W, within person.

to data sets with many observations clustered within many participants, the number of participants is more critical to estimation quality than the number of observations per participant (36).

Tests of Specific Hypotheses

Analyses were conducted in consecutive steps. We first examined the within-person effect of each overnight glucose metric on each next-day functioning variable (Fig. 1*A*). Because multiple functioning variables were considered, we estimated a model in which all functioning measures served as simultaneous (correlated) outcomes. Different glucose metrics were tested in separate models. An omnibus Wald χ^2 test was performed for each glucose metric to evaluate whether it had an overall within-person effect on all seven functioning variables in combination (df = 7); thereafter, pairwise tests evaluated effects of each glucose measure on each functioning variable. Because multiple post hoc tests were conducted, we controlled for inflation of type I error using the Benjamini-Hochberg correction (37). As a robustness check, we also examined whether the glucose measures predicted the proportion of EMA surveys and/or cognitive tests that were missed on the next day; no significant associations were found (Supplementary Table 1).

To examine within-person–mediated effects within significant glucose functioning relationships, each putative mediator was entered separately at level 1 as a within-person–centered intermediate variable of the total lagged effect of a glucose metric on a functioning outcome (Fig. 1*B*). Significance of indirect (i.e., mediated) effects was evaluated using the product of coefficients method and inspecting 95% credible intervals from Bayesian parameter estimation. To evaluate moderated effects, we examined cross-level interactions, testing each participant characteristic as a between-person predictor of individual differences in the within-person relationships between glucose and functioning variables (represented as a random regression slope in Fig. 1*C*). Finally, we explored whether individual differences in the within-person effects of glucose on functioning were associated with global patient-reported outcomes (Fig. 1*D*). To do this, we examined whether the random slope for the relationship between each glucose and functioning measure predicted the patient-reported outcome measures at the between-person level. Because these were considered exploratory, we did not adjust for multiple comparisons. All DSEM models were conducted using Mplus version 8.8 software (38). Missing values were accommodated using Bayesian estimation with default noninformative priors.

Data and Resource Availability

Data are available from the corresponding author upon reasonable request.

RESULTS

Of 196 participants who started the study protocol, 12 had no readable CGM data, and 21 had <7 days of concurrent EMA and CGM data. Thus, data from 166 participants were analyzed, as presented in Table 1 (frequency distributions are shown in Supplementary Figs. 1–3). Participants contributed, on average, 12.96 ±

Table 1—Participant demographic and clinical characteristics ($n = 166$)

	n (%)
Demographic characteristics	
Age (range 18–75 years), mean ± SD	40.99 ± 14.67
Sex	
Male	75 (45.2)
Female	91 (54.8)
Race/ethnicity	
Hispanic	66 (39.8)
Non-Hispanic White	51 (30.7)
Non-Hispanic Black	25 (15.1)
Asian	7 (4.2)
Other	4 (2.4)
More than one race/ethnicity	10 (6)
Did not wish to provide	3 (1.8)
Preferred language	
English	148 (89.2)
Spanish	18 (10.8)
Level of education	
Less than high school	14 (8.4)
High school graduate/GED	22 (13.3)
Some college but no degree	43 (25.9)
Associate degree	17 (10.2)
Bachelor degree	46 (27.7)
Graduate degree	21 (12.7)
Did not wish to provide	3 (1.8)
Annual household income, $	
<25,000	37 (22.3)
25,000–49,999	37 (22.3)
50,000–99,999	25 (15.0)
100,000–199,999	16 (9.6)
≥200,000	8 (4.8)
Did not wish to provide	43 (25.9)
Health insurance	
Government sponsored	63 (38)
Private	66 (39.8)
Both government sponsored and private	11 (6.6)
No health insurance or coverage	3 (1.8)
Did not wish to provide	23 (13.9)
Marital status	
Single (never married)	82 (49.4)
Living together/married	56 (33.7)
Separated/divorced/widowed	22 (13.3)
Other/did not wish to provide	6 (3.6)
Employment status	
Student	15 (9)
Working now full time	60 (36.1)
Working now part time	20 (12)
Full-time homemaker	7 (4.2)
Unemployed and looking for work	22 (13.3)
Disabled	19 (11.4)
Retired	15 (9)
Other/did not wish to provide	8 (4.8)
Clinical characteristics	
Treatment regimen	
Injections/insulin pen	88 (53.0)
Insulin pump	72 (43.4)
Both injections and insulin pump	5 (3.0)
Insulin delivery method not reported	1 (0.6)
CGM (non-AID)	62 (37.4)
AID	39 (23.5)
Comorbidities	
Diabetic nerve damage	21 (12.65)
Heart disease	8 (4.82)
Heart surgery (coronary artery, cardiac stent, other)	6 (3.61)

Continued on p. 1350

1.20 days of data, for a total sample size of 2,151 days; average EMA survey compliance was 88.4% (median 91.7%, interquartile range 84.5–96.4%).

As shown in Table 2, the functioning variables were generally weakly intercorrelated, suggesting that they addressed a wide range of aspects of daily functioning. Results from omnibus Wald tests showed that the next-day functioning variables in combination were significantly predicted from overnight CV (χ^2 [7] = 17.03, $P = 0.017$) and percent time >250 mg/dL (χ^2 [7] = 14.95, $P = 0.037$), while percent time <70 mg/dL had a nonsignificant effect (χ^2 [7] = 12.95, $P = 0.073$). Thus, when a participant had more variability or time >250 mg/dL overnight, they experienced poorer functioning the following day, controlling for glucose and functioning the previous day.

Results of pairwise tests evaluating effects of each glucose metric on each individual functioning variable are presented in Table 3 (for full model results, see Supplementary Tables 2–4). Three variables were not significantly associated with any glucose metrics: self-reported function, task load, and step count. Higher CV was associated with poorer sustained attention (adjusted $P = 0.028$) and lower daily activity demand (adjusted $P = 0.028$), more time <70 mg/dL was associated with poorer sustained attention (adjusted $P = 0.007$), and more time >250 mg/dL was associated with more sedentary time (adjusted $P = 0.024$) and marginally associated with worse perceptual speed (adjusted $P = 0.051$). As above, these effects indicate that within an individual, overnight glucose predicted next-day changes in functioning, while controlling for the prior day's glucose and functioning.

Among the relationships examined in Table 3, there was no evidence of moderation by race and ethnicity, sex, language, or education level (all $P > 0.10$); however, we identified moderation by mean glucose levels and treatment regimen (Supplementary Figs. 4 and 5). Among non-CGM users (compared with CGM or AID users), greater overnight variability predicted less sedentary time and more steps the following day. Among those with higher average glucose levels, more time <70 mg/dL predicted worse sustained attention, higher variability predicted less sedentary behavior, and more time >250 mg/dL predicted lower task load the following day.

Table 1—Continued

	n (%)
Osteoarthritis or degenerative arthritis that limits daily activity	4 (2.41)
Cancer (other than nonmelanoma skin cancer)	4 (2.41)
Stroke or transient ischemic attack	3 (1.81)
Chronic lung disease (COPD or chronic bronchitis or emphysema)	1 (0.60)
Nightly sleep duration, h, mean ± SD	7.27 ± 0.90
Sleep duration per night, h	
<4	38 (1.62)
4–6	376 (16.08)
6–8	1,241 (53.06)
>8	684 (29.24)
Glucose measures, mean ± SD	
Glucose management indicator[a]	7.73 ± 1.39
Overall	
Number of CGM observations	1,210.42 ± 175.31
CV	38.05 ± 7.88
Percent time in range	53.75 ± 22.14
Percent time <54 mg/dL	0.79 ± 1.61
Percent time <70 mg/dL	4.69 ± 5.40
Percent time >180 mg/dL	41.75 ± 24.31
Percent time >250 mg/dL	20.08 ± 20.67
Nighttime	
Number of CGM observations	375.84 ± 71.06
CV	36.72 ± 10.32
Percent time in range	56.05 ± 24.96
Percent time <54 mg/dL	1.53 ± 3.99
Percent time <70 mg/dL	7.07 ± 9.47
Percent time >180 mg/dL	36.88 ± 27.35
Percent time >250 mg/dL	17.18 ± 20.65
Daytime	
Number of CGM observations	843.58 ± 130.34
CV	36.93 ± 7.85
Percent time in range	52.33 ± 22.57
Percent time <54 mg/dL	0.47 ± 0.98
Percent time <70 mg/dL	3.64 ± 4.65
Percent time >180 mg/dL	44.03 ± 24.36
Percent time >250 mg/dL	21.36 ± 21.65
Functioning measures, mean ± SD	
Sustained attention d'[b]	212.87 ± 54.35
Perceptual speed, ms	1,670.38 ± 447.49
Percent time sedentary (range 0–100)	71.07 ± 10.14
Step count	9,612.23 ± 3,660.60
Self-reported function (range 0–100)	76.18 ± 10.05
Net demand daily activities (range −100 to 100)	−25.72 ± 32.14
Task load (range 0–100)	50.83 ± 11.85

COPD, chronic obstructive pulmonary disease; GED, General Educational Development. [a]Glucose management indicator % = 3.31 + 0.02392 × mean glucose in mg/dL. [b]The statistic d' was calculated as the difference in *z* scores for hits and false alarms × 100, for a possible range of approximately −500 to 500.

In within-person mediation models, greater sleep fragmentation partially accounted for the negative effect of CV on sustained attention (indirect effect estimate −0.093, 95% CI −0.246 to −0.004, $P = 0.042$). Specifically, higher overnight CV was associated with more fragmented sleep during the night (standardized effect 0.061, 95% CI 0.009–0.109, $P = 0.018$), which in turn predicted worse next-day sustained attention (standardized effect −0.060, 95% CI −0.106 to −0.009, $P = 0.024$); the direct effect of CV on sustained attention remained significant (standardized effect −0.051, 95% CI −0.096 to −0.007, $P = 0.032$). All other mediation models were nonsignificant.

Individual differences in the within-person effect of overnight time <70 mg/dL on next-day sustained attention were significantly associated with worse global patient-reported outcomes. Stronger negative effects of time <70 mg/dL predicted more illness intrusiveness (Adapted Illness Intrusiveness Rating Scale standardized effect −0.285, 95% CI −0.522 to −0.058, $P = 0.016$) and lower diabetes-related quality of life (Type 1 Diabetes and Life standardized effect 0.254, 95% CI 0.024–0.500, $P = 0.036$). Individual differences in the impact of other glucose metrics on functioning variables were not associated with global patient-reported outcomes.

CONCLUSIONS

This study adds to our understanding of how glucose metrics impact function in type 1 diabetes. Importantly, while most previous studies have investigated between-person impacts of glucose on functioning over long-term time horizons (e.g., 4–7, 10,11), this study examines how short-term fluctuations in glucose may impact an individual relative to their usual level of function, adding to a still-nascent body of literature (12,14–16). Overall, our findings indicate that overnight glucose impacts various dimensions of functioning the following day, with omnibus Wald tests indicating significant effects of CV and hyperglycemia on physical, cognitive, and self-reported function. Effect sizes for these relationships are small; for example, spending 10% more time >250 mg/dL overnight leads to ∼2 min more sedentary time the following day. Yet, these effects should be considered in the context of a lifelong chronic condition. Although experiencing slightly worse function on a given day may not be bothersome, this marginal daily impact has the potential to be repeated thousands of times over a lifetime, magnifying its overall effect on well-being and quality of life. We found evidence of such a relationship within our study: individuals for whom low glucose overnight more strongly impacted sustained attention reported more illness intrusiveness and lower diabetes-related quality of life, illustrating a broader impact on global well-being.

Glucose variability (CV) is associated with poorer sustained attention and lower engagement in demanding activities the next day, with the impact of CV on sustained attention being partially accounted for by greater sleep fragmentation. Higher variability may be a consequence of events that disrupt sleep, such as in an individual who wakes in response to a CGM alarm or hypoglycemia symptoms, treats the hypoglycemia with more glucose

Table 2—Within-person correlations among daily functioning variables

	Sustained attention	Perceptual speed	Percent time sedentary	Step count	Self-reported function	Net demand daily activities	Task load
Cognition							
Sustained attention	—						
Perceptual speed	0.061**	—					
Physical activity							
Percent time sedentary	0.054*	−0.045*	—				
Step count	−0.059**	0.046*	−0.759***	—			
Activity participation							
Self-reported function	0.042*	0.028	−0.086***	0.084***	—		
Net demand daily activities	0.008	0.057*	−0.145***	0.188***	−0.048*	—	
Task load	−0.068**	0.022	−0.193***	0.262***	−0.011	0.396***	—

*$P < 0.05$. **$P < 0.01$. ***$P < 0.001$.

than necessary, and wakes again to treat the resultant hyperglycemia: a cascade of events that would be marked by high overnight variability. This relationship, however, was not fully accounted for by sleep fragmentation, suggesting that other physiological or behavioral mechanisms also contribute to this phenomenon. Interestingly, our exploratory analyses indicated that among participants with higher average glucose and those not using CGM or AID systems, higher overnight variability is associated with increased physical activity the following day. We are unsure what accounts for this finding, and more research is needed to understand the relationship between CV and physical activity in this subgroup.

Table 3—Within-person regression effects of overnight glucose metrics on next-day functioning

Predictor and outcome	Estimate (95% CI)	Adjusted *P*
CV		
Cognition		
Sustained attention	−0.150 (−0.277 to −0.029)	0.028*
Perceptual speed	0.331 (−0.364 to 0.955)	0.496
Physical activity		
Percent time sedentary	−0.022 (−0.057 to 0.014)	0.473
Step count	4.571 (−8.723 to 16.882)	0.546
Activity participation		
Self-reported function	0.006 (−0.028 to 0.040)	0.754
Net demand daily activities	−0.219 (−0.371 to −0.069)	0.028*
Task load	−0.033 (−0.087 to 0.022)	0.473
Percent time <70 mg/dL		
Cognition		
Sustained attention	−0.143 (−0.238 to −0.055)	0.007*
Perceptual speed	0.253 (−0.242 to 0.717)	0.817
Physical activity		
Percent time sedentary	0.010 (−0.016 to 0.036)	0.817
Step count	−2.951 (−12.463 to 6.381)	0.817
Activity participation		
Self-reported function	0.005 (−0.019 to 0.031)	0.817
Net demand daily activities	0.018 (−0.096 to 0.134)	0.817
Task load	−0.004 (−0.046 to 0.036)	0.822
Percent time >250 mg/dL		
Cognition		
Sustained attention	0.043 (−0.018 to 0.098)	0.158
Perceptual speed	−0.287 (−0.627 to 0.004)	0.051‡
Physical activity		
Percent time sedentary	0.020 (0.004 to 0.036)	0.024*
Step count	−4.634 (−10.542 to 1.513)	0.116
Activity participation		
Self-reported function	0.014 (−0.002 to 0.029)	0.088
Net demand daily activities	−0.033 (−0.102 to 0.037)	0.404
Task load	−0.010 (−0.039 to 0.016)	0.440

*$P < 0.05$ after Benjamini-Hochberg correction for multiple testing. ‡$P = 0.051$ after Benjamini-Hochberg correction for multiple testing.

More time >250 mg/dL contributed to more sedentary behavior and was marginally associated with slower perceptual speed the following day. These findings are concordant with expected sequelae of elevated glucose (39,40). Additionally, in exploratory analyses, more time >250 mg/dL was associated with lower task load the following day only among those with elevated average glucose levels. Task load captures multiple dimensions of difficulty (e.g., physical, mental, frustration, time pressure) associated with activities over the course of a day, meaning that individuals with higher average glucose participated in less challenging activities on days preceded by even higher than their usual glucose level overnight. This may indicate a threshold of high glucose, in which the cumulative effect of generally high glucose coupled with a more extreme overnight glucose excursion adversely impacts one's abilities the following day, whereas individuals with lower average glucose have more capacity to tolerate one night of elevated glucose without impacting function.

More time <70 mg/dL impacts sustained attention the following day, contrary to previous research in which overnight hypoglycemia affected subjective well-being but not cognitive function (16). This was only found among individuals with higher average glucose levels; those with lower average glucose did not experience negative impacts from overnight

hypoglycemia. The reason for this finding may be that those with lower average glucose habitually spend more time at or near 70 mg/dL and are better adapted to functioning in that range; thus, the marginal impact of additional time <70 mg/dL is less than for those with higher average glucose. We additionally found that individuals whose sustained attention was more adversely affected by time <70 mg/dL experienced more illness intrusiveness and poorer diabetes-related quality of life. Taken together, these findings have implications for refining treatment: individuals with higher average glucose are more negatively impacted by overnight lows and, in turn, are more likely to have adverse impacts on quality of life. Thus, for this population, it may be especially important to prevent overnight hypoglycemia and to take this into consideration when working to achieve glycemic targets.

Strengths and Limitations

This study's strengths include a comprehensive assessment of multiple dimensions of objective and self-reported functioning; a focus on short-term, within-person relationships to illuminate how daily experiences are impacted by type 1 diabetes; and a thorough exploration of subgroup differences. Furthermore, the study was conducted among an ethnically and socioeconomically diverse population, strengthening its generalizability.

This study also has several important limitations. First, although analyzing within-person relationships and removing autoregressive effects may account for many potential confounders, the study's observational design precludes making strong causal inferences. Second, as this analysis focused on the association of overnight glucose and daily functioning, there may be within-day or longer-term effects of glucose on functioning that were not identified. These effects may differ from those reported here, given the modest observed correlations between nighttime and next-day glucose (CV $r = 0.12$, time <70 mg/dL $r = 0.22$, time >250 mg/dL $r = 0.29$). Similarly, in limiting analyses to single indices of hyperglycemia, hypoglycemia, and glucose variability, we may have missed alternate glucose metrics with different relationships with function. Third, while pairwise tests were adjusted for multiple comparisons, mediation and moderation analyses used unadjusted *P* values and should be subjected to further study. Finally, in our effort to balance objective and self-report measures, and to prioritize breadth over depth given the limited prior research in this area, we were unable to comprehensively assess each construct under study.

Implications

Overnight glucose fluctuations predict adverse impacts in physical activity, cognition, and self-reported activity participation the following day in adults with type 1 diabetes. While the observed decrements in function are small, their significance is magnified when considering their cumulative impact over a lifetime. Individualizing treatment and using diabetes technologies to minimize overnight glucose fluctuations have the potential to enhance function and quality of life for adults with type 1 diabetes.

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