# The Association Between Glycemic Variability and Macronutrients in Young Children with T1D

Alexandra D. Monzon (),<sup>1</sup> MA, Laura B. Smith,<sup>2</sup> PHD, CDE, Scott W. Powers,<sup>2</sup> PHD, ABPP, FAHS, Lawrence M. Dolan,<sup>3</sup> MD, and Susana R. Patton,<sup>4</sup>\* PHD, ABPP, CDE

<sup>1</sup>Clinical Child Psychology Program, University of Kansas, <sup>2</sup>Division of Behavioral Medicine & Clinical Psychology, Cincinnati Children's Hospital Medical Center, <sup>3</sup>Division of Endocrinology, Cincinnati Children's Hospital Medical Center, and <sup>4</sup>Nemours Center for Healthcare Delivery-Florida, Nemours Children's Health System

\*All correspondence concerning this article should be addressed to Susana R. Patton, PhD, ABPP, CDE, Nemours Center for Healthcare Delivery-Florida, Nemours Children's Health System, 807 Children's Way, Jacksonville, FL 32207, USA. E-mail: Susana.patton@nemours.org

Received 4 December 2019; revisions received 15 May 2020; accepted 29 May 2020

# Abstract

Objective There is limited information regarding the potential effect macronutrients have on postprandial glycemic variability in young children with type 1 diabetes (T1D). To date, studies examining nutrition and glycemic outcomes either assess these factors at a single timepoint, or aggregate large datasets for group level analyses. This study examined how inter- and intraindividual fluctuations in carbohydrate, fat, and protein intake impact glycemic variability in the postprandial period for young children with T1D. Methods Thirty-nine young children, aged 2-6 years, wore a continuous glucose monitor for 72 hr, while their parents completed detailed diet records of all food intake. The analyses tested three multilevel models to examine intra- and interindividual differences between food intake and postprandial glycemic variability. Results The results suggest carbohydrate intake, relates to greater postprandial glycemic variability. In contrast, the results reveal the inverse effect for protein, suggesting a tendency for young children who ate more protein at some meals to have lower postprandial glycemic variability, with the exception of lunch. There was no effect for fat on postprandial glycemic variability. Conclusion These results suggest protein consumption may be an important consideration when aiming for optimal glycemic levels for some meals. When counseling parents of young children with T1D on common behaviors underlying glycemic excursion, pediatric psychologists may consider discussing the nutritional make up of children's meals. Further, the results demonstrate retaining longitudinal data at the person level, versus aggregating individual data for group level analyses, may offer new information regarding macronutrient intake and glycemic outcomes.

Key words: glycemic variability; intraindividual differences; nutrition; type 1 diabetes; young children.

# Introduction

Young children, under the age of 7 years, with type 1 diabetes (T1D) mellitus are highly sensitive to insulin, resulting in their vulnerability to extreme variations in blood glucose levels (DiMeglio et al., 2004; Patton et al., 2011). In addition, young children can have

unpredictable eating behaviors (Patton et al., 2013), inconsistent activity levels (Sundberg et al., 2012), and limited communication skills (Desrocher & Rovet, 2004) that further complicate a family's ability to maintain glycemic levels in the target range (Streisand & Monaghan, 2014). Nutrition management has long been a part of diabetes care because the nutrients we

consume can influence postprandial blood glucose levels in different ways, such that patients with T1D can experience wide fluctuations in their postprandial glycemic levels. Unfortunately, the occurrence of extreme glycemic variability (via severe hypo- or hyperglycemia) is a risk factor for suboptimal glycated hemoglobin A1c (HbA1c) and long-term health complications including retinopathy, nephropathy, and neuropathy (Škrha et al., 2016). Pediatric psychologists frequently work alongside dietitians and diabetes educators to help families receive the necessary education related to T1D self-care and often provide behavioral support surrounding mealtime challenges. This study examined individual differences in macronutrient consumption to aid in tailoring interventions for families who may struggle with nutrition and glycemic variability (i.e., fluctuation in blood glucose levels).

Nutrition management is recommended for all children with T1D to optimize glycemic control. Carbohydrates are absorbed by the body faster than other macronutrients and can lead to postprandial excursions in blood glucose levels. Therefore, preprandial insulin dosing, up to 15–20 min before the meal, is recommended to reduce the risk of postprandial excursions (Bell et al., 2015). Overall, research has demonstrated that patients with T1D are more likely to achieve postprandial blood glycose in the target range when insulin is matched to carbohydrate ratios (MacLeod et al., 2017). However, there is some evidence in older children suggesting that meals high in fat or protein can impact early (i.e., 1–2 hr) or delayed (i.e., 3-6 hr) postprandial glycemia (Smart et al., 2013; Wolpert et al., 2013). The International Society for Pediatric and Adolescent Diabetes (ISPAD) offers dietary recommendations for macronutrient consumption and suggest that carbohydrates make up 45-50% of the total calories consumed, proteins make up 15-20% of total calories consumed, and fats make up <35% of energy with saturated fats making up <10%(Smart et al., 2018). Previous studies have demonstrated that young children with T1D do not meet the ISPAD recommendations for micro- and macronutrients, and better dietary quality associates with lower mean daily glucose levels (Patton et al., 2013). Unfortunately, no research to date has examined individual differences in macronutrient consumption and fluctuations in glucose levels in young children with T1D during the postprandial period. A deeper understanding of these relationships at the individual level may help practitioners and families optimize their child's glycemic control.

Continuous glucose monitors (CGMs) are a relatively new device that provides a near continuous glucose reading. These devices offer a more complete glucose picture, whereas traditional self-monitoring of blood glucose may miss important glucose excursions.

Families may also set alarms to indicate when their child's glucose levels are outside the target range. Therefore, in patient groups who may be more vulnerable to glycemic variability (e.g., young children), CGMs may provide more information to track glucose fluctuations and to potentially help families to optimize their T1D management (Patton et al., 2011). Yet, while CGMs provide intensive longitudinal data, in the existing research using this technology, most researchers have elected to aggregate the data into groups and/or collapse the data into summary values often at the expense of variability. This approach limits the ability to examine interindividual differences (e.g., Do young children with T1D with higher macronutrient intake have higher postprandial glycemic variability?) and intraindividual differences (e.g., does a child's postprandial glycemic variability differ on days, or by meal, when their macronutrient intake is higher/lower than their personal average?) in the data. Analyzing CGM data at the individual level may uncover new information regarding glycemic outcomes in relation to macronutrient intake and fill important gaps in the understanding of young children's glycemia in the postprandial period.

Thus, the aim of this study was to examine how interindividual (i.e., between participant) and intraindividual (i.e., within participant) fluctuations in carbohydrate, fat, and protein intake influence glycemic variability, as measured by the standard deviation of glucose values, in the postprandial period (i.e., 3 hr postmeal) for young children with T1D. The research team hypothesized that children who consume a diet high in carbohydrates would experience more glycemic variability. However, as an exploratory hypothesis the research team also examined the strength of the relationship between glycemic variability and the consumption of fats and proteins.

#### **Materials and Methods**

## **Participants**

This study enrolled 39 young children and their parents from two Midwest pediatric Endocrinology clinics. Eligibility criteria included child age between 2 and 6.99 years, a confirmed diagnosis of T1D for at least 12 months, English speaking, and intensive insulin treatment (e.g., multiple daily injections [MDI] or insulin pump). The study team recorded children's glycated hemoglobin level (HbA1c) as a proxy for child average glycemic levels to use as a covariate in the analyses.

## Procedures

The Institutional Review Board at each institution approved this study prior to recruitment. To recruit for the project, the research team sent out letters to 77

potentially eligible families. Research staff then called families to answer their questions, obtain informed consent, and enroll families in the study  $\sim 2$  weeks after mailing the letters. Thirty-nine families agreed to participate yielding a recruitment rate of 51% with no attrition during the study period. The initial study visit took place in each family's home. At this visit, research staff placed a CGM on the back of the child's arm, on their stomach, or on their buttocks to measure daily fluctuations in glucose. Children wore the CGM for 72 hr, after which the parents removed the sensor and returned the monitor. In addition, research staff trained parents how to accurately measure their child's liquid and solid food intake, and how to complete a 3-day diet diary. Research staff asked parents to weigh or measure all food and beverages their child consumed (i.e., breakfast, lunch, dinner, and snacks) while their child wore the CGM on a standardized diet diary. Research staff gave parents a digital scale and food measuring cups/spoons for consistent measurement across families, and instructed parents to weigh foods and beverages pre- and postfeeding. In addition to recording foods and beverages, parents recorded the time, dose, and type of insulin that they gave to their child. Research staff asked parents to maintain their child's typical diet and daily activities during the 72-hr monitoring period. Research staff returned to each families' home a week later to collect all data and study materials and used the electronic medical record to collect other relevant child T1D health outcomes (e.g., frequency of hypoglycemia, most recent HbA1c) that corresponded with the time of data collection. The data from this study were derived from a larger study examining dietary adherence and mealtime behaviors in young children with T1D (Patton et al., 2013). Data were collected between 2007 and 2008.

# Measures

## **Detailed Diet Records**

Parents monitored their child's food and beverage intake using a weighed diet diary on the 3 consecutive days their child wore the CGM (typically including at least 1 weekend day). Researchers used a studyspecific food diary, reviewed and approved by a research dietitian, who then analyzed the food recall with the Nutrition Data System for Research (NDSR) software version 2009 analyses. This dietary analysis program calculated, in grams, the total carbohydrates, proteins, and fats for each food item the child consumed. These macronutrients can be further broken down into more specific categories (i.e., protein from animals, protein from vegetables, saturated fats, etc.); however for this study, the various types of carbohydrates, proteins, and fats were not examined. NDSR uses the appropriate nutritional information and food

composition data available at the time of data collection and is the gold-standard for nutritional analyses. Families also videotaped their child's meals at home as part of the protocol of the larger study. This extra procedure gave research staff the opportunity to "visually verify" the food and beverages parents recorded on the diet diaries and offered additional evidence supporting the validity of the nutritional data parents reported. In addition, in real-time as research staff collected the diet diaries from families; a research dietitian reviewed the records and contacted families to verify weights, measures, and foods when she had any concerns about the accuracy of the diaries.

## **Continuous Glucose Monitor**

Researchers used the Medtronic Minimed CGM System Gold to measure glucose concentrations over a continuous 72-hr period. The researchers selected this device for use in this study because of its wearability and accuracy in (Gandrud et al., 2007; Patton et al., 2011). CGMs were blinded to participants for the duration of the study and all participants wore the study issued CGM. Of note, at the time of data collection, there was no personal CGM use in children under the age of 18 years old and the researchers had to get an Investigational Device Exemption (per Code of Federal Regulations 812.2[b]) to complete the study. The study team instructed parents to calibrate the CGM twice daily, to ensure validity of glucose data. Once placed just under the skin, this CGM measured glucose in interstitial fluid every 10 s. The device then related these interstitial fluid glucose measurements, using a computer driven algorithm, into a mean glucose level every 5 min. The research team calculated the average and standard deviation of glucose levels in the 3 hr postmeal to reflect young children's glycemic variability. The standard deviation of glucose levels is a common metric for glycemic variability when utilizing CGM data (Jung, 2015). Further the standard deviation of glucose levels has demonstrated usefulness in clinical practice for predicting hyperglycemia and hypoglycemia (Saisho et al., 2015).

#### **Demographic Form**

Parents reported descriptive information regarding their family (e.g. child age, biological sex, family income, and race/ethnicity) at the time of the initial study visit.

#### Data Analysis Plan

This study assessed both inter- (i.e., the variability of responses across participants) and intraindividual variance (i.e., the variability of an individual's responses over time). To model these two sources of variability, researchers included a grand mean centered and person mean centered independent variable in each

	Ν	%
Child sex		
Males	20	51.3
Females	19	48.7
Child ethnicity		
Caucasian	32	82.1
Non-Caucasian	7	17.9
Child insulin regimen		
Pump	25	64.1
Multiple daily injections	14	35.9
Participating parent		
Mother	33	84.6
Father	4	10.3
Stepmother	2	5.1
Parent marital status		
Married	30	76.9
Single	3	7.7
Divorced	2	5.1
Separated	4	10.3
Parent education		
Some high school	1	2.6
High school graduate	5	12.8
Trade school	2	5.1
Some college	11	28.2
College graduate	14	35.9
Graduate school	6	15.4
Hollingshead		
4-Factor Socioeconomic		
Scale		
I (lowest level)	2	5.1
II	4	10.3
III	11	28.2
IV	14	35.9
V (highest level)	8	20.5
	M(SD)	Range
Child HbA1c	8.6 mmol/mol	6.9–12.7
	(1.34)	mmol/mol
Child age	5.08 years (1.13)	2-6 years
Child BMI	17.06 (1.59)	15.10-21.81
Parent age	35.11 years (6.36)	22-50 years

**Table I.** Descriptive Information for Participating Familiesof Children With Type 1 Diabetes (N = 39)

Note. M = mean; SD = standard deviation; BMI = body mass index.

model. To grand mean center independent variables, the researchers subtracted the grand mean from each observation. Then, researchers aggregated the grand mean centered variable within each participant to form the interindividual variable. Finally, to form the intraindividual variable, the researchers subtracted the between person variable from each observation.

Using SAS PROC MIXED, this study tested three multilevel models to examine intra- and interindividual differences between food intake (i.e., carbohydrate, protein, and fat) and postprandial glycemic variability. The researcher used a categorical variable of meal type (i.e., breakfast, lunch, snacks, and dinner) as a moderator in the relationship between food intake and glycemic variability. Each model included HbA1c, the total grams of the meal, glycemic index, and grams of fiber as covariates. The research team managed missing data using full information maximum likelihood estimation (Enders, 2001) with the assumption that data were missing at random. Each set of analyses entered time as a linear, random linear, quadratic, and random quadratic predictor in four separate models, to explicitly test for the influence of time. Finally, the researchers conducted nested model comparisons and determined that a random linear effect of time was the best fitting model for each set of analyses.

# Results

The average child age was 5.08 years (SD = 1.1) and 51% of children were girls. The average glycated HbA1c for children was 8.6% (*SD* = 1.34). This mean is higher than the current American Diabetes Association (ADA) recommended value of  $\leq 7.5\%$ (American Diabetes Association, 2020b), but was only just above the ADA recommended target of < 8.5%for young children at the time of data collection (Silverstein et al., 2005). There were no significant differences in child age and glycemic levels (HbA1c) for the families who consented to participate in the project versus the families of young children who made up the respective clinic populations. Further, there was low variability in body mass index (BMI) across young children and there were no significant differences among percentile categories. In the sample, 87% of BMI values were in classified in the healthy percentile range. Table I provides additional descriptive information regarding the participating families. Average child carbohydrate, protein, and fat consumption can be found in Table II, along with average postprandial glucose levels.

There were no significant differences with regards to macronutrient consumption and glycemic variability across family socioeconomic status, marital status, and child ethnicity. There was a significant difference in HbA1c for children using insulin pumps (M = 8.27, SD = 1.25) and those using MDI (M = 9.22, SD =1.33), such that youth using insulin pumps had a lower HbA1c; t(35) = -2.16, p < .05. There were no significant differences between macronutrient consumption, or glycemic variability, between youth using insulin pumps and MDI. Further, there were no significant associations between HbA1c and each macronutrient, or between HbA1c and glycemic variability. Parents reported administering insulin before the meal ~75% of the time and administering insulin during or after the meal 25% of the time. There were no significant differences in glycemic variability between insulin administration before and after the meal. Table III provides the associations of macronutrient predictors and covariates with glycemic variability as the outcome.

	Amount consumed		% calories consumed	
	M(SD)	Range	M (SD)	Range
Carbohydrate intako	e			
Breakfast	47.32 g (28.67)	3.46–152.34 g	62.08 (17.02)	8.13-84.92
Lunch	51.98 g (28.06)	2.20–171.76 g	48.76 (14.05)	3.99-86.46
Snacks	20.70 g (17.61)	0.00–98.18 g	56.50 (28.28)	0.00-100.00
Dinner	51.40 g (31.62)	2.82–179.60 g	43.69 (13.75)	9.13-74.60
Protein Intake		C		
Breakfast	10.09 g (7.05)	0.79–48.00 g	12.80 (4.85)	3.20-27.91
Lunch	17.15 g (12.31)	1.07–90.25 g	15.74 (6.59)	5.59-38.07
Snacks	3.93 g (4.76)	0.00–26.06 g	14.29 (21.73)	0.00-100.00
Dinner	21.86 g (24.35)	0.39–243.97 g	19.26 (8.74)	5.27-46.72
Fat intake		U		
Breakfast	9.72 g (9.45)	0.19–48.14 g	25.01 (14.60)	1.68-63.83
Lunch	17.72 g (10.36)	0.46–54.81 g	35.48 (12.67)	4.71-72.66
Snacks	5.66 g (6.83)	0.00–42.24 g	27.43 (21.06)	0.00-76.87
Dinner	18.88 g (11.16)	0.26–51.47 g	37.00 (12.10)	9.56-67.22
Postprandial BG lev	el	0	× ,	
Breakfast	251.64 mg/dl (82.25)	94-400 mg/dl		
Lunch	211.27 mg/dl (88.66)	76–400 mg/dl		
Snacks	203.33 mg/dl (85.56)	53–400 mg/dl		
Dinner	204.55 mg/dl (77.29)	63–385 mg/dl		

|--|

Note. M = mean; SD = standard deviation; BG, blood glucose. Current International Society for Pediatric and Adolescent Diabetes recommendations suggest that carbohydrates make up 45–50% of the total calories consumed, proteins make up 15–20% of total calories consumed, and fats make up <35% of energy with saturated fats making up <10% (Smart et al., 2018).

The research team first examined unconditional models in order to calculate the intraclass correlation coefficient (ICC) which provides an assessment of inter- and intraindividual variability for each variable of interest. The ICC for glucose was .289, which indicated that 28.9% of the variability in glucose was between person and 71.1% of the variability was within person. The ICC for carbohydrates was .203, which indicated that 20.3% of the variability in carbohydrates was between person and 79.7% of the variability was within person. The ICC for protein was .114, which indicated that 11.4% of the variability in protein was between person and 88.6% of the variability was within person. Last, the ICC for fats was .049, which indicated that 4.9% of the variability in fats was between person and 95.1% of the variability was within person.

## Carbohydrates

Results of the multilevel models indicated that there was a fixed linear effect for total meal carbohydrate prospectively associated with postprandial glycemic variability between individuals. This finding suggests that the children who ate a greater number of carbohydrates during their meal ( $\beta$  = .31, *p* < .05) had higher postprandial glycemic variability, while controlling for total meal grams. Further, there was an interaction between meal type and intraindividual carbohydrates consumed, such that children who ate a greater number of carbohydrates for lunch than

typical for themselves ( $\beta = .31$ , p < .05) had higher postprandial glycemic variability.

#### Proteins

There was a fixed linear effect for total meal protein prospectively associated with postprandial glycemic variability within individuals. This finding suggests that children who ate more protein than typical for themselves during their meal ( $\beta = -.29$ , p < .05) had lower postprandial glycemic variability, while controlling for total meal grams. Further, there was an interaction between meal type and intraindividual protein consumed, such that children who ate more protein for lunch than typical for themselves ( $\beta = .59$ , p < .05) had higher postprandial glycemic variability.

## Fats

There were no significant interactions or linear effects for inter- or intraindividual fat consumption and postprandial glycemic variability.

## Meal Type

When the research team assessed meal type independent of food consumption, there was a significant association for snacks and postprandial glycemic variability ( $\beta = -10.11$ , p < .05), suggesting lower glycemic variability following snacks, in general. There was also a significant association for breakfast and average postprandial glycemic values ( $\beta = 47.97$ ,

	Glycemic variability	
	$\beta$ (SE)	p
Carbohydrates		
Fixed effects		
Intercept	36.88 (7.05)	<.0001
Time	58 (1.27)	.65
BP CHO	.31 (0.12)	.01
WP CHO	13 (0.10)	.22
WP CHO*breakfast	11 (0.16)	.50
WP CHO*lunch	.31 (0.15)	.04
WP CHO*snacks	.27 (0.14)	.06
WP CHO*dinner	.16 (0.12)	.10
Random effects		
Intercept variance	197.36 (77.16)	.01
Time slope variance	12.68 (8.55)	.07
Intercept-time slope covariance	-48.39 (24.50)	.05
Residual	517.56 (40.93)	<.0001
Proteins		
Fixed effects		
Intercept	41.91 (6.20)	<.0001
Time	60 (1.30)	.65
BP PRO	.52 (0.30)	.09
WP PRO	29 (0.12)	.02
WP PRO*breakfast	31 (0.36)	.38
WP PRO*lunch	59 (0.27)	.03
WP PRO*snacks	.62 (0.35)	.08
WP PRO*dinner	.42 (0.25)	.12
Random effects		
Intercept variance	211.71 (81.64)	.01
Time slope variance	14.76 (9.23)	.05
Intercept-time slope covariance	-53.90 (26.44)	.04
Residual	515.71 (40.72)	<.0001
Fats		
Fixed effects		
Intercept	38.67 (7.82)	<.0001
Time	43 (1.32)	.75
BP fats	.83 (0.46)	.07
WP fats	40 (0.25)	.11
WP fats* breakfast	25(0.40)	.53
WP fats*lunch	.58 (0.37)	.12
WP fats*snacks	.40 (0.37)	.28
WP fats*dinner	.38 (0.26)	.36
Random effects		
Intercept variance	202.72 (80.65)	.01
I ime slope variance	14.54 (9.31)	.06
Intercept-time slope covariance	-52.41(26.57)	.05
Kesidual	522.44 (41.28)	<.0001

 
 Table III. Associations of Macronutrient Predictors and Covariates With Glycemic Variability as the Outcome

Note. SE = standard error; BP = between person; WP = within person; CHO = carbohydrates; PRO = proteins; Bolded lines indiacte p < .05.

p < .05), suggesting higher mean glucose values following breakfast, in general for all young children.

## Discussion

This study examined how inter- (i.e., between child) and intra-individual (i.e., within child) fluctuations in carbohydrate, fat, and protein intake impact glycemic

variability in the postprandial period for young children with T1D. The results suggest carbohydrate intake, and particularly a high intake of carbohydrates, relates to greater postprandial glycemic variability. In contrast, the results demonstrated an inverse effect for protein, suggesting young children who ate more protein were more likely to have lower postprandial glycemic variability. However, there was also an interaction between meal type and protein consumption, suggesting higher postprandial glycemic variability may follow lunches where young children eat more protein than typical for themselves. This study builds upon previous work conducted by Smart et al. (2013) in older children with T1D. Specifically, their results suggested that the addition of protein and/or fat to a carbohydrate meal had no significant difference on glycemia in the first 3 hr postmeal, but significantly increased glucose between 3 and 5 hr postmeal. In this study, the results demonstrate a stronger effect for intraindividual protein consumption during the early postprandial period in young children with T1D and highlights the importance of examining these data at the individual level (vs. group level) in order to model intraindividual differences in macronutrient consumption in children. The results of this study also point to the need for more longitudinal research to understand glycemic data at the individual level in youth with T1D. Indeed, aggregating glucose data over several days or an entire study period may miss important glucose patterns made possible for discovery by CGM devices, while maintaining individual data within a multilevel framework offers unique information which psychologists and other diabetes care providers may use to tailor treatment in children.

The results suggest an interesting pattern related to meal timing and size. For example, postprandial glycemic variability was greater for children who ate more protein and carbohydrates, than typical for themselves, during lunch. Families consumed their lunch over a wide span of time in the middle of the day, with some eating lunch in late morning and some eating in the late afternoon. It is possible that this difference in time may have contributed to the large glycemic variability observed after lunch (Table II). However, specific to meal size, the study results also suggest that glycemic variability may be heavily influenced by insulin therapy and the caregivers' ability to accurately estimate mealtime insulin requirements. For example, the results suggest higher glycemic variability when children with T1D consumed larger meals than typical, regardless of meal composition, indicating parents may have experienced more difficulty estimating insulin needs for larger meals. Previous research in families of older youth have shown that both parents and youth have more difficulty estimating carbohydrate content for larger meals versus smaller meals and snacks (Smart et al., 2010). Therefore, the results of this study appear to extend these results to families of young children as well. Interestingly, in this study, researchers found that snacks were generally associated with lower glycemic variability and demonstrated the lowest variability in the amount of carbohydrate, protein, and fat young children consumed. It is possible that the low variability in carbohydrate, protein, and fat content in children's snacks combined with the number of snacks children consumed during the day aided in relatively tight glycemic levels for the young children in this study.

Consistent with previous findings (Patton et al., 2013) there is newer evidence suggesting that young children with T1D continue to fall short of meeting nutritional recommendations regarding macronutrient consumption (Mackey et al., 2020). Further, there is evidence that children with suboptimal glycemic levels report higher carbohydrate intake while those with more optimal glycemic levels report higher protein intake at breakfast (Mackey et al., 2020). However, these previous studies examined overall group means and proxies for glycemic control (i.e., child HbA1c), while this study examined individual variation in macronutrient intake and glycemic variability. Therefore, the researchers assert that this study builds upon these previous studies by adding a level of detail to the evidence that can better inform pediatric psychologists and other clinic-based educators on how to approach individual counseling with parents regarding feeding behavior and insulin administration, two cornerstones of T1D self-care.

Although not included as a variable in this study, problematic child mealtime behavior (i.e., low appetite, picky eating, tantrums) can also pose an important challenge to optimal child nutrition intake and be a common referral concern for pediatric psychologists. Specific to young children with T1D, previous studies reveal associations between child nutrition, child mealtime behavior, and child picky eating (Patton et al., 2013). Moreover, the literature in families of young children with T1D reveals significant positive associations between child disruptive mealtime behaviors and their average daily glycemic levels (Patton et al., 2006). What is not yet known is how child disruptive mealtime behaviors may influence glycemic variability beyond the potential influence of the meal's macronutrient composition. However, the results of this study suggest that behavioral interventions should also consider the nutritional make up of children's meals and the fluctuations in postprandial glucose levels that children may experience based on their intake of carbohydrate, protein, and fat during their meals.

The results of this study have important implications for parent education and glycemic control. Some evidence suggests that insulin dosing based on

carbohydrate, fat, and protein grams could lead to lower postprandial glycemic levels than conventional carbohydrate counting (Bell et al., 2015; Kordonouri et al., 2012). Although most of the available literature draws from adult samples, this study is one of the first to report on the effect of person-level macronutrient consumption on glycemic variability in young children. This study results suggest that protein consumption is an important consideration when aiming for optimal glycemic levels for some meal types. Therefore, in working with families of young children who are struggling with glycemic variability and suboptimal glycemic levels, it is possible that a pediatric psychologist could help by offering updated nutritional education so that parents would have adequate knowledge to consider whether adding protein to their child's meals could help with reducing their child's glycemic variability and meeting their child's glucose target.

There is evidence of at least one parent intervention, targeting nutrition education, food shopping, and meal preparation in families of young children with T1D which found that this education led to a decrease in children's mean daily glucose values (Patton et al., 2014). This intervention was designed and delivered by pediatric psychologists in collaboration with clinic-based educators, suggesting that families of young children with T1D may be receptive to learning about their child's nutrition from multiple professionals. However, beyond that, the authors would assert that pediatric psychologists are in the unique position to deliver education and intervention that may focus on diet and food intake because their training teaches them to consider individual, family, and physiological factors that can impede disease management. Furthermore, psychologists have the training and experience to assess for barriers related to parent and child mood or behavior and to intervene with motivational interviewing strategies, cognitive-behavioral therapy, problem-solving and goal-setting, or behavioral parent training to help reduce the impact of these barriers.

This study has particular strengths worth noting. First, the intraindividual level of analyses provides more information about the individual child regarding the relationships examined than traditional statistical approaches can offer. Second, the real-time glucose measurement via CGM during the postprandial period provides a highly specific picture of glycemic variability that would otherwise be missed by self-monitoring blood glucose data or HbA1c. There are, however, some limitations to acknowledge when conceptualizing the results. First, the current study is limited by a small sample size. Although a small sample size is a common limitation for most studies recruiting young children in T1D (Mackey et al., 2020; Seckold et al., 2019), nonetheless here, the small sample and homogeneous demographic make-up of the children limits the ability to generalize the results to young children from other ethnic or racial groups or children who may still be on a conventional insulin regimen, even though the American Diabetes Association recommends that most children with T1D use intensive insulin therapy (American Diabetes Association, 2020a). Second, in the larger study there was no way to evaluate the accuracy of parents' insulin dosing without moving the study outside of the home environment. Unfortunately, this means that if parents had difficulty dosing for insulin at a meal or purposefully administered a low dose of insulin for a meal, these dosing decisions, or the intermittent use of extended or delayed insulin bolusing could impact the some of the variability observed in children's postprandial glycemia independent of the nutrient content of the meal. Along this same notion is a potential Hawthorne effect. Parents may have misreported portion size of meals or snacks during the day because they knew they were being studied, which could impact the internal validity of their data. Third, CGMs do not measure glucose values over 400 mg/dl. Therefore, it is possible that the glycemic variability observed in this study may be an underrepresentation of the true postprandial glycemic range children experienced. However, clinically speaking, because diabetes care teams would consider all glucose values above 250 mg/dl to be very high (Battelino et al., 2019) and would provide similar treatment recommendations for values above 250 or 400 mg/dl (i.e., monitor ketones, increase blood glucose monitoring), we anticipate any impact device limitations may have had on our analyses to be minor. Related, due to the evolving nature of diabetes technology, there may be a limitation specific to the CGM model used in the current study. Although there is no evidence to suggest that these CGMs failed to provide accurate glucose data, future studies may consider examining similar relationships in newer devices that can provide a longer observation period (e.g., 7-10 days) as well as real-time data on child glycemic levels. Fourth, this study did not include a measure of physical activity. Young children who were physically active before or during the postprandial period may have experienced less glycemic variability. A child could be more insulin sensitive as a result of exercise versus their nutrient intake. While parents were asked to record physical activity on the diet diaries, it was not clear that all parents did this and children did not wear an accelerometer to objectively measure their physical activity levels. Last, this study examined glycemic variability in a 3-hr postprandial period; however, both fats and proteins can impact glycemia beyond a 3-hr period. Therefore, the longer-term impact of fat and protein intake on young

children's glycemia outside of the immediate postprandial period remains unknown.

## Conclusion

The results of this study suggest a clear pattern regarding the average amount of macronutrients a young child consumes and their postprandial glycemic variability. If young children consume a similar amount of proteins and carbohydrates per meal, it is possible that they may experience a greater likelihood of lowering their glycemic variability postmeal. Future studies should consider examining additional macronutrients and micronutrients in a larger sample of children. Further, it would be helpful to understand how physical activity influences this relationship since other studies (Leclair et al., 2013) have shown a link between glucose values and exercise in other persons with T1D. The findings from this study have important clinical implications for pediatric psychologists. Specifically, the results suggest that psychologists working with families of youth with T1D may consider counseling parents of young children on not just if or how much their child eats, but what their child eats for their meals and snacks. This broader perspective of child feeding/eating as a self-care behavior may help augment what pediatric psychologists already provide with respect to counseling and behavioral parent training for mealtimes.

# Acknowledgments

The authors would like to thank Ram Menon, MD, for his assistance in the implementation of this study. The authors also thank the families who participated in this study. Through their participation, the study team can continue to advance diabetes research in young children. The data analyzed for this article come from a study that was conducted at the University of Michigan/C.S. Mott Children's Hospital and the University of Cincinnati. The authors have received permission from those named in the acknowledgements.

## Funding

This study was supported in part by grants K24-DK59973 and K23-DK076921 from the National Institutes of Health/ National Institute of Diabetes and Digestive and Kidney Diseases.

Conflicts of interest: None declared.

## References

- American Diabetes Association. (2020a). 13. Children and Adolescents: Standards of Medical Care in Diabetes— 2020. *Diabetes Care*, 43, S163–S182.
- American Diabetes Association. (2020b). 6. Glycemic targets: Standards of medical care in diabetes—2020. *Diabetes Care*, 43, S66–S76. https://doi.org/10.2337/dc20-S006.

- Battelino, T., Danne, T., Bergenstal, R. M., Amiel, S. A., Beck, R., Biester, T., Bosi, E., Buckingham, B. A., Cefalu, W. T., Close, K. L., Cobelli, C., Dassau, E., DeVries, J. H., Donaghue, K. C., Dovc, K., Doyle, F. J., Garg, S., Grunberger, G., Heller, S., ... Phillip, M. (2019). Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. *Diabetes Care*, 42, 1593–1603. 10.2337/ dci19-0028
- Bell, K. J., Smart, C. E., Steil, G. M., Brand-Miller, J. C., King, B., & Wolpert, H. A. (2015). Impact of fat, protein, and glycemic index on postprandial glucose control in type 1diabetes: Implications for intensive diabetes management in the continuous glucose monitoring era. *Diabetes Care*, 38, 1008–1015. https://doi.org/10.2337/dc15-0100
- Desrocher, M., & Rovet, J. (2004). Neurocognitive correlates of type 1 diabetes mellitus in childhood. *Child Neuropsychology*, 10, 36–52. https://doi.org/10.1076/ chin.10.1.36.26241
- DiMeglio, L. A., Boyd, S. R., Pottorff, T. M., Cleveland, J. L., Fineberg, N., & Eugster, E. A. (2004). Preschoolers are not miniature adolescents: A comparison of insulin pump doses in two groups of children with type 1 diabetes mellitus. *Journal of Pediatric Endocrinology and Metabolism*, 17, 865–870.
- Enders, C. K. (2001). The performance of the full information maximum likelihood estimator in multiple regression models with missing data. *Educational and Psychological Measurement*, 61, 713–740. https://doi.org/10.1177/ 0013164401615001
- Gandrud, L. M., Xing, D., Kollman, C., Block, J. M., Kunselman, B., Wilson, D. M., & Buckingham, B. A. (2007). The Medtronic MiniMed gold continuous glucose monitoring system: An effective means to discover hypoand hyperglycemia in children under 7 years of age. *Diabetes Technology & Therapeutics*, 9, 307–316. https:// doi.org/10.1089/dia.2007.0026
- Jung, H. S. (2015). Clinical implications of glucose variability: Chronic complications of diabetes. *Endocrinology and Metabolism*, 30, 167–174. https://doi.org/10.3803/EnM. 2015.30.2.167
- Kordonouri, O., Hartmann, R., Remus, K., Bläsig, S., Sadeghian, E., & Danne, T. (2012). Benefit of supplementary fat plus protein counting as compared with conventional carbohydrate counting for insulin bolus calculation in children with pump therapy. *Pediatric Diabetes*, 13, 540–544. https://doi.org/10.1111/j.1399-5448.2012. 00880.x
- Leclair, E., de Kerdanet, M., Riddell, M., & Heyman, E. (2013). Type 1 diabetes and physical activity in children and adolescents. *Journal of Diabetes & Metabolism, S10*, 004. https://doi.org/10.4172/2155-6156.S10-004
- Mackey, E. R., Rose, M., Tully, C., Monaghan, M., Hamburger, S., Herrera, N., & Streisand, R. (2020). The current state of parent feeding behavior, child eating behavior, and nutrition intake in young children with type 1 diabetes. *Pediatric Diabetes*, https://doi.org/10.1111/pedi. 12997
- MacLeod, J., Franz, M. J., Handu, D., Gradwell, E., Brown, C., Evert, A., ... Robinson, M. (2017). Academy of Nutrition and Dietetics Nutrition Practice Guideline for

type 1 and type 2 diabetes in adults: Nutrition intervention evidence reviews and recommendations. *Journal of the Academy of Nutrition and Dietetics*, 117, 1637–1658.

- Patton, S. R., Dolan, L. M., Chen, M., & Powers, S. W. (2013). Dietary adherence and mealtime behaviors in young children with type 1 diabetes on intensive insulin therapy. *Journal of the Academy of Nutrition and Dietetics*, 113, 258–262. https://doi.org/10.1037/ a0033615
- Patton, S. R., Dolan, L. M., & Powers, S. W. (2006). Mealtime interactions relate to dietary adherence and glycemic control in young children with type 1 diabetes. *Diabetes Care*, 29, 1002–1006. https://doi.org/10.2337/ dc05-2354
- Patton, S. R., Odar, C., Midyett, L. K., & Clements, M. A. (2014). Pilot study results for a novel behavior plus nutrition intervention for caregivers of young children with type 1 diabetes. *Journal of Nutrition Education and Behavior*, 46, 429–433. https://doi.org/10.1016/j.jneb. 2013.11.007
- Patton, S. R., Williams, L. B., Eder, S. J., Crawford, M. J., Dolan, L., & Powers, S. W. (2011). Use of continuous glucose monitoring in young children with type 1 diabetes: Implications for behavioral research. *Pediatric Diabetes*, 12, 18–24. https://doi.org/10.1111/j.1399-5448.2010. 00649.x
- Saisho, Y., Tanaka, C., Tanaka, K., Roberts, R., Abe, T., Tanaka, M., ... Itoh, H. (2015). Relationships among different glycemic variability indices obtained by continuous glucose monitoring. *Primary Care Diabetes*, 9, 290–296.
- Seckold, R., Howley, P., King, B. R., Bell, K., Smith, A., & Smart, C. E. (2019). Dietary intake and eating patterns of young children with type 1 diabetes achieving glycemic targets. *BMJ Open Diabetes Research and Care*, 7, e000663.
- Silverstein, J., Klingensmith, G., Copeland, K., Plotnick, L., Kaufman, F., Laffel, L., ... Clark, N.; American Diabetes Association. (2005). Care of children and adolescents with type 1 diabetes: A statement of the American Diabetes Association. *Diabetes Care*, 28, 186–212. https://doi.org/ 10.2337/DIACARE.28.1.186
- Škrha, J., Šoupal, J., Škrha, J., & Prázný, M. (2016). Glucose variability, HbA1c and microvascular complications. *Reviews in Endocrine and Metabolic Disorders*, 17, 103–110. In (Vol. Issue Springer US. https://doi.org/10. 1007/s11154-016-9347-2
- Smart, C. E. M., Evans, M., O'Connell, S. M., McElduff, P., Lopez, P. E., Jones, T. W., ... King, B. R. (2013). Both dietary protein and fat increase postprandial glucose excursions in childrenwith type 1 diabetes, and the effect is additive. *Diabetes Care*, 36, 3897–3902. https://doi.org/ 10.2337/dc13-1195
- Smart, C. E., Ross, K., Edge, J. A., King, B. R., McElduff, P., & Collins, C. E. (2010). Can children with type 1 diabetes and their caregivers estimate the carbohydrate content of meals and snacks? *Diabetic Medicine*, 27, 348–353. https://doi.org/10.1111/j.1464-5491.2010.02945.x
- Smart, C. E., Annan, F., Higgins, L. A., Jelleryd, E., Lopez, M., & Acerini, C. L. (2018). ISPAD Clinical Practice Consensus Guidelines 2018: Nutritional management in

children and adolescents with diabetes. *Pediatric Diabetes*, 19, 136–154. https://doi.org/10.1111/pedi.12738

- Streisand, R., & Monaghan, M. (2014). Young children with type 1 diabetes: Challenges, research, and future directions. *Current Diabetes Reports*, 14, 520.
- Sundberg, F., Forsander, G., Fasth, A., & Ekelund, U. (2012). Children younger than 7 years with type 1 diabetes are less physically active than healthy controls. *Acta Paediatrica, International Journal of Paediatrics*, 101,

1164–1169. https://doi.org/10.1111/j.1651-2227.2012. 02803.x

Wolpert, H. A., Atakov-Castillo, A., Smith, S. A., & Steil, G. M. (2013). Dietary fat acutely increases glucose concentrations and insulin requirements in patients with type 1 diabetes: Implications for carbohydrate-based bolus dose calculation and intensive diabetes management. *Diabetes Care*, 36, 810–816. https://doi.org/10.2337/dc12-0092