Assessing dynamic cognitive function in the daily lives of youth with and without Type 1 Diabetes (T1D): a pilot and feasibility study

Mary Katherine Ray, Jorie Fleming, Andrew Aschenbrenner, Jason Hassenstab, Brooke Redwine, Carissa Burns, Ana Maria Arbelaez, Mary Ellen Vajravelu, Tamara Hershey

Submitted to: JMIR Diabetes
on: May 06, 2024

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Abstract

Background: Studies have shown a relationship between worse glycemic control and lower cognitive scores in youth with Type 1 Diabetes (T1D). However, most studies only assessed long-term glucose control (e.g., years-decades) and cognition at a single time point. Understanding this relationship at a higher temporal resolution (e.g., minutes-hours) and in naturalistic settings has potential clinical implications. Newer technology (e.g., continuous glucose monitoring [CGM] and ecological momentary assessment [EMA]) provides a unique opportunity to explore the specific glucose dynamics that influence dynamic cognition; that is, cognitive functions that fluctuate in the short-term and are influenced by environmental factors.

Objective: Before we can assess this relationship, we first need to determine the feasibility of measuring cognition in youth in daily life and the practicality of integrating EMAs of cognition and continuously measured glucose—the purpose of this study. Specifically, we assessed the acceptability of measuring dynamic cognition using a smartphone application (app), the youngest age at which it was feasible to use a smartphone app, and adherence to cognitive testing in daily life in youth with and without T1D. Further, we illustrated integration of dynamic cognitive performance scores from the smartphone app and glucose from CGM in youth with T1D.

Methods: The study was conducted in three phases including one in-lab study and two remote studies. For all phases, youth were asked to complete cognitive tests on the Ambulatory Research in Cognition (ARC) smartphone app that measured processing speed, associative memory, and working memory. For the in-lab study, youth completed app testing four times during their session. For the remote phases, youth were asked to complete cognitive tests five times per day for either 10 or 14 consecutive days in daily life. Youth were asked to rate their impressions of the app. Youth with T1D wore a CGM.

Results: N=74 youth (N=53 Control; N=21 T1D) aged 4-16 participated. Youth generally reported liking/understanding the ARC app tasks in a lab and remote setting. Age was significantly correlated with task performance such that younger youth performed more poorly; around age 9 is when youth started to perform well. Youth had high mean testing adherence in daily life completing between 76.3%-80.2% of tasks. EMAs of cognition and glucose data were successfully integrated at two distinct temporal resolutions for each participant with T1D—for each day of participation and for each individual cognitive test.

Conclusions: Data from this pilot and feasibility study support the use of an app to measure dynamic cognitive function in youth ?9 years old in naturalistic settings and the feasibility of integrating EMAs of cognition and glucose. Next steps include using EMA in a fully powered study to determine the relationship between short-term glycemic control and cognition in youth with T1D.

(JMIR Preprints 06/05/2024:60275)

DOI: https://doi.org/10.2196/preprints.60275

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Conclusions: Data from this pilot and feasibility study support the use of an app to measure dynamic cognitive function in youth ≥9 years old in naturalistic settings and the feasibility of integrating EMAs of cognition and glucose. Next steps include using EMA in a fully powered study to determine the relationship between short-term glycemic control and cognition in youth with T1D.

Keywords

Ecological Momentary Assessment; EMA; ambulatory; smartphone; continuous glucose monitoring; CGM

Introduction

Studies have shown subtly lower cognitive scores in youth with Type 1 diabetes (T1D) compared to their peers without T1D, and a relationship between worse glycemic control and lower cognitive scores[1-11]. These results highlight an important relationship between glucose and cognition in T1D. However, they are based on measures of long-term glucose control over long periods (e.g., years-decades) and cognitive function tested in a lab setting at a single time point. Understanding this relationship at a higher temporal resolution (e.g., minutes-hours) and in naturalistic settings has potential clinical implications. Newer technology (e.g., continuous glucose monitoring [CGM] and ecological momentary assessment [EMA]) provides a unique opportunity to explore the specific glucose dynamics that influence dynamic cognition; that is, cognitive functions that fluctuate in the short-term and are easily influenced by environmental factors[12-13]. Using these approaches in adults with T1D, significant glucose fluctuations were shown to be related to slower processing speed in the moment[14]. However, whether this relationship or others are seen in youth with T1D is unknown. Before we can assess this relationship, we need to determine the feasibility and practicality of measuring dynamic cognition in youth in daily life using a smartphone app (initially designed for adults[15-17]) and integrating these results with CGM data.

Methods

We assessed the acceptability of measuring dynamic cognition in youth, the youngest age at which it is feasible to use a smartphone app for this purpose, and adherence to testing in daily life in youth with and without T1D. Further, we illustrated integration of dynamic cognitive performance scores from the app and glucose from CGM in youth with T1D at two temporal resolutions.

Participants and Procedures:

The study was conducted in three phases. Phase 1 was conducted in the lab setting. Phase 2 and Phase 3 were conducted in a remote setting. The Washington University HRPO approved procedures, and participants provided consent/assent. Inclusion and exclusion criteria are outlined in *Table 1*. *In Lab Study: Phase 1:* Participants completed app testing four times with five minute breaks. *Remote Study- Phase 2:* Participants had a video call with researchers to practice the app tasks. The following day, youth were asked to complete testing in daily life five times per day for 14 consecutive days —they were prompted to take the tests randomly and had two hours to complete them. They had a video call with the research team one and two weeks later to complete an Experiential Interview. *Remote Study- Phase 3*: Participants had a video call or visited the laboratory to practice the app tasks. The following day, youth were asked to complete testing in daily life five times per day for 10 consecutive days —they were prompted to take the tests randomly and had two hours to complete them. For both *Remote Study Phases*, monetary incentives were provided to encourage adherence ($5 per day when ≥2/5 tests were completed; $0.50

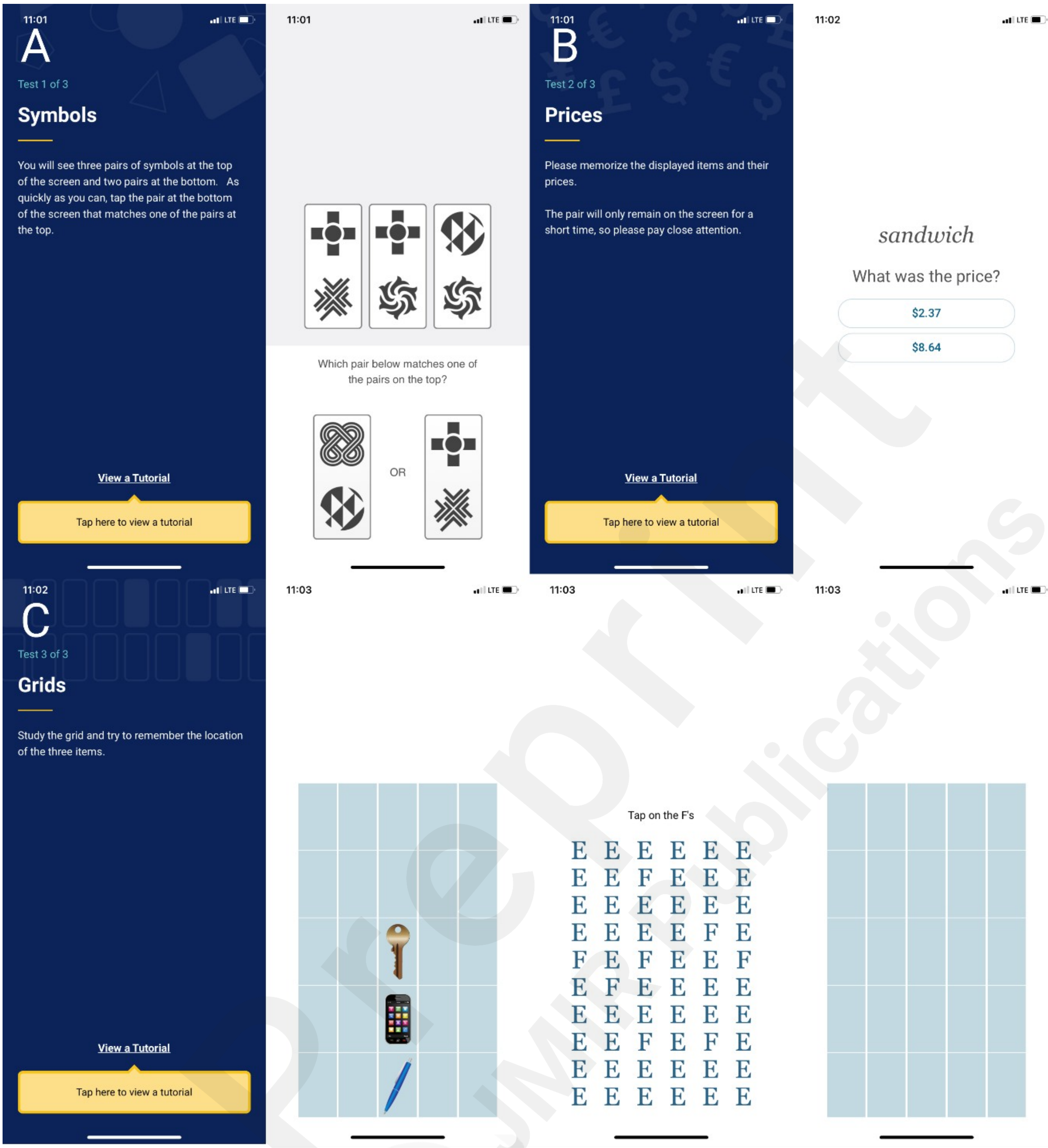
per completed test).

Table 1. Inclusion and exclusion criteria for all 3 phases of the pilot and feasibility study.			
Study	Phase	Inclusion	Exclusion
In-Lab	1	• Age 4-16	• No English fluency • Unable to use a smartphone • Severe mental, neurological, medical condition that would make them unable to complete tasks • Use of medications with known effects on the central nervous system (except ADHD meds)
Real World	2	• Age 9-16 • iPhone ownership (6s or newer) • Established use of Dexcom G5/G6 CGM	• No English fluency • Unable to use a smartphone • Severe mental, neurological, medical condition that would make them unable to complete tasks • Use of medications with known effects on the central nervous system (except ADHD meds) • No parent-approved screen time for participation • No tablet/computer with reliable internet connection • Severe phone screen cracks that would affect testing
Real World	3	• Age 9-16 • *Youth without a phone or CGM were provided one for the study*	• No English fluency • Unable to use a smartphone • Severe mental, neurological, medical condition that would make them unable to complete tasks • Use of medications with known effects on the central nervous system (except ADHD meds) • No parent-approved screen time for participation • No tablet/computer with reliable internet connection • Severe phone screen cracks that would affect testing

Measures

Ambulatory Research in Cognition (ARC) App: The app is comprised of three tasks. The Symbols Task assesses processing speed by asking participants to compare visual stimuli. Participants are shown three cards with two images at the top of a screen and two cards with two images at the bottom of a screen and asked to determine which card on the bottom matches a card on the top as quickly as possible (*Figure 1A*). There are 12 trials. The performance score is median reaction time (RT), calculated for trials with correct responses and RTs above 150ms to avoid anticipatory responses. The Prices Task assesses associative memory. Participants are given a household item and an associated price. They are shown 10 pairs and asked to recall the price (*Figure 1B*). The performance score is percent error (0%=all correct, 100%=all incorrect). The Grids Task assesses working memory. Participants are shown a grid with three items and asked to remember their location (*Figure 1C*). They are presented with a distraction task where they are shown a screen of "E" s with sporadic "F" s and asked to select the "F" s. Then they are presented with a blank grid and asked to choose where the items were located. Participants are presented with this task twice per session. The performance score is the average Euclidean distance from the selected response to the correct placement (0=perfect placement of all items and trials). Each session, including all three tasks, only takes about three minutes to complete.

Figure 1. The Ambulatory Research in Cognition (ARC) App. (A) The Symbols Task assesses processing speed. (B) The Prices Task assesses associative memory. (C) The Grids Task assesses working memory.



Continuous Glucose Monitor (CGM): Participants with T1D wore a Dexcom G5/G6 CGM to measure glucose every 5 minutes. Data sharing privileges from Dexcom Clarity were established at study onset to reduce the likelihood of missing glucose data.

Experiential Interview: For each task, youth were asked to rate on a scale of 1-5 how challenging or easy the task was, how confusing or clear the instructions were, how confusing or clear the task was, and how boring or fun the task was.

Statistical Analysis

Data were analyzed with R and SPSS. *In-Lab Study: Phase 1*- Pearson correlations assessed the relationship between age and ARC task performance to determine at what age it was feasible for youth to use the app (Kendall's Tau for non-normal data). *Real-World Study: Phase 2 and Phase 3*: Testing adherence was calculated as number of tests completed/number of tests offered. To integrate cognitive and glucose data, glucose obtained from the CGM were matched to the corresponding cognitive test by timestamps within each system, both set to CST. Given that glucose was assessed every 5 minutes, the closest glucose measure from CGM was taken within 5 minutes of each cognitive session.

Results

Participants

There were N=74 participants across all Phases. *In-Lab Study: Phase 1:* N=12 youth without T1D aged 4-16 completed the study (N=11 had app performance data). *Real-World Study: Phase 2:* N=44 youth aged 9-16 completed the study (N=30 Control, N=14 T1D). *Real-World Study: Phase 3:* N=18 youth aged 9-16 completed the study (N=11 Control, N=7 T1D). As shown in *Table 2*, the study samples were homogenous, with most participants being Non-Hispanic white. Glycemic measures for youth with T1D are shown in *Table 3*.

Table 2. Demographic data for the *In-Lab Study* and *Real-World Study* populations. For the Real-World Studies, the sample included youth with and without Type 1 Diabetes (T1D).

In-Lab Study: Phase 1	Overall	≥9 Years Old
Age: Mean (SD) (N)	10.6 (3.6) (12)	13.1 (2.3) (7)
Sex: N Female/N Male	7/5	5/2
Race/Ethnicity: N (%)		
Black	3 (25%)	2 (29%)
Hispanic/White	1 (8%)	1 (14%)
Non-Hispanic White	8 (67%)	4 (57%)
Mixed Race		
Real-World Study: Phase 2	**Control**	**T1D**
Age: Mean (SD) (N)	13.6 (1.7) (30)	14.0 (2.0) (14)
Sex: N Female/N Male	17/13	7/7
Race/Ethnicity: N (%)		
Black	2 (7%)	0 (0%)
Hispanic	1 (3%)	0 (0%)
Non-Hispanic White	25 (83%)	14 (100%)
Mixed Race	2 (7%)	0 (0%)
Annual Household Income: Mean (SD) (N)	$138,907 (71,860) (27)	$125,231 (44,129) (13)
Real-World Study: Phase 3	**Control**	**T1D**
Age: Mean (SD) (N)	13.0 (2.3) (11)	12.4 (2.2) (7)
Sex: N Female/N Male	5/6	1/6
Race/Ethnicity: N (%)		
Black	0 (0%)	0 (0%)
Hispanic	0 (0%)	0 (0%)
White	11 (100%)	7(100%)
Mixed Race	0 (0%)	0 (0%)
Annual Household Income: Mean (SD) (N)	$91,818 (37,031) (11)	$120,000 (47,010) (6)

Table 3. Glycemic measures for youth with Type 1 Diabetes (T1D) as measured by continuous glucose monitoring (CGM) across the whole study. Data are presented as mean (standard deviation). N=20; we were unable to collect CGM data in N=1 participant with T1D.

Mean Glucose	176.0 mg/dL (46.0)
Standard Deviation of Glucose	63.9 mg/dL (17.7)
Percent Time in Range (TIR)	58.7% (20.6)
Percent Time Below Range	2.5% (3.3)
Percent Time > 180mg/dL	38.8% (22.3)
Percent Time > 250 mg/dL	17.2% (19.1)

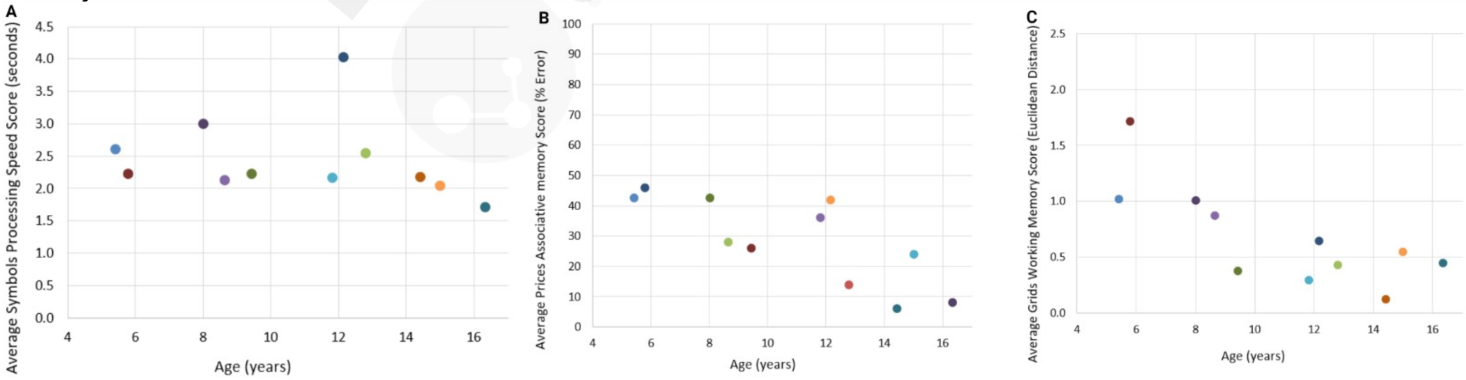
Feasibility of Using a Smartphone App to Assess Dynamic Cognitive Function in Youth

In-Lab Study: Phase 1: Youth reported liking and understanding the Grids and Symbols Tasks but not the Prices Task (*Table 4*). Performance on the tasks correlated with age (Grids: R=-0.77, *P*=.006, N=11; Prices: R=-0.77, *P*=.005, N=11; Symbols: Tau=-0.42, *P*=.07, N=11), such that younger youth performed worse than older youth. Around age 9 is when youth started performing well (*Figure 2*). These data guided our decision to include ages 9-16 in the *Real-World Phases*. As shown in *Table 4*, youth reported positive impressions of the Grids and Symbols Tasks but not the Prices Task. On average, youth asked to complete testing for 14 days completed 76.3% (SD=19.0) of offered tasks, and youth asked to complete testing for 10 days completed 80.2% (SD=13.0).

Table 4. Youth's performance on and impressions of the Ambulatory Research in Cognition (ARC) smartphone app cognitive tasks.

	Symbols (Processing Speed)	Prices (Associative Memory)	Grids (Working Memory)
Performance (Mean, SD) (lower score = better)	Median Reaction Time	% Error Score	Euclidean Distance
In-Lab: Phase 1 (N = 11)	2.4 (0.6)	28.6 (14.5)	0.7 (0.4)
Real-World: Phase 2 (N = 44)	1.8 (0.4)	40.6 (7.7)	0.5 (0.2)
Real-World: Phase 3 (N = 18)	1.9 (0.5)	40.1 (6.7)	0.5 (0.2)
Impressions (Mean, SD, Range)			
How hard/easy was the task? *(1 = very hard, 5 = very easy)*			
In-Lab: Phase 1 (N = 12)	4.2 (0.7, 3-5)	2.3 (0.8, 1-4)	3.3 (1.4, 1-5)
Real-World - Week 1 (N = 42)	4.3 (0.8, 2-5)	2.2 (1.1, 1-4)	4.0 (1.0, 2-5)
Real-World - Week 2 (N = 43)	4.5 (0.8, 2-5)	2.6 (1.2, 1-5)	4.1 (0.9, 2-5)
How confusing/clear were the task instructions? *(1 = very confusing, 5 = very clear)*			
In-Lab: Phase 1 (N = 12)	4.4 (1.1, 2-5)	4.4 (1.0, 2-5)	4.5 (0.9, 3-5)
Real-World - Week 1 (N = 42)	4.9 (0.3, 4-5)	4.8 (0.4, 4-5)	4.9 (0.4, 3-5)
Real-World - Week 2 (N = 43)	4.9 (0.4, 3-5)	4.9 (0.4, 3-5)	4.9 (0.4, 3-5)
How confusing/clear was the task itself? *(1 = very confusing, 5 = very clear)*			
In-Lab: Phase 1 (N = 12)	4.7 (0.7, 3-5)	3.8 (1.4, 2-5)	4.3 (1.4, 1-5)
Real-World - Week 1 (N = 42)	4.7 (0.7, 2-5)	4.3 (1.1, 2-5)	4.7 (0.7, 2-5)
Real-World - Week 2 (N = 43)	4.8 (0.4, 4-5)	4.4 (0.9, 2-5)	4.7 (0.6, 2-5)
How boring/fun was the task? *(1 = very boring, 5 = very fun)*			
In-Lab: Phase 1 (N = 12)	3.6 (1.0, 2-5)	3.8 (0.8, 3-5)	4.5 (0.7, 3-5)
Real-World - Week 1 (N = 42)	3.8 (0.9, 2-5)	2.8 (1.1, 1-5)	4.1 (0.8, 2-5)
Real-World - Week 2 (N = 43)	3.8 (1.0, 1-5)	2.7 (1.0, 1-5)	4.0 (0.6, 3-5)

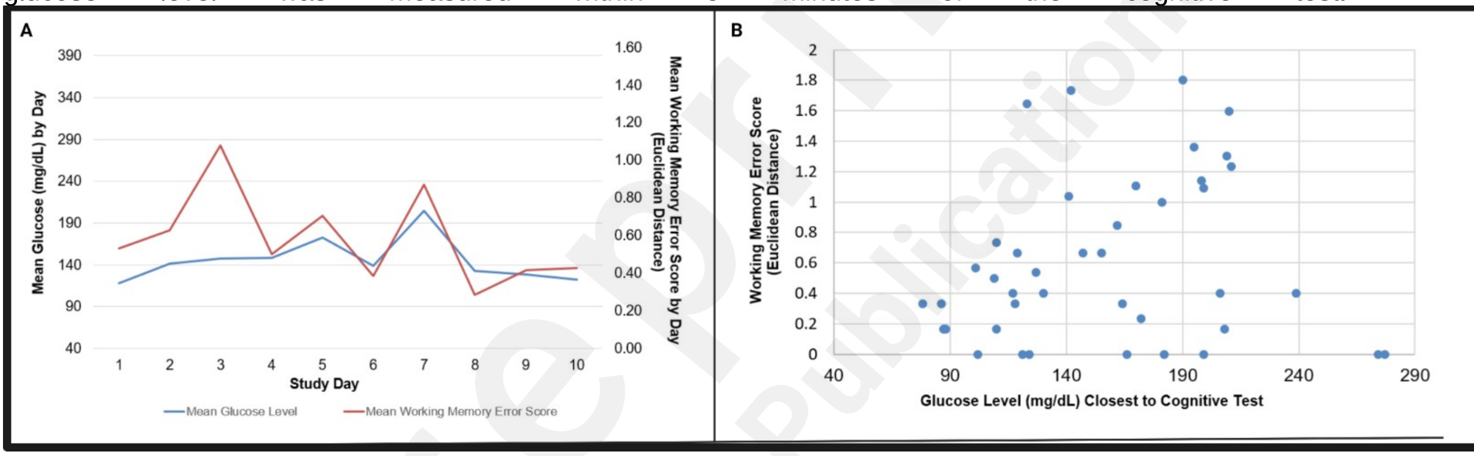
Figure 2. Scatterplots representing performance on each of the Ambulatory Research in Cognition (ARC) smartphone application tasks and age during the *In-Lab Study*. Each dot represents an individual participant. Lower scores on each task represent better cognitive performance. The (A) Symbols Task assesses processing speed, (B) Prices Task assesses associative memory, and (C) Grids Task assesses working memory.



Integrating Cognition and Continuously Measured Glucose in Youth with T1D

Cognitive and glucose data collected over the same time period were successfully integrated at distinct temporal resolutions for N=20 participants with T1D. Specifically, data were integrated for each day of participation and for each individual cognitive test (*Figure 3*).

Figure 3. Example of data integration for glucose measured via CGM and cognitive function measured via the Ambulatory Research in Cognition app for a participant with Type 1 Diabetes (T1D). Higher Working Memory Error Scores represent worse performance. A) Mean Glucose against mean Working Memory Error Score for each day of study participation. B) Glucose level closest to the time of each individual cognitive test; the glucose level was measured within 5 minutes of the cognitive test.



Discussion

This study aimed to assess the feasibility of using a smartphone app to measure dynamic cognitive function in youth in daily life and to integrate this information with data from CGM for youth with T1D. Youth performed well on 2/3 app tasks (Symbols, Grids), rated them highly (e.g., fun, understandable), and had high testing adherence (76%-80%) in daily life. This compliance is similar to that of adults from a previous study (~80%)[16]. Therefore, our data support the use of a smartphone app to measure dynamic cognition in youth aged 9-16 years, with and without T1D in daily life. Future studies could use this methodology to determine the relationship between short-term glycemic control and dynamic cognitive function in youth with T1D.

There were limitations. Our sample was homogenous—mostly non-Hispanic white with high household incomes. Studies are needed to develop protocols that will make participation more feasible for youth from underserved communities. Our cognitive app was only usable for age ≥9; further research is needed to determine what stimuli are appropriate for cognitive testing in younger youth. It is also important to note that there is a documented lag between interstitial glucose obtained from CGM and blood glucose in past literature[18-19]. Given that lag time is patient-specific[20], we chose to use the glucose measurement obtained closest to each individual cognitive test to illustrate the integration of glucose measured via CGM and cognition measured via the smartphone app; future studies assessing the relationship between short-term glucose control and dynamic cognitive function need to consider multiple glycemic features that account for lag.

In conclusion, we found that it is feasible to obtain measures of dynamic cognitive function in youth in daily life and integrate cognition measures and continuously measured glucose. This approach will move the field towards a fuller understanding of cognitive function variability in youth with T1D in naturalistic settings.

Acknowledgements

This work was made possible with support from Washington University in St. Louis WU-CDTR (P30DK092950), Washington University in St. Louis Diabetes Research Center (P30DK020579), and Washington University in St. Louis and BJC Healthcare Innovation Lab Big Ideas grant. MKR was supported by National Center for Advancing Translational Sciences of the National Institutes of Health Career Development Award (KL2TR002346), National Institute of Diabetes and Digestive and Kidney Diseases Career Development Award (1K01DK131339), Washington University in St. Louis Biomedical Research Training in Drug Abuse training grant (T32DA007261), and Washington University in St. Louis Transdisciplinary Postdoctoral Training Program in Obesity and Cardiovascular Disease

(T32HL130357). AA was supported by NIA K01AG071847. MEV was supported by NIDDK K23DK125719 The content is solely the responsibility of the authors and does not necessarily represent the official views of the WU-CDTR, DRC, NIDDK, NIA, or Healthcare Innovation Lab.

Conflicts of Interest

None declared.

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Abbreviations

Type 1 Diabetes: T1D

Ecological Momentary Assessment: EMA

ARC app: Ambulatory Research in Cognition App

Continuous Glucose Monitoring: CGM