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Original Article



# Differential longitudinal effects of frequent sweetened food consumption at different exposure ages on child cognitive, language, and motor development

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## ABSTRACT

**Background:** Evidence reveals frequent sugar consumption worsens cognition in animal models, and similar effects on child development are probable. We aimed to investigate the influence of sweetened foods (SFs) on child developmental trajectories.

**Methods:** The prospective cohort recruited 3-month-old children in Taiwan from 1st April 2016 to 30th June 2017. Developmental inventories including cognitive, language, and motor domains, were measured at the age of 3-, 12-, 24-, and 36 months old via in-person interviews. We constructed latent growth models with covariates to estimate the influence of SFs on child development.

**Results:** Ultimately, 4782 children (50.7% boys) were included in the statistical analysis. In the cognitive domain, consumption at one year of age significantly affected the intercept, but not the linear slope and quadratic term (intercept: estimate =  $-0.054$ ,  $p < .001$ ); consumption at two years of age significantly affected the intercept and quadratic term (intercept: estimate =  $-0.08$ ,  $p < .001$ ; quadratic term: estimate =  $-0.093$ ,  $p = .026$ ), but not the linear slope. In the language domain, only consumption at two years of age significantly affected the intercept (estimate =  $-0.054$ ,  $p < .001$ ). In the motor domain, consumption at two years of age significantly affected the linear slope and quadratic term (estimate =  $0.080$ ,  $p = .011$  and estimate =  $-0.082$ ,  $p = .048$ , respectively).

**Conclusion:** We found SFs exposure at different times has different negative effects on child development. Early exposure to SFs harmed children's cognitive function. Relatively late exposure to SFs not only deteriorated children's cognitive and language abilities but also decelerated developmental velocity in cognitive and motor domains.

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**At a glance commentary***Scientific background on the subject*

Evidence reveals that frequent sugar consumption worsens cognition in animal models, with similar effects on child development likely.

*What this study adds to the field*

Child development is prone to interference by frequent sweetened food consumption, and the influence varies among domains and ages. Early exposure to sweetened foods harmed children's cognitive function. Relatively late exposure to sweetened food deteriorates children's cognitive and language abilities and decelerates developmental velocity in the cognitive and motor domains.

**Introduction**

Sweetened foods (SFs) with pleasant flavors created by adding sugars are always attractive to children; even infants innately prefer a sweet taste. Sugar-sweetened beverages (SSBs) account for nearly 80% of the increased sugar intake and have recently become the largest source of artificially added sugar consumption [1,2]. However, sweetened delicacies are not nutritious. The main constituents of SFs are easily digested carbohydrates, which provide many calories, causing rapid weight gain. Moreover, SFs and SSBs possess high glycemic indexes and cause rapid increases in blood sugar levels and increased insulin resistance, which may eventually develop into diabetes [3]. The rising prevalence of obesity and diabetes is attributed to SFs [4–6] and the negative consequences of SF intake have global impacts. In 2015, the World Health Organization suggested that children and adults consume <10% free sugars in their diet [7].

Poorer cognitive function in children was recently correlated to maternal SSB intake in a dose-dependent manner [8]. Evidence in animal-based research linked sugar to reduced cognition, executive function, and abnormal behavior [4–6]. Impaired reward systems were noted in rodents, with abnormal risk-taking and delayed decision-making strategies after low-dose but frequent SSB intake [6]. Persistent and harmful effects on memory function were described in mouse models even if only exposed to sugars in early life [9]. However, no large sample study investigating the long-term developmental influence on children has been conducted. Previous studies focused on the dose effects of SSBs and the specific time point of maternal or childhood SF exposure connecting these to poor developmental outcomes at an older age, although they lacked a series of follow-ups [8,10]. Moreover, these studies emphasize the effects of SFs on cognitive function, while the effects on other important domains such as language and motor development are rarely mentioned.

To the best of our knowledge, no study has investigated the causal relationship between the exposure age to SF and long-term child developmental growth velocity. We hypothesized that the influence of SFs on child developmental growth velocity depends on exposure age, which differs in various domains. To expand on previous research, this cohort study was designed using a multivariable latent growth model (LGM) [11], and aimed to investigate the longitudinal effects of SF consumption at different exposure ages on the development of the cognitive, language, and motor domains in Taiwanese children.

**Material and methods***Study participants and recruitment*

This study is based on a national prospective project “Kids in Taiwan: National Longitudinal Study of Child Development & Care (KIT).” The

KIT project was a prospective cohort study that investigated potential factors influencing children's developmental characteristics. Potential participants were sampled using the method of probability proportional to size sampling within the framework of the national census register. An invitation letter with information and an introduction to the KIT project were mailed to each of the sampled families. Young children who had achieved developmental milestones were enrolled in this study. The exclusion criteria were as follows: (1) disability, (2) developmental delay, (3) neurological disorders or any congenital diseases, and (4) diagnosis of special educational needs.

A total of 6588 children in Taiwan completed the first step of data collection from April 1, 2016 to June 30, 2017, without statistically significant sex differences when compared with the national population ( $n = 250, 246; p = .175$ ). In total, 451, 775, and 177 participants were lost to follow-up among the 12-, 24-, and 36-month-old children, respectively. Sample attrition resulted in a reduction from 6588 to 4782 participants in the KIT-M3 cohort.

*Study design and data collection*

All children underwent assessments of the child development inventory at the ages of 3, 12, 24, and 36-months. We used questionnaires to collect information regarding the frequency of SF consumption for each child at the ages of 12 and 24 months, and covariates at 12 months. Well-trained personnel administered the related questionnaire and a 30-min child development inventory via home visits.

*Frequency of SF consumption*

SFs include liquid, semi-solid, and solid forms of food with artificially added sucrose or glucose, such as SSBs, sweet soup, candy, and cake. The frequency of SF consumption was categorized into four grades: grade 1, never; grade 2, seldom (<1 time per week); grade 3, usually ( $\geq 1$  time per week and <1 time per day); and grade 4, always ( $\geq 1$  time per day).

*Child developmental inventory*

Two versions of child development inventories were included in this cohort study, featuring 3–24- and 36–72-month-old participants with common items. The child development inventory included a four-point rating scale (grade 1, unable; 2, unskilled; 3, semi-skilled; and 4, skillful) and included the cognitive, language, and motor domains. The cognitive domain contained memory and executive function evaluations; the language domain comprised communication, comprehension, expression, and emergent literacy. The motor domain encompasses assessment of body coordination, locomotion, visual-motor integration, and manipulation. The internal consistency reliability, concurrent validity, and test-retest reliability were all adequate in the two versions of developmental inventories as reported in previous published studies [12–14]. The Cronbach's  $\alpha$  values for the cognitive, language, and motor domains were 0.96, 0.94 to 0.95, and 0.94 to 0.99, respectively. The concurrent validity values for the cognitive, language, and motor domains were 0.86, 0.71 to 0.89, and 0.74 to 1.00, respectively. The test-retest reliability values were 0.65–0.69 in the cognitive domain, 0.86 to 0.93 in the language domain, and 0.98 to 0.99 in the motor domain. The well-trained personnel interviewed the main caregivers to answer each item in the developmental inventories, based on the children's standard performance via home visits.

*Covariates*

Risk factors associated with children's development were examined in previous studies [15]. The following variables were adopted as covariates: preterm birth (<36 weeks), very low birth weight (<1500 g), young maternal age at childbirth (<20 years), parents' education level,

**Table 1**  
Demographic characteristics of the participants (N = 4782).

	No exposure to SFs n = 3050	Exposed to SFs n = 1732	p-value
<b>Demographic characteristics</b>			
<b>Sex</b>	..	..	0.140
<b>Boy</b>	1572 (51.5%)	854 (49.3%)	..
<b>Girl</b>	1478 (48.5%)	868 (50.7%)	..
<b>Birth weight (M ± SD)/ grams}</b>	3024.13 ± 464.79	3054.28 ± 434.16	0.062
<b>Very low birth weight</b>	29 (0.9%)	8 (0.5%)	0.084
<b>Preterm birth</b>	160 (5.2%)	68 (3.9%)	0.040 *
<b>Maternal age (M ± SD)</b>	32.41 ± 4.57	31.34 ± 5.06	<0.001 ***
<b>Young maternal age</b>	25 (0.8%)	25 (1.4%)	0.042 *
<b>Maternal education level</b>	..	..	<0.001 ***
Junior high school	78 (2.6%)	113 (6.5%)	..
Senior high school	850 (27.9%)	666 (38.5%)	..
Bachelor's degree	1675 (54.9%)	795 (45.9%)	..
Master's degree	447 (14.7%)	158 (9.1%)	..
<b>Paternal education level</b>	..	..	<0.001 ***
Junior high school	101 (3.3%)	120 (6.9%)	..
Senior high school	956 (31.3%)	716 (41.3%)	..
Bachelor's degree	1333 (43.7%)	659 (38.0%)	..
Master's degree	660 (21.6%)	237 (13.7%)	..
<b>Socioeconomic status</b>	..	..	<0.001 ***
<b>10,000 TWD/month</b>			
0-5	704 (23.1%)	567 (32.7%)	..
5-10	1656 (54.3%)	874 (50.5%)	..
10-20	607 (19.9%)	256 (14.8%)	..
>20	83 (2.7%)	35 (2.0%)	..

socioeconomic status, disability, neurologic disorders, and congenital disorders. Preterm birth, very low birth weight, young maternal age at childbirth, parents' educational level, and socioeconomic status were included in the statistical analysis, while disability, neurologic disorders, and congenital disorders were excluded by the exclusion criteria. Information regarding these variables [Table 1] was collected from parents or caregivers during the home-visit interviews. [Table S1] in the Supplement shows the correlations among covariates.

#### Statistical analysis

IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA), ACER ConQuest 5.0 (Australian Council for Educational Research, Adelaide SA, Australia), and Mplus 8.3 (Muthen & Muthen, Los Angeles, CA, USA) were used for the statistical analysis; a total of 4782 participants from the KIT-M3 were included. We performed Rasch analysis to examine item difficulty for each question and developmental ability estimates for each child. We used the statistical method known as "Expected A Posteriori" to compare the results of two different versions of child development inventories. Based on the shared items between the two versions of the inventory, we were able to quantify the developmental ability estimates for each child using the same metric. After ability estimates for cognitive, language, and motor domains (four waves: 3, 12, 24, and 36 months old) were obtained, all variables were examined for absolute values of skewness and kurtosis to ensure the underlying assumption of normal univariate distribution. The skewness and kurtosis values should be lower than 3.0 and 8.0, respectively.

We used LGM as a suitable method for analysis because the children's developmental abilities were assessed at four different points in time, namely 3, 12, 24, and 36 months old, and because children's development is a continuous process that evolves over time. LGM analyses were based on repeated measures in four waves for the cognitive, language, and motor domains. Univariate LGM was designed to assess the change-over-time relationship (trajectory) between the frequency of SF consumption and developmental scores. To find the best fit for the univariate LGM, linear and nonlinear design models were tested, and the

three-factor LGM was finally chosen as the best fit for the model. Cognitive, language, and motor models were designed with ended-point codes; covariates (preterm birth, very low birth weight, young maternal age at childbirth, parents' education, and socioeconomic status) were included in the multivariable LGM. In addition, we added sex as a covariate in our unpublished study. The goodness-of-fit parameters of the LGM were as follows:

Statistics of (1)  $\chi^2$  with the degree of freedom (*df*), (2) comparative fit index (CFI) [16], (3) root mean square error of approximation (RMSEA) [17], and (4) standardized root mean square residual (SRMR) have been reported [18]. The threshold values were as follows:  $\chi^2/df \leq 2$ ; CFI  $\geq 0.90$ ; RMSEA  $\leq 0.08$ , and SRMR  $\leq 0.06$ . Furthermore, the values of  $\Delta\chi^2$  and  $\Delta CFI$  were compared between the linear slope and quadratic growth models to identify the better-fitting model. Statistical significance was set at  $p < .05$ .

## Results

### Descriptive statistics

This study included 4782 participants (boys: 2426 [50.7%]; girls: 2356 [49.3%]). [Table 1] presents the demographic information for the KIT-M3 cohort. We noticed the elder average maternal age, higher preterm birth rate, parental education level, and socioeconomic status in the group with no exposure to SFs compared to the exposed group.

### Univariate LGMs

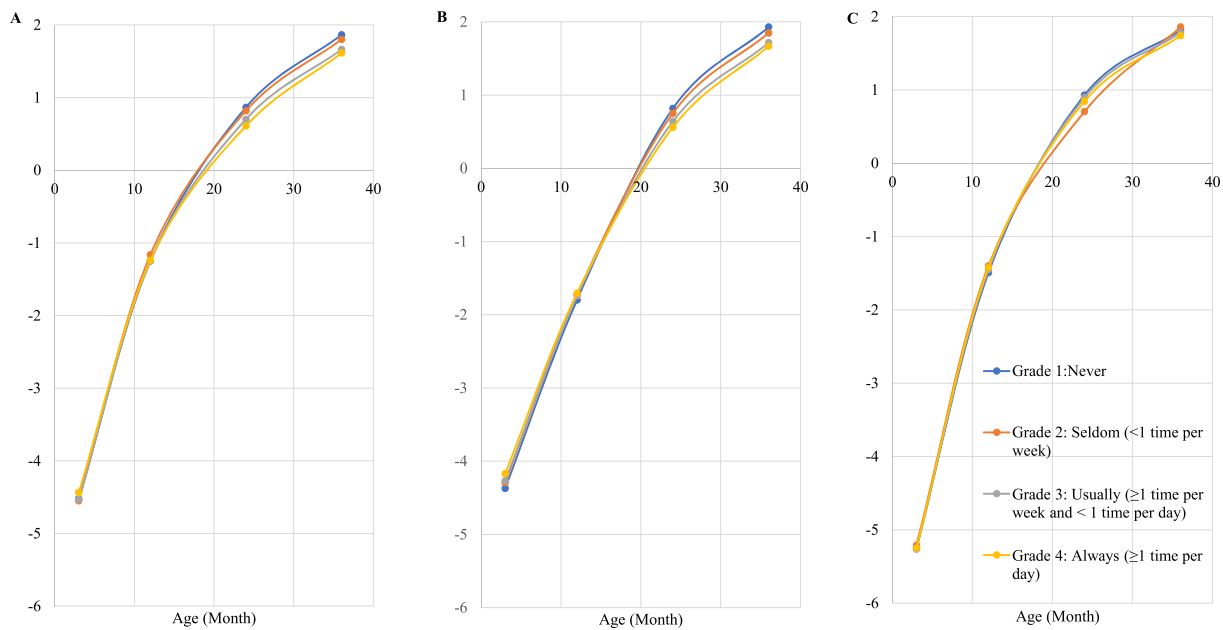
The intercept-only univariate LGMs were first analyzed, and two-factor LGMs with intercept and slope parameters were formulated. Three-factor curve models were established by adding a quadratic factor. Better model fits of the final quadratic growth models were reported (CFI: 0.984, 0.980, 1.000 and RMSEA: 0.052, 0.054, 0.019 in cognitive, language, and motor measures, respectively). The growth trajectories of the measures were checked by graphing; [Figs. 1 and 2] display different categories of SF consumption frequency at one and two years of age to developmental scores of children, and the trends of quadratic growth curves were appropriate. Three-factor LGMs with intercepts, linear slopes, and quadratic factors were established.

### LGMs with covariates

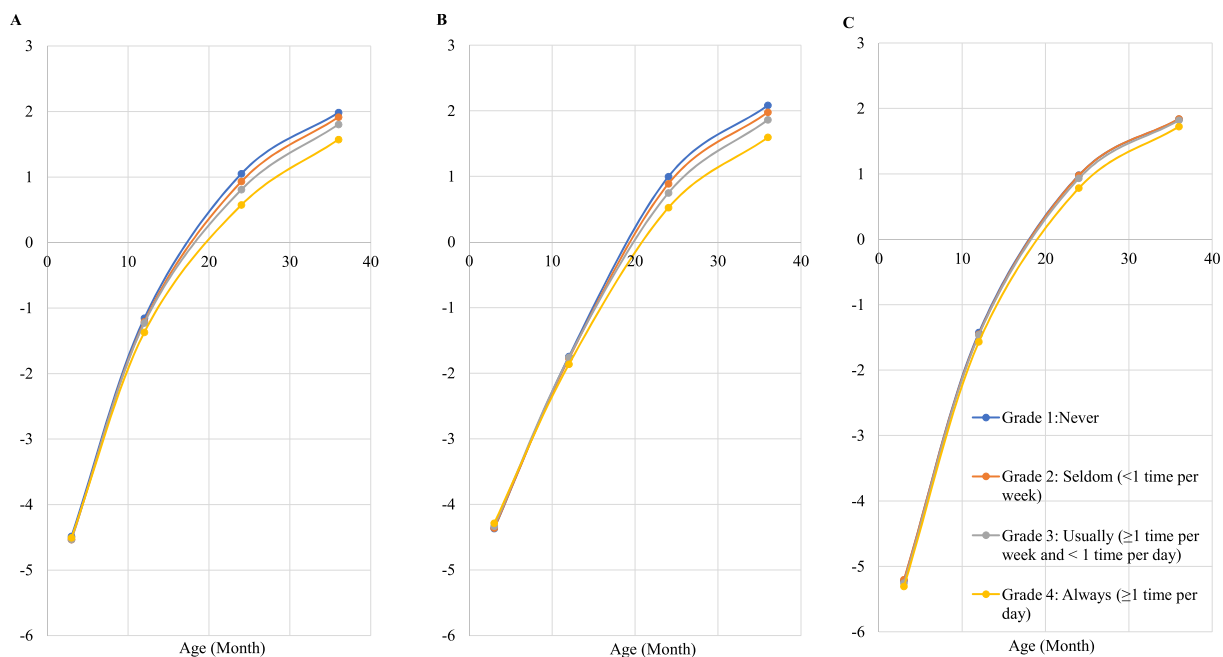
The frequency of SF consumption and covariates were added to the quadratic growth model (three domains) to determine whether the characteristics of individuals influenced the trajectories of child developmental scores. [Table 2] shows the results of the model fit and the values of  $\Delta\chi^2$  and  $\Delta CFI$  between the linear and quadratic growth models with covariates. The effects of the SF consumption frequency on cognitive, language, and motor development are presented in [Table 3]. As the LGMs with covariates had quadratic trends, we emphasized the interpretation of quadratic terms, which could reveal an acceleration/ deceleration effect on the growth curve. Furthermore, due to the endpoint code design in the cognitive, language, and motor models, the intercept of covariates could be regarded as a developmental effect at three years of age.

In the cognitive domain, the frequency of SF consumption at one year of age (SF1) had statistically significant effects on the intercept (estimate =  $-0.054$ ,  $t = -3.248$ ,  $p < .001$ ), but not on the linear and quadratic terms. The frequency of SF consumption at two years of age (SF2) had significant effects on the intercept and quadratic term (estimate =  $-0.081$ ,  $t = -4.598$ ,  $p < .001$ ; estimate =  $-0.093$ ,  $t = -2.230$ ,  $p = .026$ , respectively), but not on the linear slope.

In the language domain, SF consumption at two years of age (SF2), but not SF1, had significant effects on the intercept (estimate =  $-0.054$ ,  $t = -3.518$ ,  $p < .001$ ). Neither SF1 nor SF2 had significant effects on the linear or quadratic terms.



**Fig. 1.** Parts A-C. Comparison of different categories of sweetened food consumption frequency at one-year-old to developmental trajectories of children (A: Cognitive; B: Language; C: Motor).



**Fig. 2.** Parts A-C. Comparison of different categories of sweetened food consumption frequency at two-years-old to developmental trajectories of children (A: Cognitive; B: Language; C: Motor)

In the motor domain, SF2 exhibited significant effects on the linear slope and quadratic term (estimate = 0.080,  $t = 2.547$ ,  $p = .011$ ; estimate =  $-0.082$ ,  $t = -1.979$ ,  $p = .048$ , respectively) but not on the intercept. SF1 had no significant effect on the intercept, linear slope, or quadratic term.

*Covariate effects on each LGM domain*

Sex had significant effects on the intercepts in the cognitive, language, and motor domains, with significant estimated values of 0.150\*\*, 0.101\*\*, and 0.130\*\*, respectively. Furthermore, sex had significant effects on the quadratic terms in the cognitive and language models

(estimate: 0.186\*\* and 0.188\*\*, respectively). Preterm birth significantly affected the intercepts in the cognitive, language, and motor domains (estimate:  $-0.056$ \*\*,  $-0.041$ \*\*,  $-0.059$ \*\*, respectively), with no significant effects on the linear slope and quadratic term. Very low birth weight exerted significant effects on the quadratic terms in the cognitive, language, and motor models (estimate:  $-0.089$ \*\*,  $-0.096$ \*\*, and  $-0.068$ \*, respectively). Maternal and paternal education levels had significant effects on the intercepts in cognition and language domains (maternal education estimate: 0.106\*\* and 0.075\*\* in the cognitive and language domains, respectively; paternal education estimate: 0.083\*\* and 0.047\*\* in the cognitive and language domains, respectively). Paternal education level had significant effects on the quadratic term in

**Table 2**  
Model fit of child developmental latent growth models with covariates.

	Model fit					
	$\chi^2/df$	CFI	RMSEA	SRMR	$\Delta\chi^2$	$\Delta CFI$
<b>Cognitive</b>	87.393/12	0.981	0.044	0.017	215.494**	0.053
<b>Language</b>	138.873/12	0.963	0.054	0.022	259.312**	0.072
<b>Motor</b>	113.75/23	0.973	0.034	0.020	123.25**	0.034

Abbreviations:  $\chi^2$  : Values of chi-squared; df : Degrees of freedom; CFI=Comparative Fit Index; RMSEA : Root Mean Square Error of Approximation; SRMR: Standardized Root Mean Square Residual;  $\Delta\chi^2$  : Difference  $\chi^2$  between linear and quadratic growth model, \* $\alpha < 0.05$ , \*\*  $\alpha < 0.01$ ;  $\Delta CFI$  : Difference value of CFI between linear and quadratic growth model.

**Table 3**  
The standardized estimated effects of frequent SF consumption on cognitive, language, and motor in multivariable latent growth models.

	Estimate	S.E.	Est/S.E.	p-value
<b>Cognitive</b>				
<b>SF1</b>				
Intercept	-0.054	0.017	-3.248	<0.001***
Linear slope	-0.026	0.035	-0.733	0.463
Quadratic term	0.004	0.036	0.118	0.906
<b>SF2..</b>				
Intercept	-0.081	0.018	-4.598	<0.001***
Linear slope	0.062	0.038	1.629	0.103
Quadratic term	-0.093	0.042	-2.230	0.026*
<b>Language</b>				
<b>SF1</b>				
Intercept	-0.028	0.015	-1.889	0.059
Linear slope	0.015	0.028	0.531	0.595
Quadratic term	-0.053	0.035	-1.515	0.130
<b>SF2..</b>				
Intercept	-0.054	0.015	-3.518	<0.001***
Linear slope	0.003	0.025	0.132	0.895
Quadratic term	-0.032	0.034	-0.943	0.346
<b>Motor</b>				
<b>SF1..</b>				
Intercept	0.004	0.017	0.239	0.811
Linear slope	0.008	0.030	0.257	0.797
Quadratic term	-0.022	0.036	-0.593	0.553
<b>SF2..</b>				
Intercept	-0.008	0.018	-0.452	0.651
Linear slope	0.080	0.031	2.547	0.011*
Quadratic term	-0.082	0.041	-1.979	0.048*

SF1: Frequency of sweetened food consumption at 1-year-old; SF2: Frequency of sweetened food consumption at 2-year-old; Est: Estimate; S.E: Standard error \* $p < .05$ ; \*\* $p < .01$ , \*\*\* $p < .001$ .

the cognitive, language, and motor models (estimate: 0.136\*\*, 0.072\*, and 0.084\*, respectively). Family income also showed significant effects on the intercepts in the cognitive, language, and motor domains (estimates: 0.100\*\*, 0.063\*\*, and 0.038\*, respectively), without significant effects on linear slopes and quadratic terms.

## Discussion

This is the first prospective cohort study to investigate the effects of SF consumption at different exposure times on developmental growth trajectories in children with typical development using the method of LGMs with covariates. The different timings of exposure to SFs exerted different effects on various domains. The results revealed that the more frequently children consumed SFs at the ages of one and two years, the poorer their cognitive abilities at three years of age. Frequent exposure to SFs at two years of age worsens language ability in three-year-old children. Furthermore, children who frequently consumed SFs at two years of age exhibited decelerated developmental growth velocity in the cognitive and motor domains. These findings reveal that exposure to SFs at different times has diverse effects on child development in various

domains. Early SF exposure has a negative impact on cognitive performance in children. Relatively late exposure to SFs not only deteriorated children's cognitive and language function but also decelerated the growth velocity in cognitive and motor development. The developmental gap would widen if children retained their habits. The results of this study may offer evidence to help establish policy-making guidelines regarding SFs exposure during development in early childhood.

Our longitudinal evidence suggests that early exposure to SFs in children aged 1–2 years profoundly harms cognitive function and decelerates cognitive developmental velocity. This finding suggests that if children habitually consume SFs, the gap in cognitive function is expected to widen with increasing age. A similar study concluded that childhood consumption of SSBs harmed children's cognition [8]. Evidence in animal models provided a possible mechanism, which described that SF consumption, even low-dose but frequent, would impair the reward system and alert brain neurochemistry in mice [4,6,9]. The results of the rodent model may correspond with the results of our study and provide an excellent explanation of how frequent SF consumption in early childhood worsens cognitive function and decelerates developmental velocity.

The KIT-M3 cohort found that SF exposure in children aged two years deteriorated their language ability at three years of age. Although previous studies reported that SSBs and SF consumption were associated with worse cognition, studies investigating the effects of SFs on language development and the possible underlying mechanism in children are rare. One study reported no significant correlations between SSB consumption and English Language Arts Score in 8–12-year-old children [19]; however, this study did not include younger children. SSBs and SFs are widely known to contain high concentrations of fructose or sucrose, which lead to dramatic changes in blood sugar and contribute to spikes in insulin levels, even in healthy individuals [20]. A study demonstrated that poor blood sugar control related to worse neurocognitive function in preschool-age children with type 1 diabetes, concluding that children with higher blood sugar exhibited poor receptive language [21]. The overall findings of these studies suggest the adverse effects of frequent SF consumption on language development. It is logical to presume that SFs cause fluctuations in blood sugar levels, potentially influencing children's receptive language abilities.

The KIT-M3 cohort also revealed that SF consumption at two years of age decelerated the motor growth velocity. This finding shows the time point at which SF exposure started to slow motor development. Previous studies have reported that maternal SSB consumption during early lactation affects children's cognitive, language, and fine motor development [8,10]. The motor development gap is expected to widen over time if dietary habits are retained.

Furthermore, our cohort controlled for potential factors influencing the child's developmental outcome as covariables. The covariable effects are listed in [Table S2] of the Supplement. We found that girls exhibited more rapid growth velocity and better achievement in the cognitive and language domains than boys. Children born preterm displayed poor developmental performance in the cognitive, language, and motor domains without decreasing developmental growth velocity. Children born with very low birth weights showed decelerated cognitive, language, and motor growth velocities. Higher maternal and paternal education levels were associated with better developmental performance in the cognitive and language domains. Additionally, higher paternal education levels accelerated the growth velocity of children in all three domains. We found that a higher household income yielded better outcomes in the cognitive and language abilities of children in the KIT-M3 cohort. Our results are consistent with those of the previous studies. Previous studies found that preterm birth and low birth weight increased the risk of developmental delays [22,23]; disabilities and neurologic defects occur in severe cases [24]. Paternal education level was associated with child development in the literature [25]. Highly educated mothers tended to purchase more books and had higher academic expectations for their children [26,27]. Household income

positively affected cognitive development, whereas low family income and poverty negatively impacted cognitive development [28,29].

This study had some limitations. The KIT-M3 cohort was primarily from Taiwan. As dietary habits may differ across races and cultures, it should be noted that generalizability of the results may not extend beyond the samples. Another limitation is the method of SF analysis. We used frequency, although not quantitative, analysis of SF consumption in this cohort study, implying that the effect of low frequency was possibly underestimated despite large doses of SFs in some participants.

Another concern was the statistical values of  $\chi^2/\text{degree of freedom (df)}$  in cognitive, language, and motor domains, which were not included in the appropriate range of model fit, and the condition was possibly associated with a relatively large sample size in this cohort study. Moreover, the inapplicable values for the intercepts of young maternal age and very low birth weight resulted from large skewness and kurtosis values and, subsequently, no convergence in the LGMs.

At the end of the limitations section, we noted a significant correlation between frequent SFs consumption, parental education level, and young maternal age at birth. However, frequent SFs consumption and these covariates had varying accelerated or decelerated effects. Therefore, the influence of frequent SFs consumption and these covariates on children's development changed dynamically over time. It was difficult to precisely quantify the impact of SFs consumption and each covariate on a child's development.

## Conclusions

The KIT-M3 cohort study revealed crucial findings regarding child developmental trajectories within the framework of LGMs. Our longitudinal evidence supports the idea that different SF exposure timings have diverse influences on cognitive, language, and motor development. In summary, cognition is prone to worsening with early exposure to SFs in children, and the negative influence will increase over time. The negative influence of SF exposure exhibits relatively late onset in the language and motor domains; there is a quantitative effect in the language domain with a decelerated effect on motor growth velocity in children. This study expands on previous studies and supports the potentially negative influence of SFs on child development. We recommend that parents be attentive to the dietary habits of their offspring, and that the government formulate appropriate policies to decrease children's exposure to SFs.

## Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the National Taiwan University. The project identification codes were 201408ES007 and 201707HS003 (approved on October 16, 2014 and October 27, 2017, respectively). Written informed consent was obtained from the parents or guardians of all participants.

## Conflicts of interest

None.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bj.2023.100608>.

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